



September 25, 2025

PALSONIFY™ (paltusotine)
FDA Approval



Forward Looking Statements

This presentation contains forward-looking statements. Crinetics Pharmaceuticals, Inc. (“Crinetics,” the “company,” “we,” “us,” or “our”) cautions you that all statements other than statements of historical facts contained in this presentation are forward-looking statements. Such forward-looking statements include, but are not limited to, statements regarding: the estimates relating to market size, our ability to optimize the launch or ensure broad access to Palsonify™ or our ability to drive diagnosis and treatment for undiagnosed patients; the plans and timelines regulatory filings or approval of paltusotine outside the US; the expected timing of patient enrollment in the Phase 3 program of paltusotine for carcinoid syndrome; the expected timing of patient enrollment in additional studies of atumelnant in CAH or our plans or timing for a phase 2/3 study of atumelnant in Cushing’s syndrome; the plans and timelines for the clinical development of our drug candidates, including the therapeutic potential and clinical benefits or safety profile thereof; and the expected timing for the initiation of clinical trials or the potential benefits of our development candidates in patients across multiple indications; the expected timing of additional research pipeline updates or the expected timing of the advancement of those programs; and the company’s anticipated cash runway or its operating cash burn guidance. 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,” “aim,” “potential,” “target,” or other similar terms or the negatives thereof.

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: estimates relating to market size and growth potential, which involve a number of assumptions and limitations, particularly about any projections, assumptions, and estimates of our future performance; the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk; the possibility of unfavorable new clinical data and further analyses of existing clinical data; potential delays in the commencement, enrollment and completion of clinical trials and the reporting of data therefrom; 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; regulatory developments or political changes, including policies related to pricing and pharmaceutical drug reimbursement 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 or our cash burn rate may accelerate; 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.

INTRODUCTORY REMARKS

Scott Struthers, Ph.D.

Founder & Chief Executive Officer



Our Mission:

To be **the world's leading endocrine company** that consistently pioneers new therapeutics to help patients better control their disease and improve their daily lives



Tony



Ellen



Wendy



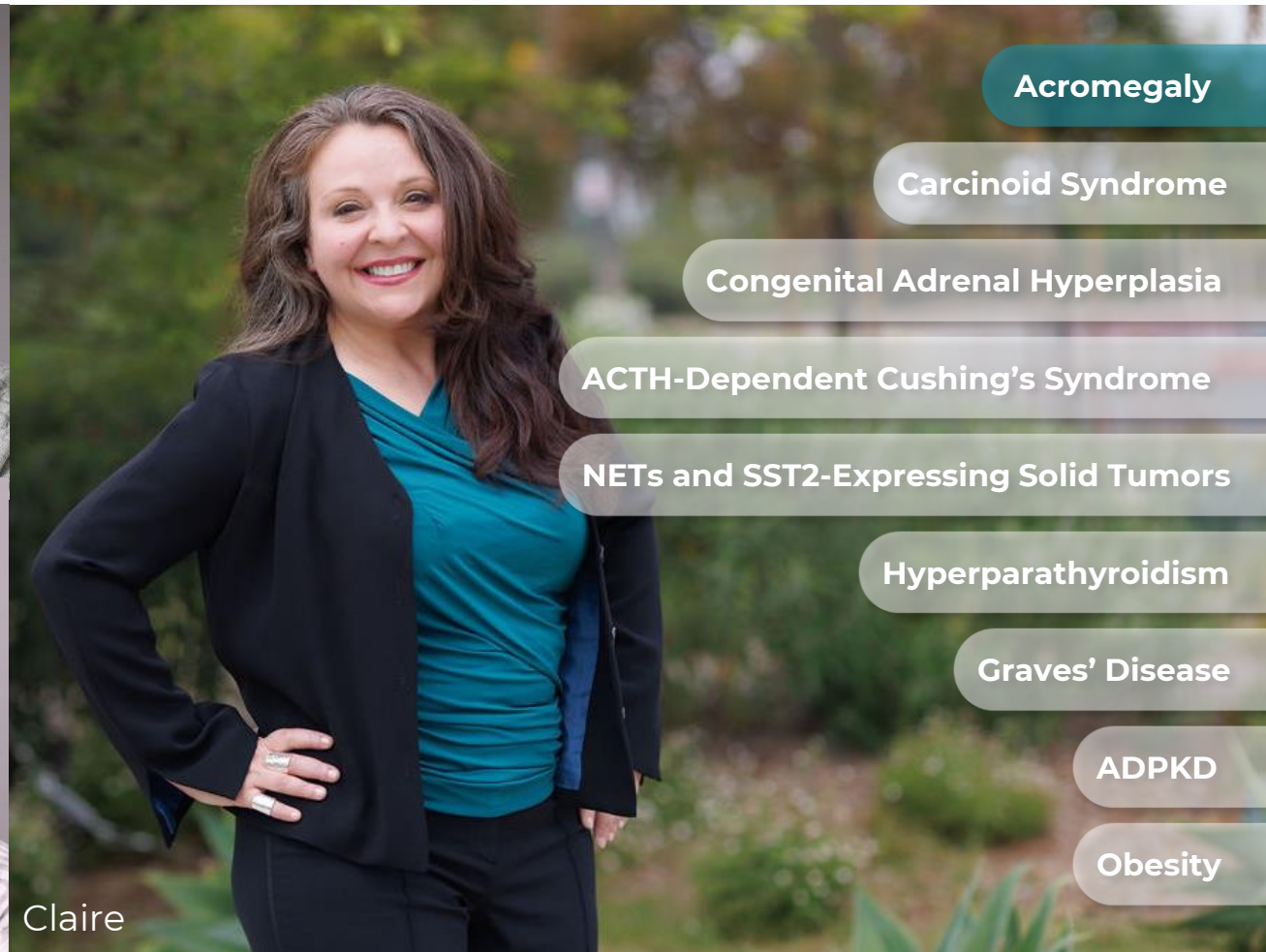
Stacey



Dee



Matthew



Claire

Acromegaly

Carcinoid Syndrome

Congenital Adrenal Hyperplasia

ACTH-Dependent Cushing's Syndrome

NETs and SST2-Expressing Solid Tumors

Hyperparathyroidism

Graves' Disease

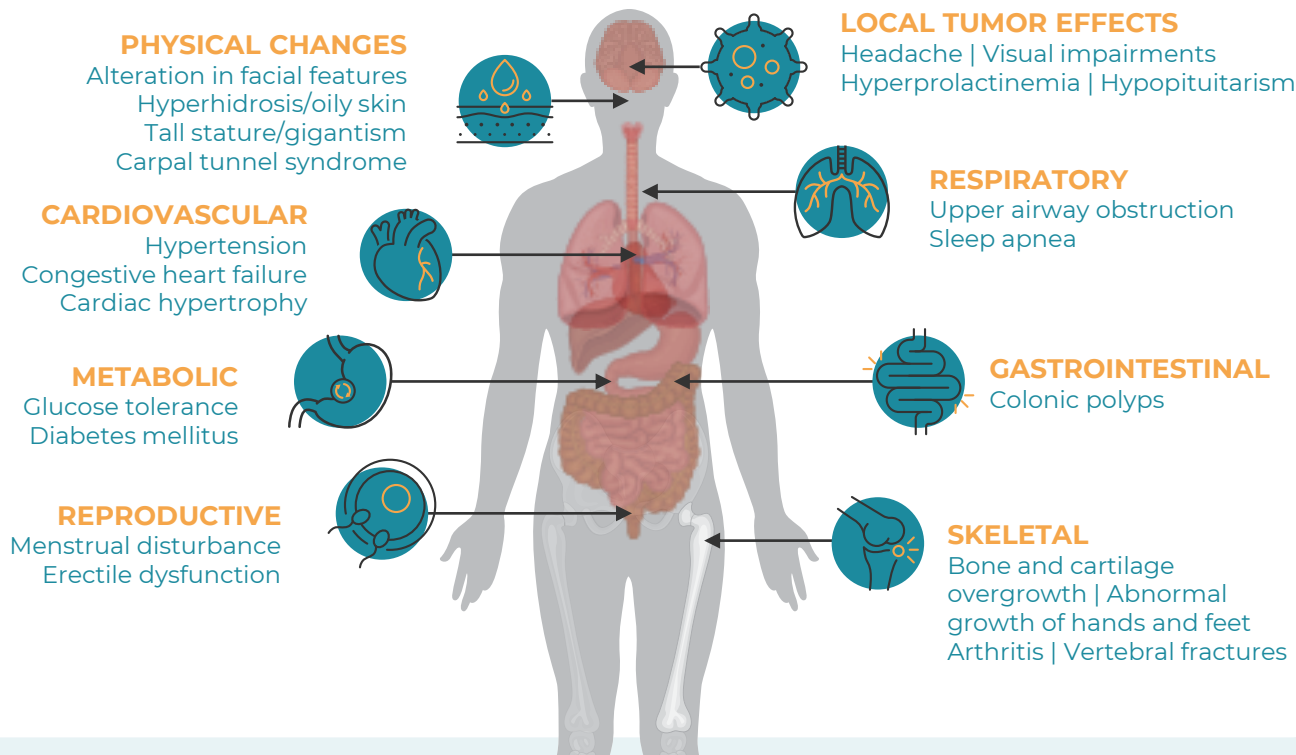
ADPKD

Obesity






Acromegaly Symptoms Take a Toll on Patients

Acromegaly is a rare chronic disease caused by a pituitary adenoma that secretes excess GH, resulting in hypersecretion of IGF-I^{1,2}

Effects of Prolonged Exposure to IGF-I and GH^{1,2}



Patient Symptoms³⁻⁴

-  Enlarged hands, feet, lips, nose, tongue, and jaw
-  Skin changes: oily skin, thickened skin, excessive sweating
-  Headaches, which may be frequent and/or severe
-  Joint pain, vertebral fractures
-  Peripheral neuropathy, carpal tunnel syndrome

GHRH = growth hormone-releasing hormone; IGF-1 = insulin-like growth factor 1.

1. Colao A, et al. *Nat Rev Dis Primers*. 2019;5(1):20. 2. Gomes-Porras M, et al. *Int J Mol Sci*. 2020;21(5):1682.

Figure adapted with permission from Colao A, et al. *Nat Rev Dis Primers*. 2019;5(1):20. 3. Fliseriu M, et al. *Lancet Diabetes Endocrinol*. 2022;10(11):804-826.

4. Slagboom TNA, et al. *Pituitary*. 2023;23(4):319-332.

“

Acromegaly is a cage... I've been dealing with this a long time. And there are medicines out there that will let you live life somewhat...I'm not symptom-free...If I was better controlled, I wouldn't have to take that 30-minute nap when I get home or feel like my head is dragging. Because of acromegaly, I stopped singing and playing music...

I have hope to actually get parts of my life back that I had thought I'd lost...I hope everyone living with acromegaly can get their song back.

”

- Dave, living with acromegaly



NOW FDA APPROVED

Once-Daily Oral



PalsonifyTM
(paltusotine) tablets

**A New Era in
Acromegaly
Treatment**

CLINICAL DATA REVIEW

Dana Pizzuti, M.D.

Chief Medical Officer



PALSONIFY's Broad Label Supported by Robust Clinical Database

Highlights of Prescribing Information

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use PALSONIFY™ safely and effectively. See full prescribing information for PALSONIFY.

PALSONIFY (paltusotine) tablets, for oral use
Initial U.S. Approval: 2025

INDICATIONS AND USAGE

PALSONIFY is a somatostatin receptor agonist indicated for the treatment of adults with acromegaly who had an inadequate response to surgery and/or for whom surgery is not an option (1).

DOSAGE AND ADMINISTRATION

- Take orally once daily with water on an empty stomach (at least 6 hours after a meal) and at least 1 hour before the next meal (2.1).
- Recommended initial dosage is 40 mg once daily. During initiation, PALSONIFY may be temporarily reduced to 20 mg once daily if needed, based on tolerability. Once adverse reactions have resolved, resume PALSONIFY 40 mg once daily (2.2).
- After 2 to 4 weeks, based on IGF-1 levels, titrate to 60 mg once daily (2.2).

DOSAGE FORMS AND STRENGTHS

Tablets: 20 mg, 30 mg (3)

CONTRAINDICATIONS

- None (4)

WARNINGS AND PRECAUTIONS

- Cholelithiasis and its Complications: Monitor periodically. If complications of cholelithiasis occur, discontinue PALSONIFY and treat appropriately (5.1).
- Hyperglycemia and Hypoglycemia: Monitor glucose and adjust antidiabetic treatment as needed (5.2).

- Cardiovascular Abnormalities: Bradycardia or conduction abnormalities may occur. Dosage adjustments of concomitantly used drugs with bradycardia effects may be necessary (5.3).
- Thyroid Function Abnormalities: Hypothyroidism may occur. Assess thyroid function periodically (5.4).
- Steatorrhea and Malabsorption of Dietary Fats: New onset steatorrhea, stool discoloration, loose stools, abdominal bloating, and weight loss may occur. If new occurrence or worsening of these symptoms are reported, evaluate for potential pancreatic exocrine insufficiency (5.5).
- Vitamin B₁₂ Deficiency: Monitor vitamin B₁₂ levels during treatment if indicated (5.6).

ADVERSE REACTIONS

Most common adverse reactions (≥5%) are diarrhea, abdominal pain, nausea, decreased appetite, sinus bradycardia, hyperglycemia, palpitations, and gastroenteritis (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Crinetics Pharmaceuticals, Inc. at toll-free phone 1-833-CRN-INFO or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

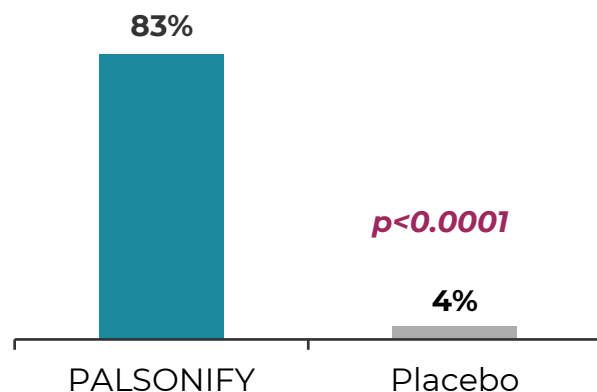
DRUG INTERACTIONS

- Strong CYP3A4 Inducers: may decrease paltusotine exposure. May require PALSONIFY dosage increase (2.3, 7.1).
- Moderate CYP3A4 Inducers: may decrease paltusotine exposure. May require PALSONIFY dosage increase (2.3, 7.1).
- Proton Pump Inhibitors: may decrease paltusotine exposure. May require PALSONIFY dosage increase (2.3, 7.1).
- Cyclosporine: may decrease cyclosporine exposure. May require cyclosporine dosage adjustment (7.2).

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

In Phase 3 Studies, PALSONIFY Achieved Rapid, Reliable and Consistent Biochemical Control in Switch Patients

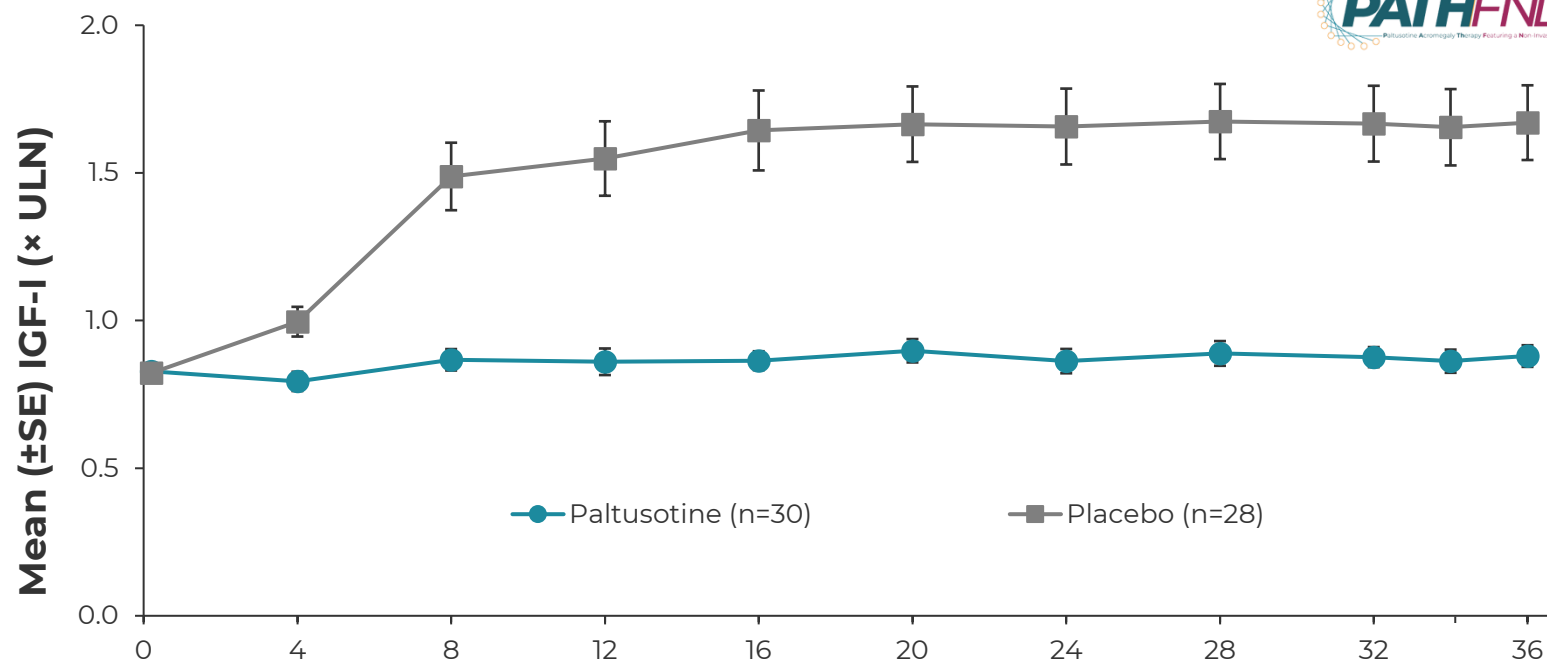
Patients Switching From Standard-of-Care



**PRIMARY
ENDPOINT**

Maintained
IGF-1 $\leq 1.0 \times \text{ULN}$

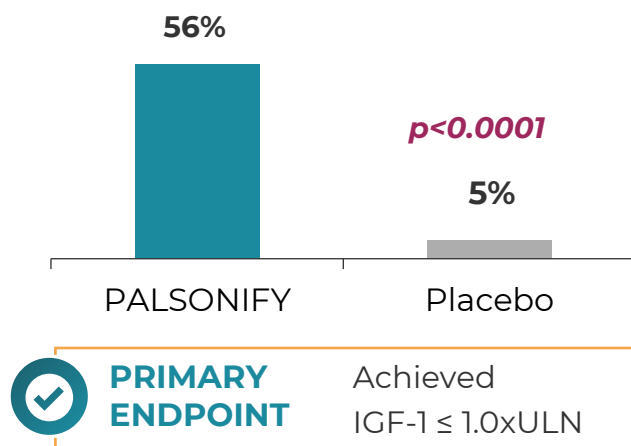
PALSONIFY Treatment Maintained IGF-1 Control in Patients who Switched from SRL Injections



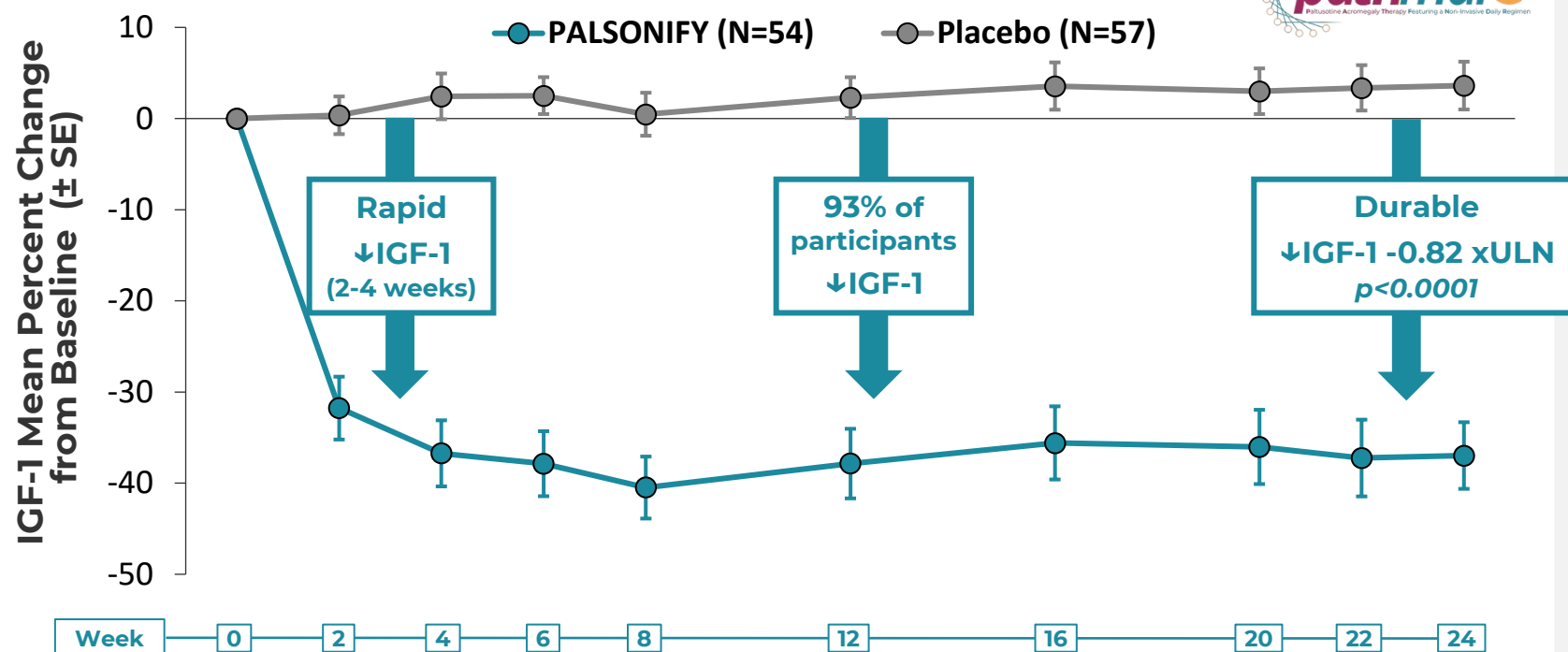
Only 1 patient taking PALSONIFY in PATHFINDER-1 had an IGF-1 above 1.1x ULN at EOT*

In Phase 3 Studies, PALSONIFY Achieved Rapid, Reliable and Consistent Biochemical Control in Naïve Patients

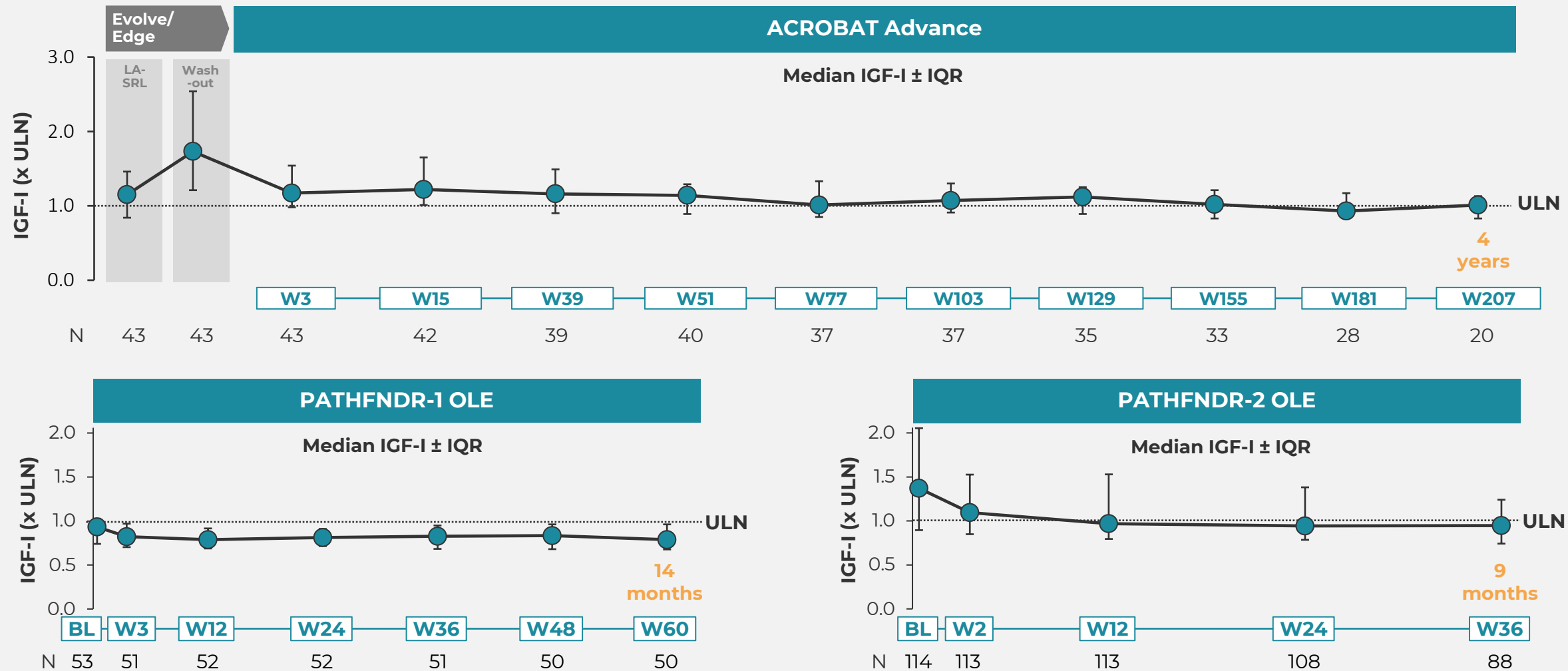
Non-Pharmacologically-Treated Patients



Percent Change from Baseline in IGF-1 Level by Visit

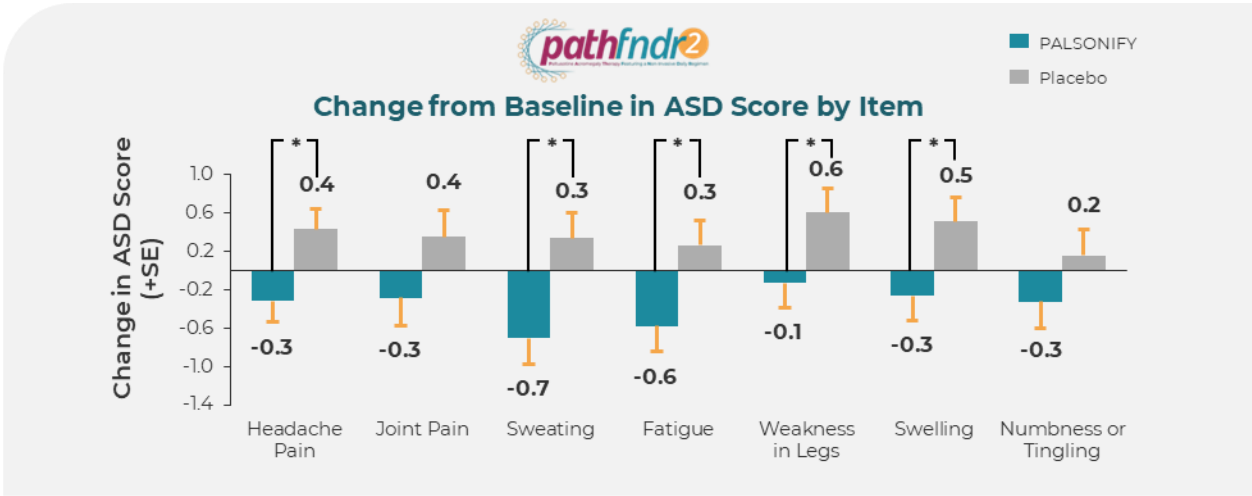
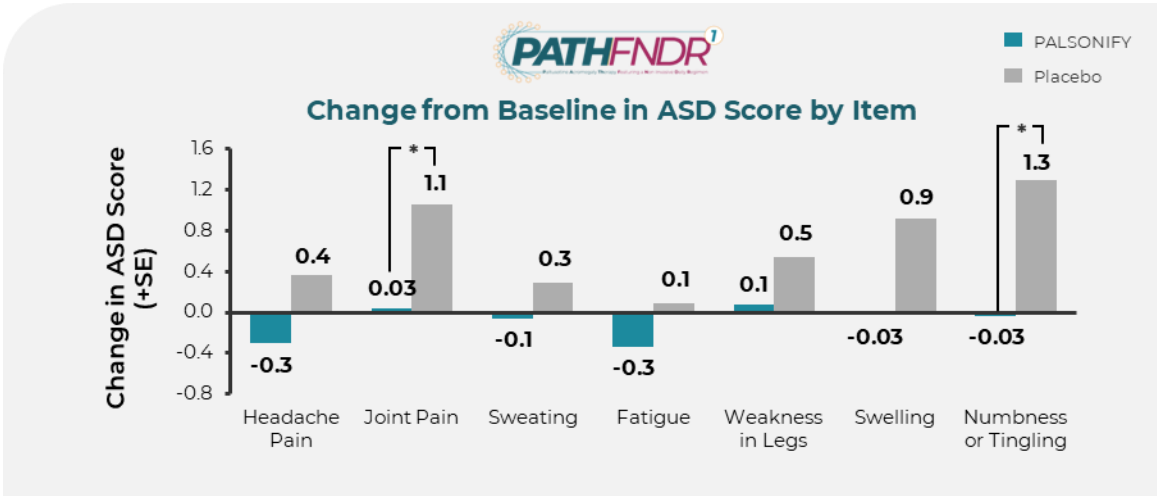


PALSONIFY Treatment Results in Long-Term, Stable Biochemical Control Across a Range of Acromegaly Patients

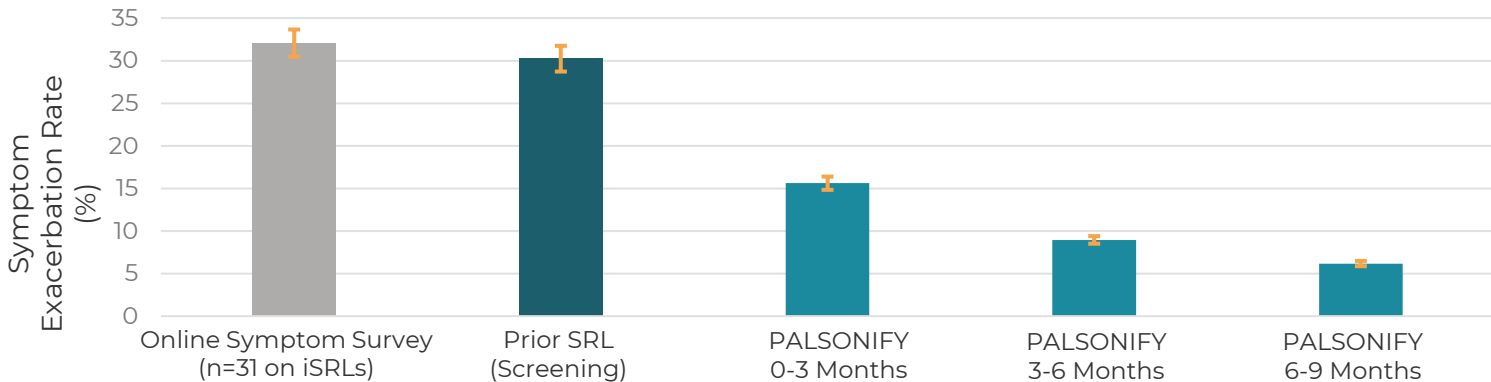


In Phase 3 Studies, PALSONIFY Achieved Consistent Control of Symptoms and Reduced Frequency of Symptom Exacerbations

✓ Label includes reduced severity of 7 key symptoms in both randomized trials



✓ Symptom exacerbation frequency continued to decline throughout the 9-month study



PATHFINDER¹
Palosinate Acromegaly Therapy Featuring a Non-Invasive Daily Regimen

Exploratory Post-Hoc Analyses with Acromegaly Symptom Diary (ASD)

(Exploratory Analysis n=22, Exploratory post hoc analysis; should not be interpreted as establishing clinical significance)

PALSONIFY was Well-Tolerated with No Severe or Serious Adverse Events

Key safety outcomes from the randomized control period of Phase 3 studies

- **No serious adverse events**
None occurred with PALSONIFY vs 2.4% with placebo
- **GI AEs resolved**
Most GI AEs occurred within the first 2 months (median duration of 6 to 18 days), were generally mild to moderate and resolved without discontinuing PALSONIFY
- **Low discontinuation rate**
<4% of patients taking PALSONIFY discontinued due to AEs
- **Stability or reduction in size of pituitary tumors**
No patients receiving PALSONIFY had clinically significant increases in tumor volume; clinically significant decreases were observed in 4 patients taking PALSONIFY but not in any patients taking placebo



Adverse Reaction	PALSONIFY N=30 n(%)	Placebo N=28 n(%)
Diarrhea	7 (23)	3 (11)
Nausea	4 (13)	1 (4)
Decreased appetite	3 (10)	0
Palpitation	2 (7)	0
Gastroenteritis	2 (7)	0



Adverse Reaction	PALSONIFY N=54 n(%)	Placebo N=57 n(%)
Diarrhea	18 (33)	8 (14)
Abdominal pain	10 (19)	3 (5)
Nausea	5 (9)	1 (2)
Sinus bradycardia	4 (7)	0 (0)
Hyperglycemia	4 (7)	1 (2)

COMMERCIAL LAUNCH STRATEGY

Isabel Kalofonos

Chief Commercial Officer



Four Pillars to Optimize the Launch of PALSONIFY



ACTIVATE

SHIFT THE MINDSET

Success isn't just about IGF-1 control, it's about helping patients feel better and live better



ADOPT

WIN ON EFFICACY

Switch and naïve patients deserve a therapy that works fast, lasts and controls symptoms



ACCESS

ENSURE ACCESS

Removing friction to help more patients get the therapy that is right for them



ADHERE

DRIVE ADHERENCE

With the right support, patients stay on therapy longer and see better outcomes

Experienced Team in Place with Comprehensive Engagement Plan

36 Sales Team

14 Medical Science Liaisons

5 Nurse Educators

6 CrinetiCARE Specialists

4 Field Reimbursement Liaisons

4 Payer National Account Directors

Sales Talent Metrics

Mean years of experience



9.2
years

in rare disease



19.7
years

in pharma/biotech



8.7
years

in endocrinology

~3,600

Community
HCP Targets

~1,800

PTC + Academic
HCP Targets

45

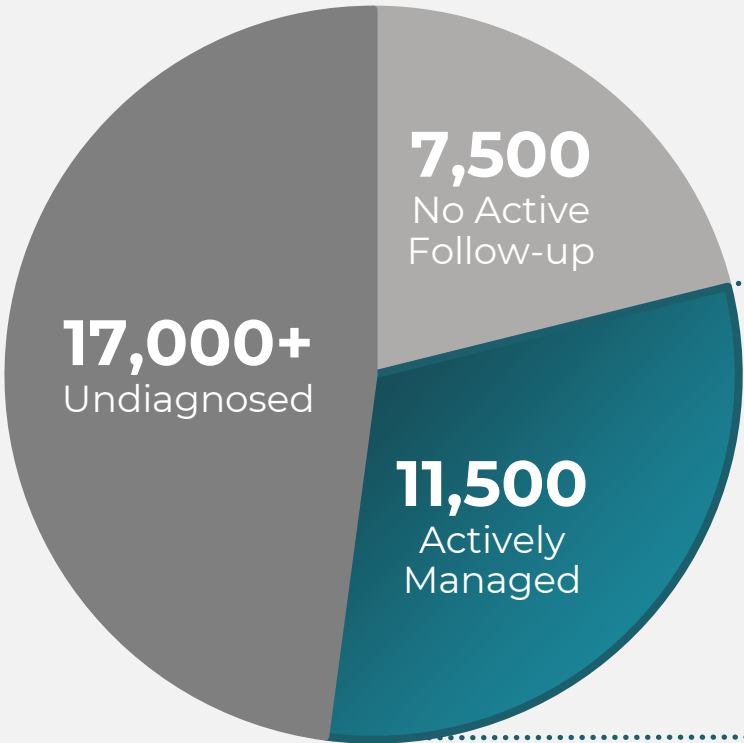
Core Pituitary
Treatment Centers

60%

of patients are treated in the
community

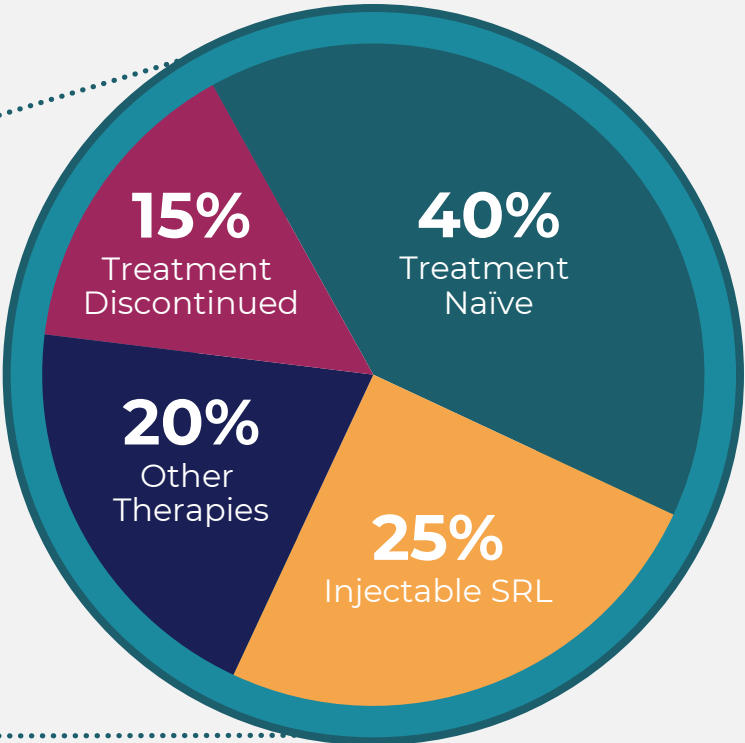
Acromegaly Patient Reach

36,000 People Living with Acromegaly in the US



1,500/yr diagnosed

11,500 Actively Managed and Addressable in Short-Term



500/yr initiating pharmacotherapy

Note: Prevalence and incidence are estimates.
Sources: Crisafulli S, et al. European Journal of Endocrinology. 2021;185(2):251-263. Komodo Claims Data Analysis and Symphony Data.

Education and Engagement Required to Empower Patients to Demand More

PATIENT ACTIVATION

ACROMEGALY REALITY

Disease education campaign to raise awareness of the lived realities of acromegaly and support earlier recognition and diagnosis



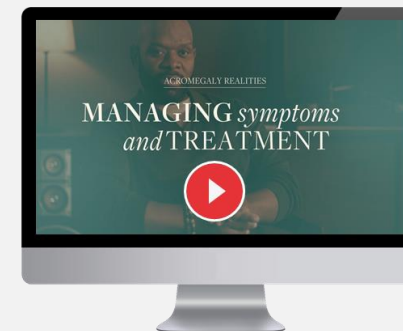
CrinetiCARE™

Comprehensive patient support services to assist with access, adherence and personalized care throughout the treatment journey



PATIENT ADVOCACY

Strengthening patient engagement through events, surveys and toolkits designed to elevate the patient voice and build community



Omnichannel Approach to Support Patients with an Acromegaly Diagnosis

Pre-Launch Engagement with Payers to Facilitate Post-Launch Formulary Access

Strong value proposition to payers includes:



Unprecedented Safety and Efficacy

Ability to achieve rapid biochemical and symptom control based on Phase 3 data



Maintain Control

Limit patient and societal burden of uncontrolled acromegaly



Optimize Treatment Paradigm

Ensure patients getting intended clinical benefit



Improve Patient Adherence and Outcomes

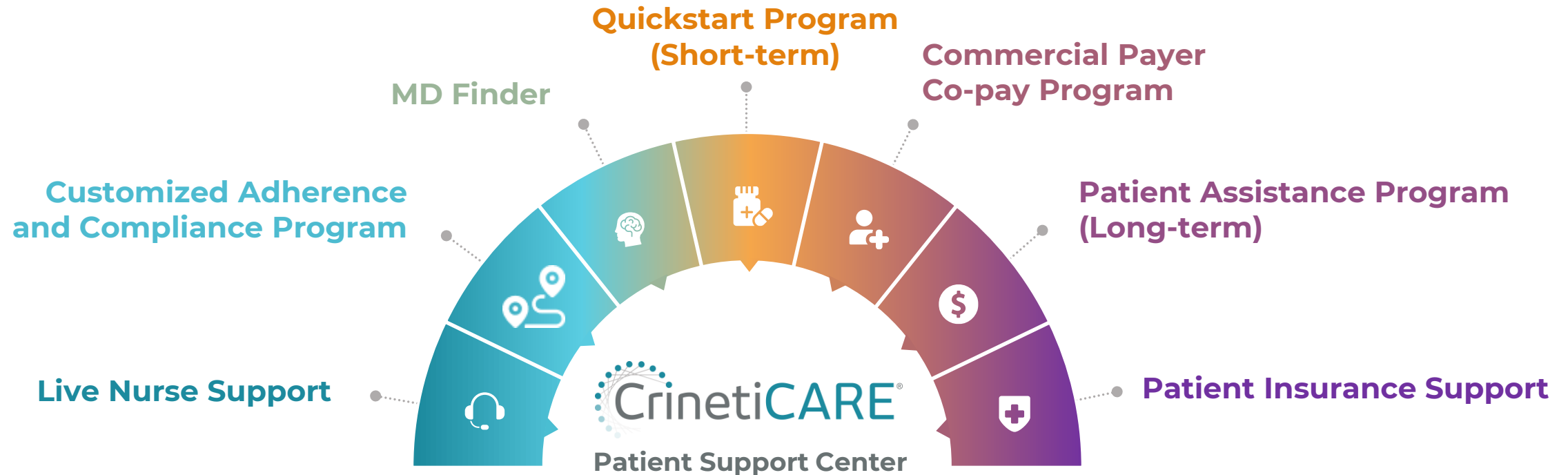
Once-daily oral dosing

60%
Commercial

30%
Medicare

10%
Medicaid

Supporting Patients at Every Step of Their Journey





Tony, living with acromegaly

A New Era in Acromegaly Has Started

**Palsonify is here to transform
acromegaly care**

- ✓ Broad Label and Strong Data
- ✓ Patient Focus
- ✓ Experienced Team

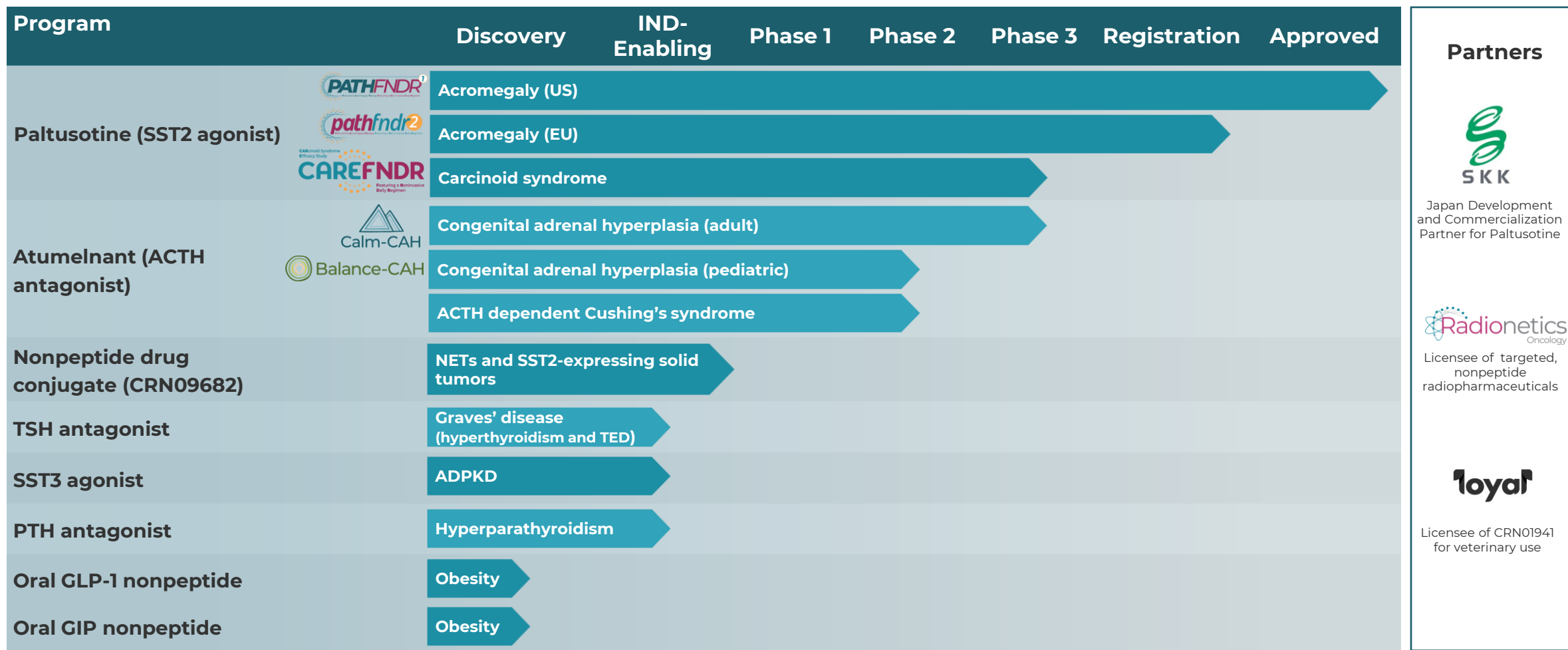
CLOSING REMARKS

Scott Struthers, Ph.D.

Founder & Chief Executive Officer



Palsonify is Just the Beginning: Building the Foundation for Our Pipeline





Crinetics
Pharmaceuticals

THANK YOU

Q&A

