ACADIA

DAYBUE™ (trofinetide) FDA Approval Call

March 13, 2023

Daybue™ (trofinetide)

FDA Approval Call Agenda

Welcome	**Mark Johnson** | Vice President, Investor Relations
Introduction	**Steve Davis** | Chief Executive Officer
DAYBUE Label and Data	**Kathie Bishop Ph.D.** | Chief Scientific Officer, Head of Rare Disease
Commercialization Strategy	**Brendan Teehan** | Chief Operating Officer, Head of Commercial
Financial Considerations	**Mark Schneyer** | Chief Financial Officer
Closing Remarks	**Steve Davis** | Chief Executive Officer
Q&A Session	**Doug Williamson M.D.** | Head of Research and Development, *available for Q&A* **Parag Meswani, Pharm.D.** | SVP, Trofinetide – Rare Disease Franchise, *available for Q&A*

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Provided March 13, 2023 as part of an oral presentation and is qualified by such; contains forward-looking statements; actual results may vary materially; Acadia disclaims any duty to update.

Forward-Looking Statements

This presentation contains forward-looking statements. These statements relate to future events and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed in or implied by such forward-looking statements. Each of these statements is based only on current information, assumptions and expectations that are inherently subject to change and involve a number of risks and uncertainties. Forward-looking statements include, but are not limited to, statements about (i) plans for, including timing and progress of commercialization of, DAYBUE; (ii) benefits to be derived from and efficacy of our product candidates, including the potential advantages of DAYBUE and expansion opportunities for DAYBUE; (iii) estimates regarding the prevalence of Rett syndrome; (iv) potential markets for any of our products, including NUPLAZID® and DAYBUE; (v) our estimates regarding our future financial performance, cash position or capital requirements.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “could,” “would,” “expects,” “plans,” “anticipates,” “believes,” “estimates,” “projects,” “predicts,” “potential” and similar expressions (including the negative thereof) intended to identify forward-looking statements. Given the risks and uncertainties, you should not place undue reliance on these forward-looking statements. For a discussion of the risks and other factors that may cause our actual results, performance or achievements to differ, please refer to our annual report on Form 10-K for the year ended December 31, 2022 as well as our subsequent filings with the SEC. The forward-looking statements contained herein are made as of the date hereof, and we undertake no obligation to update them for future events.

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Introduction

DAYBUE (trofinetide) Now Approved

DAYBUE is the first and only drug approved for the treatment of Rett syndrome

DAYBUE (trofinetide) is now approved for the treatment of Rett syndrome in adults and pediatric patients 2 years of age and older

Daybue™
(trofinetide)

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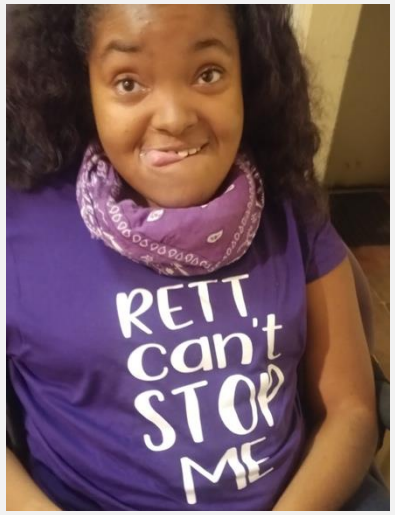
DAYBUE (trofinetide)

Label and Clinical Data

Rett Syndrome



HIGH UNMET NEED

ESTIMATED
6,000 - 9,000 PATIENTS IN THE U.S.[1]

Primarily affects females but also some males

Debilitating Symptoms[2]:

- Fine and gross motor impairment
- Loss of verbal and nonverbal communication
- Hand stereotypies
- Seizures
- G.I. symptoms, including severe constipation
- Loss of independence and require 24/7 support

[1]U.S. prevalence estimate based on incidence rates from the National Institutes of Health – National Institute of Neurological Disorders and Stroke.
[2]Acadia market research, Neul JL et al, Annal Neurol. 2010;68;944-50 and and https://www.rettsyndrome.org/about-rett-syndrome/what-is-rett-syndrome/.
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U.S. Prescribing Information

Highlights of Prescribing Information	
Indications and Usage	DAYBUE is indicated for the treatment of Rett syndrome in adults and pediatric patients 2 years of age and older.
Dosage and Administration	Administer DAYBUE orally twice daily, in the morning and evening, according to patient weight.
Dosage Forms and Strengths	Oral solution: 200 mg/mL of a pink to red, strawberry flavored solution.
Boxed Warning	None
Contraindications	None
Warnings and Precautions	• Diarrhea • Weight Loss
Adverse Reactions	Most common adverse reaction were diarrhea (82%) and vomiting (29%)
Risk Evaluation and Mitigation Strategy	None
In addition, there are no restrictions related to gender or severity of disease	

Visit DAYBUE.com for more information, including full Prescribing Information.

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Warnings and Precautions and Adverse Drug Reaction Table

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Warnings Precautions

- **Diarrhea:** Most patients experience diarrhea during treatment with DAYBUE.
- Advise patients to stop laxatives before starting DAYBUE. If diarrhea occurs, patients should start antidiarrheal treatment, increase oral fluids, and notify their healthcare provider. Interrupt, reduce dose, or discontinue DAYBUE if severe diarrhea occurs or if dehydration is suspected.
- **Weight Loss:** Weight loss may occur in patients treated with DAYBUE. Monitor weight and interrupt, reduce dose, or discontinue DAYBUE if significant weight loss occurs.

Adverse Reactions in at Least 5% of Patients Treated With DAYBUE and at Least 2% Greater than Placebo in Lavender

Adverse Reaction	DAYBUE (N=93) %	Placebo (N=94) %
Diarrhea	82	20
Vomiting	29	12
Fever	9	4
Seizure	9	6
Anxiety	8	1
Decreased appetite	8	2
Fatigue	8	2
Nasopharyngitis	5	1

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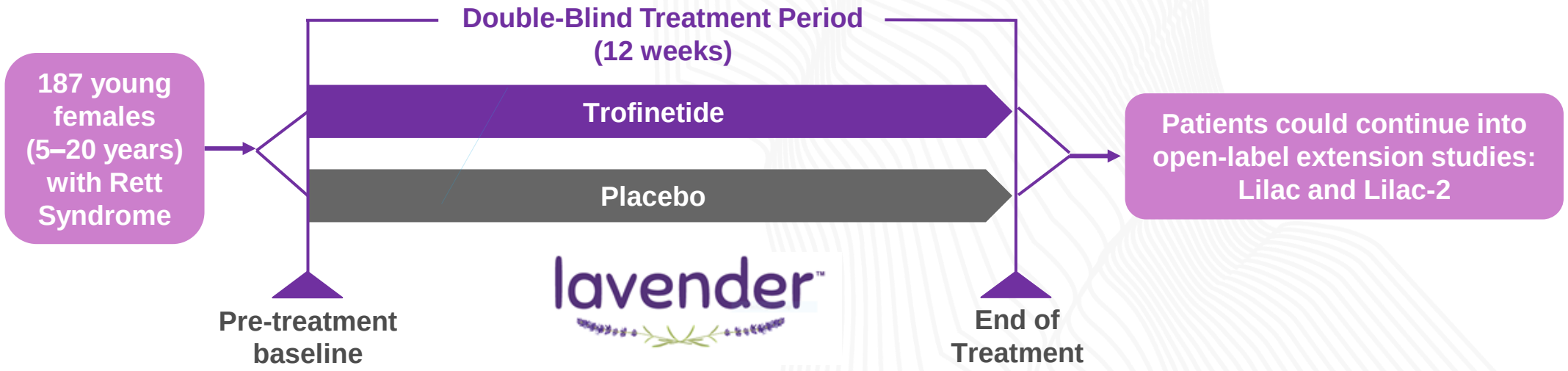
Phase 3 Lavender Study Design

Pivotal, Randomized, Double-Blind, Placebo-Controlled, Multi-Center Study



Positive Results Achieved on Co-Primary Endpoints:	
RSBQ (Change from baseline to week 12)	**CGI-I** (Score at week 12)
Two-sided p-value = 0.018	*Two-sided p-value = 0.003*
Effect Size; Cohen's d = 0.37	Effect Size; Cohen's d = 0.47

RSBQ = Rett Syndrome Behavioural Questionnaire (caregiver assessment); CGI-I = Clinical Global Impression Scale-Improvement (physician assessment).
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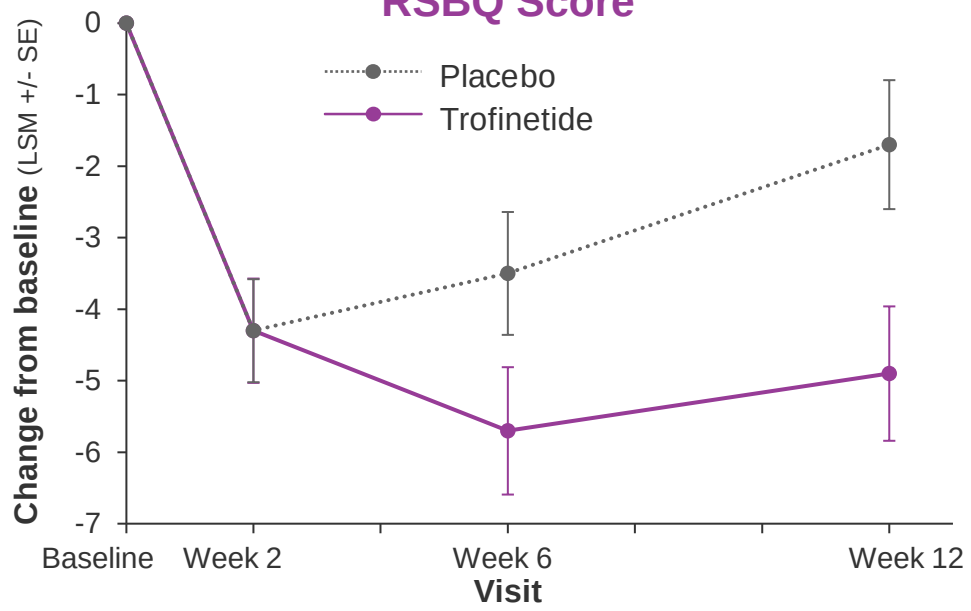
Positive Co-Primary Endpoint: RSBQ

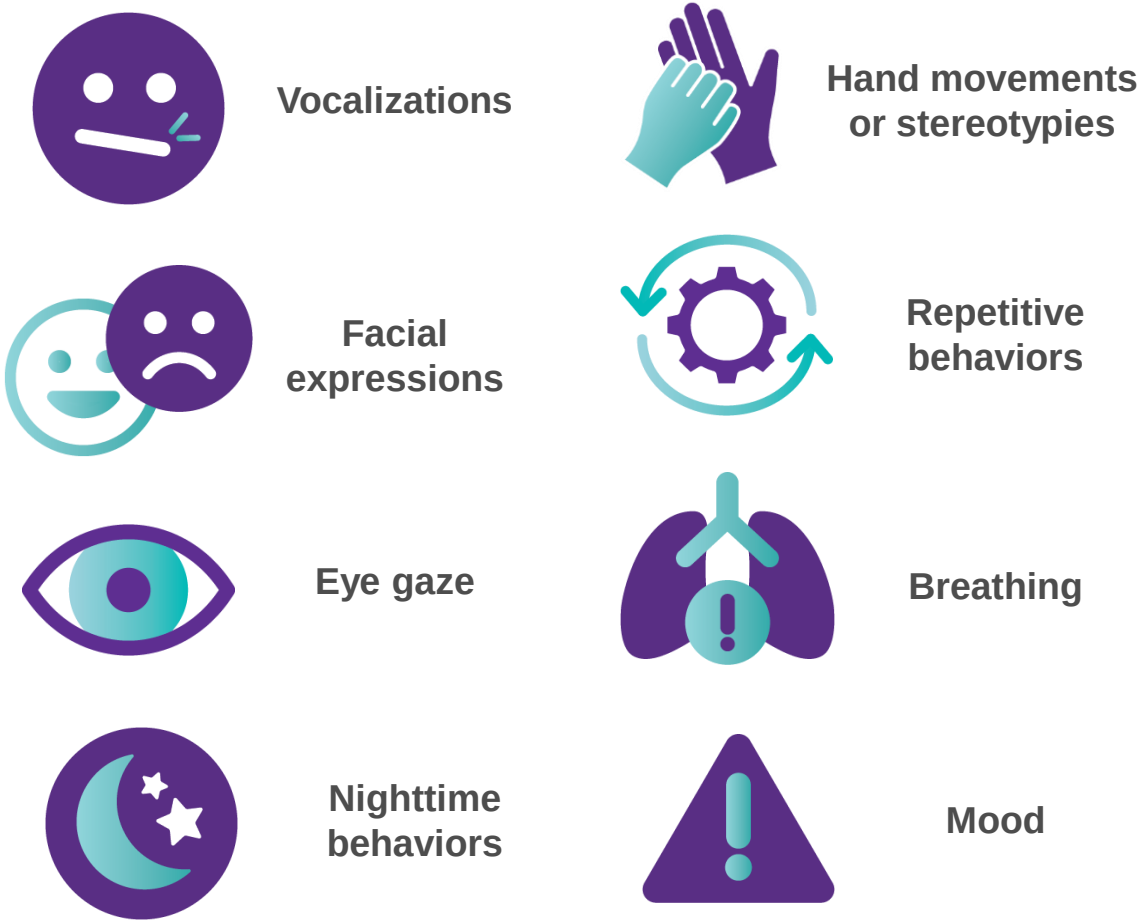
Change From Baseline in RSBQ Score



	Baseline	Week 2	Week 6	Week 12
Placebo, n=	93	90	92	85
Trofinetide, n=	91	90	83	76

RSBQ (Change from baseline to week 12)*
Two-sided p-value = 0.018
Effect Size; Cohen's d = 0.37

Signs and Symptoms Assessed by RSBQ



*RSBQ mean (SE) baseline score placebo = 44.5 (1.26) and trofinetide = 43.7 (1.21). RSBQ: n=161 for Lavender at 12 weeks.
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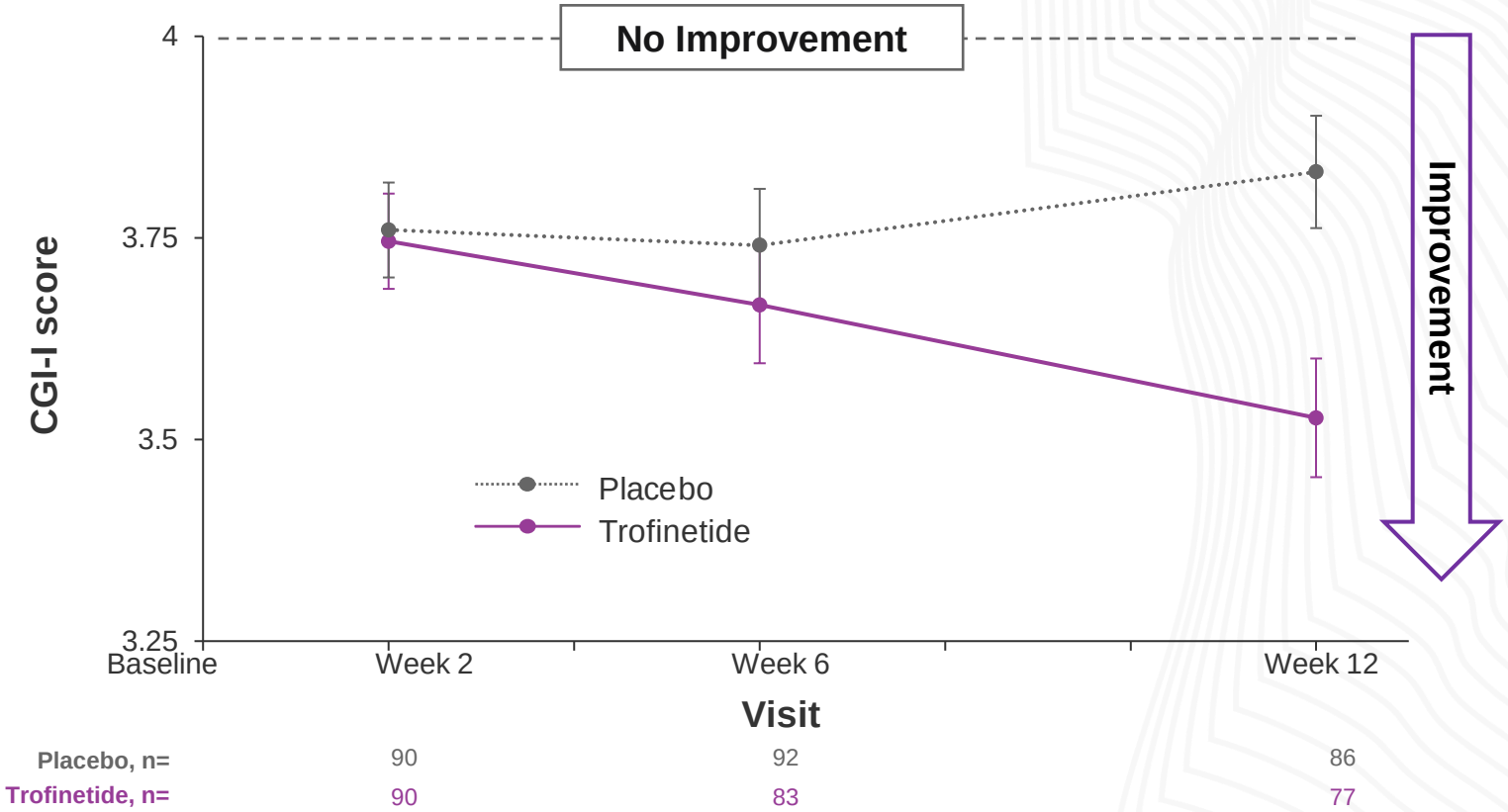
Positive Co-Primary Endpoint: CGI-I

Clinical Global Impression – Improvement (CGI-I)



	Baseline	Week 2	Week 6	Week 12
Placebo, n=		90	92	86
Trofinetide, n=		90	83	77

CGI-I uses a 7-point Likert scale:

- a score of 4 = no improvement
- >4 = worsening
- <4 = improvement

CGI-I (Score at week 12)*
Two-sided p-value = 0.003
Effect Size; Cohen's d = 0.47

*CGI-I no baseline score. CGI-I: n=163 for Lavender at 12 weeks.

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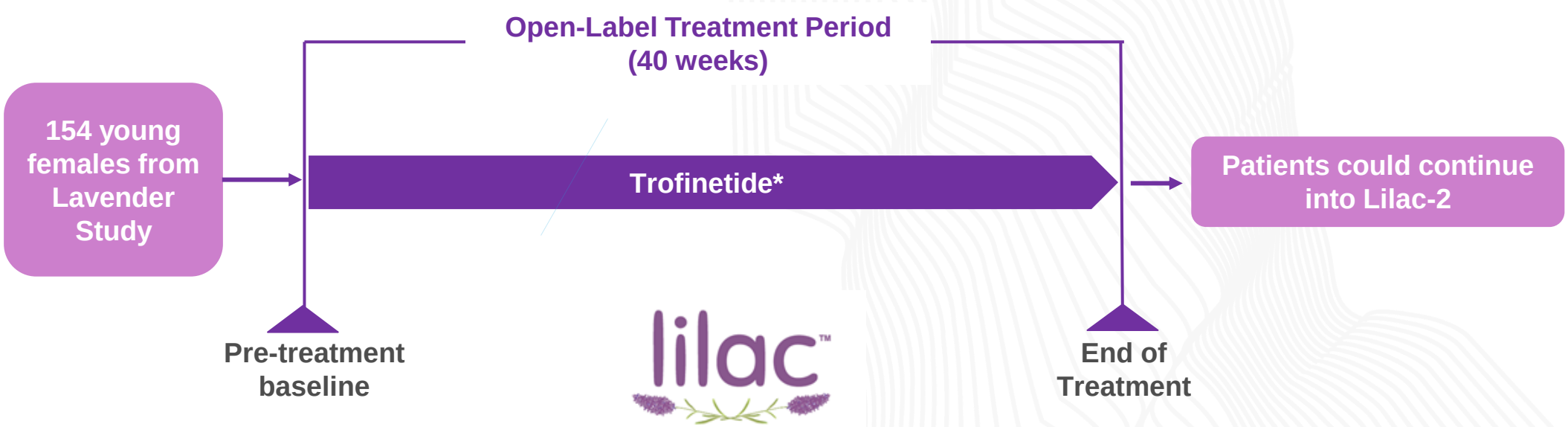
Recently Completed OLE Study: Lilac



Safety data:

- Types of Adverse events reported were similar to Lavender study and the label
- Most common adverse events (>10%) were diarrhea (74.7%), vomiting (28.6%) and COVID-19 (11%)

Efficacy assessments:

- RSBQ* (n=88) decreased on average 7.2 points; assessed from Lavender baseline
- CGI-I* (n=91) average score for patients completing Lilac was 3.1; assessed from Lilac baseline

*RSBQ mean (SE) baseline score placebo = 44.5 (1.26) and trofinetide = 43.7 (1.21). RSBQ: n=161 for Lavender at 12 weeks; n=88 for Lilac at 40 weeks.
*CGI-I no baseline score. CGI-I: n=163 for Lavender at 12 weeks; n=91 for Lilac at 40 weeks. CGI-I uses a 7-point Likert scale; with a score of 4 = no improvement; >4 = worsening and <4 = improvement
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Post-Marketing Commitments

- Renal impairment Phase 1 study
  - ✓ Already completed
- Drug-drug interaction work
- Additional nonclinical studies
- **No additional clinical studies in Rett syndrome patients**

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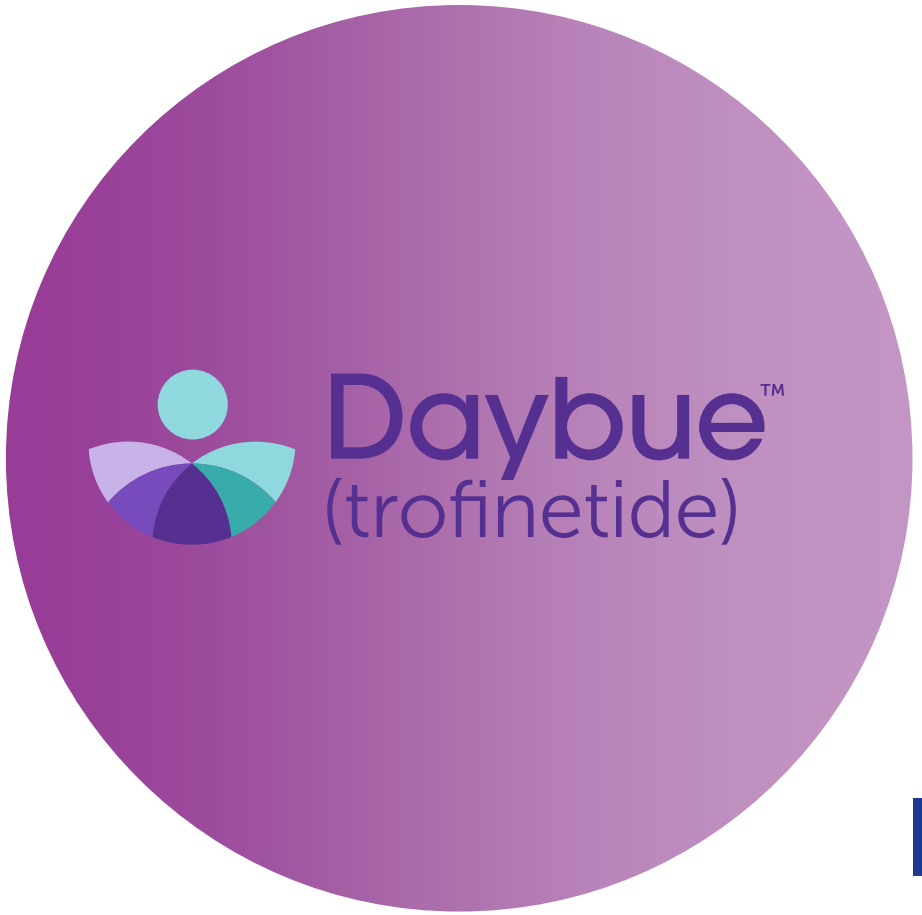
Commercialization Strategy

DAYBUE Key Launch Initiatives



- **Educate:** Drive Disease State Awareness and Education on Compelling Value of DAYBUE
- **Identify:** HCPs, Rett Patients and Families to Seek Out Treatment with DAYBUE
- **Facilitate:** Support Services, Access and Affordability

DAYBUE to be available by end of April 2023

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Educate: HCPs, Caregiver and Payors

Treatment Journey

Stage	*Market Development*	*Rett Awareness + Diagnosis*	Treatment Decision	Start Therapy	Stay on Therapy
Acadia goal	IDENTIFY Target patients and HCPs, Priority Payor Targets		DRIVE DEMAND & TREATMENT INITIATION		MAINTAIN PATIENTS ON THERAPY

Key Stakeholders to Educate

Caregivers & Rett Community

Healthcare Professionals

Practice Staff

Payors

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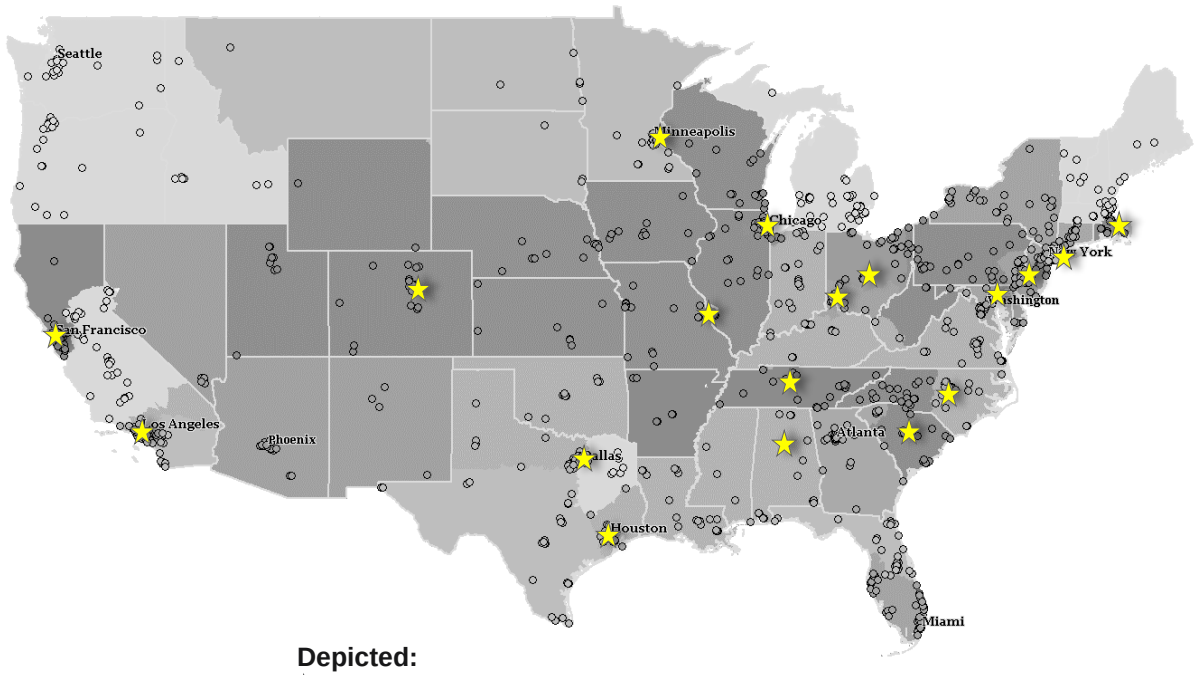
Identify: Patients and HCPs

National view of Rett Syndrome targets



Depicted:
- ★ IRSF designated Centers of Excellence
- ○ High volume institutions outside of "COEs"

1 **~20**
Centers of Excellence designated by the International Rett Syndrome Foundation[1] and similar type clinics

>200
Key opinion leaders identified in the US Rett Syndrome community

2 **~300**
Large institutions including academic hospitals prioritized for engagement at launch, containing the bolus of Rett HCP & patients

~2,250
HCP targets actively involved in diagnosing & caring for Rett syndrome today

3 **~2,700**
Community HCPs – the long-tail of opportunity, crucial for rare disease patient identification

~4,500
Diagnosed U.S. Rett syndrome patients today

Highly experienced and integrated commercial organization to fully support HCP launch targets and patients/families including field force, patient support services, medical education

[1] Source: IRSF Centers of Excellence Rett Syndrome Clinics - International Rett Syndrome Foundation

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Facilitate: Support through Acadia Connect®

Program Offerings

acadia connect®

Cost & insurance
Providing insurance coverage assistance and financial support resources

Filling prescriptions
Coordinates prescription details with patient families/caregivers and Specialty Pharmacy to help get prescriptions filled and delivered on time

Support & education
Regularly touches base to help patient families/caregivers with their insurance, provides appropriate financial assistance options, and assists with prescription delivery

Dedicated, Experienced Support Team

Nurse Care Coordinators
Welcomes patient families/caregivers to Acadia Connect and provides ongoing support throughout the DAYBUE treatment journey

Family Access Managers (FAM)
Helps patient families/caregivers understand their insurance coverage, provides information about DAYBUE, and delivers education about potential side effects, tools, and resources

Specialty Pharmacy

Process and fill DAYBUE prescriptions with clinical pharmacists, available 24/7, to:

- Answer questions and offer treatment support for DAYBUE
- Provide information about potential side effects
- Offer clinical recommendation(s) when appropriate

Acadia Connect is a patient and family support program that provides educational support and resources through the DAYBUE treatment journey

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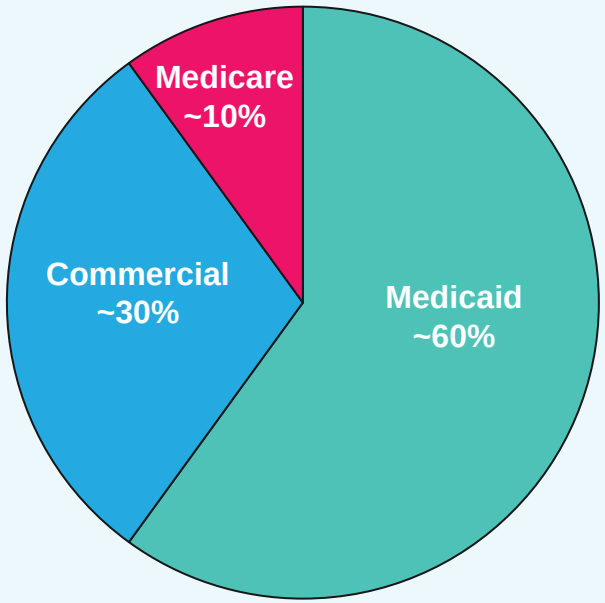
Facilitate: Patient Access and Affordability

We believe cost should never be a barrier to treatment

Projected Payor Mix and Drug Out-of-Pocket (OOP) Costs

Medicare
Nominal OOP or Qualify for Patient Assistance Program



Commercial
As Little as $0 With Acadia Connect Co-pay Card

Medicaid
Nominal OOP or Qualify for Patient Assistance Program

Acadia Connect Financial Assistance

❖ Co-Pay Program:

- Eligible patients with commercial insurance may pay as little as $0 per month for DAYBUE after being automatically enrolled in the **Acadia Connect Commercial Copay Program***

❖ Patient Assistance Program:

- For patients who do not have insurance, or situations in which DAYBUE is not covered by their insurance plan, Acadia can provide appropriate financial assistance options, such as the **Acadia Connect Patient Assistance Program**

Acadia Connect will offer personalized insurance assistance, financial resources and prescription support to patients and caregivers starting and continuing appropriate DAYBUE therapy

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DAYBUE Value Proposition and Pricing

Compelling value proposition based on key factors

- **Significant Burden of Disease**
- **High Unmet Need – First Approved Treatment**
- **DAYBUE Established Efficacy and Safety Profile**
- **Rare and Well-Defined Patient Population**
- **Development Pathway to Approval**

✓ **Innovation:** Acadia is committed to bring innovative and first-in-class CNS products to the marketplace that provide hope and opportunity.

✓ **Value:** Pricing reflects clinical benefits Acadia products bring to patients.

✓ **Access & Affordability:** Acadia believes that affordability should never prevent access to our medicines and that patients and caregivers receive the ongoing support they may need – Acadia Connect™ is the cornerstone of that commitment.

✓ **Support:** Acadia is committed to the Rett patient community of patients, caregivers and treating physicians.

Price: Expect the annual average net realized cost of DAYBUE to be ~$375,000.

- Includes assumptions for average weight of expected patient population, compliance rates to therapy and mandatory government discounts.
- The list price will be $21.10 per mL.

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Beginning Treatment with DAYBUE

Commercial Product Available by end of April 2023

Acadia Connect Patient Access Services now active

Acadia Connect information:

acadiaconnect.com

1-844-737-2223

Learn more about DAYBUE through the brand website:

DAYBUE.com

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Financial Considerations

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Acadia licensed North America rights for trofinetide from partner Neuren Pharmaceuticals in 2018

Upcoming Milestone Payment

- Acadia owes Neuren $40M within 60 days of first commercial sale in the U.S.

Received Priority Review Voucher from FDA

- Acadia owes Neuren 1/3 value at the time it is used by Acadia or sold by Acadia

Tiered Royalty Rates (annual net sales)*	
≤$250M	10%
>$250M, but ≤$500M	12%
>$500M, but ≤$750M	14%
>$750M	15%

Potential Sales Milestones	
Net Sales ≥$250M in one calendar year	$50M
Net Sales ≥$500M in one calendar year	$50M
Net Sales ≥$750M in one calendar year	$100M
Net Sales ≥$1B in one calendar year	$150M

*Royalty rates payable on the portion of annual net sales that fall within the applicable range.
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Closing Remarks

THANK YOU

Thank you to all the patients and their families who participated in our clinical studies

Thank you to the investigators, nurses, support staff and KOLs

Thank you to the patient advocacy organizations

And thank you to the Acadia team who worked so hard to deliver DAYBUE to the Rett community

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Q&A Session