



Fourth Quarter and Full Year 2022 Earnings Call

February 27, 2023



4Q and Full Year 2022 Earnings Call Agenda



Introduction | **Mark Johnson** | Vice President, Investor Relations

CEO Opening Remarks | **Steve Davis** | Chief Executive Officer

Financial Update | **Mark Schneyer** | Chief Financial Officer

NUPLAZID Update | **Brendan Teehan** | Chief Operating Officer, Head of Commercial

Trofinetide Update | **Kathie Bishop Ph.D.** | Chief Scientific Officer, Head of Rare Disease and External Innovation
| **Brendan Teehan** | Chief Operating Officer, Head of Commercial

R&D Update | **Doug Williamson M.D.** | Head of Research and Development

CEO Closing Remarks | **Steve Davis** | Chief Executive Officer

Q&A

Forward-Looking Statements

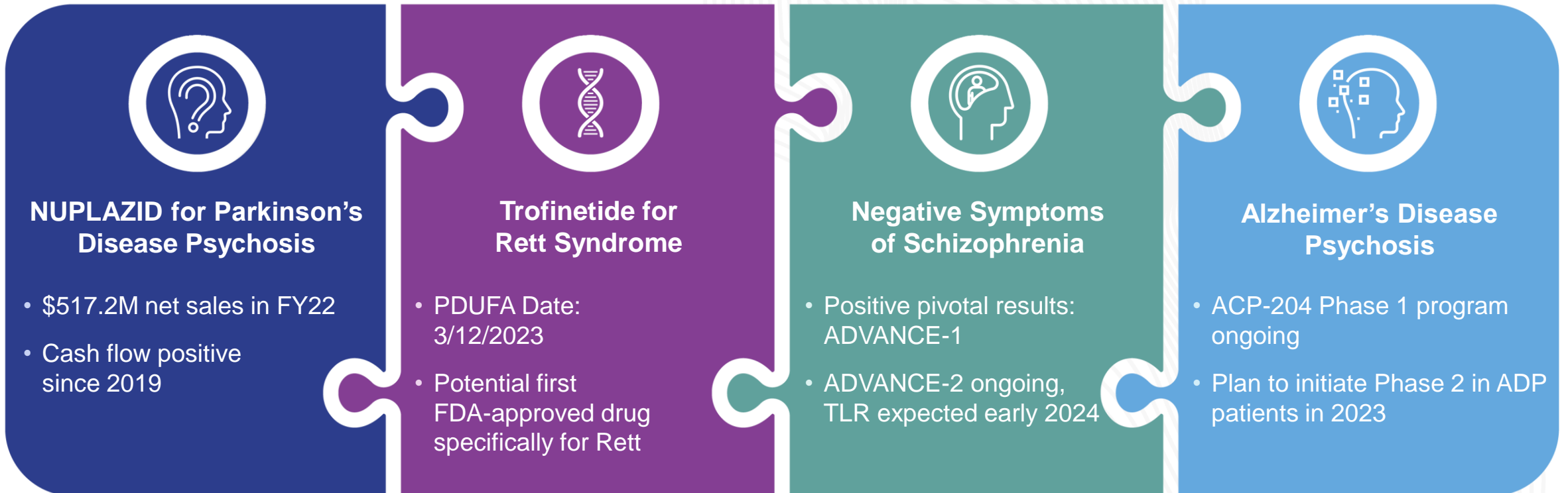


This presentation contains forward-looking statements. These statements relate to future events and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements 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, NUPLAZID® or for the clinical development of our product candidates, including pimavanserin and trofinetide; (ii) benefits to be derived from and efficacy of our product candidates, including the use of pimavanserin in dementia-related psychosis, schizophrenia or other neurological or psychiatric indications, potential advantages of NUPLAZID versus existing antipsychotics or antidepressants, and expansion opportunities for NUPLAZID; (iii) estimates regarding the prevalence of Parkinson's disease psychosis, dementia-related psychosis, schizophrenia and the potential use of trofinetide in Rett syndrome; (iv) potential markets for any of our products, including NUPLAZID and trofinetide; (v) our estimates regarding our future financial performance, cash position or capital requirements; and (vi) currently anticipated impacts of COVID-19 on Acadia's business, including its commercial sales operations, current and planned clinical trials, supply chain, and guidance for full-year 2023 NUPLAZID net sales and certain expense line items.

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, 2021 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.

Opening Remarks

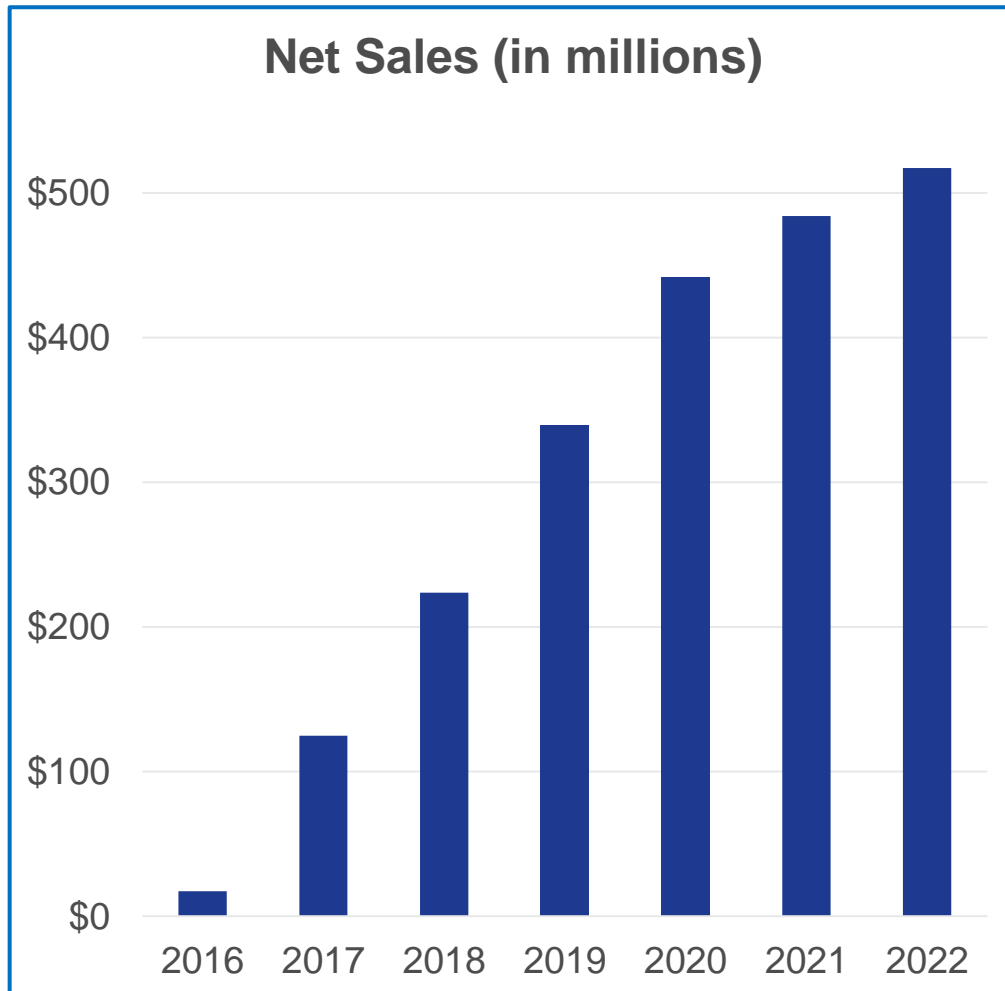
Four Strategic Priorities for Acadia



ACAD able to fund all four strategic priorities with existing cash balance

NUPLAZID (pimavanserin) is only approved in the U.S. by the FDA for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis. Provided February 27, 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.

NUPLAZID® Franchise Performance



Highlights:

- PDP franchise cash flow positive since 2019
 - \$517.2M net sales in FY22; 7% YoY growth
 - Overall demand relatively steady YoY
 - LTC channel growth improved; up 5% YoY
 - Office-based channel declined; -3% YoY
- RWE studies being shared across channels with HCPs, LTC facilities and payers

**FY23 Net Sales Guidance for PDP =
\$520 - \$550M**

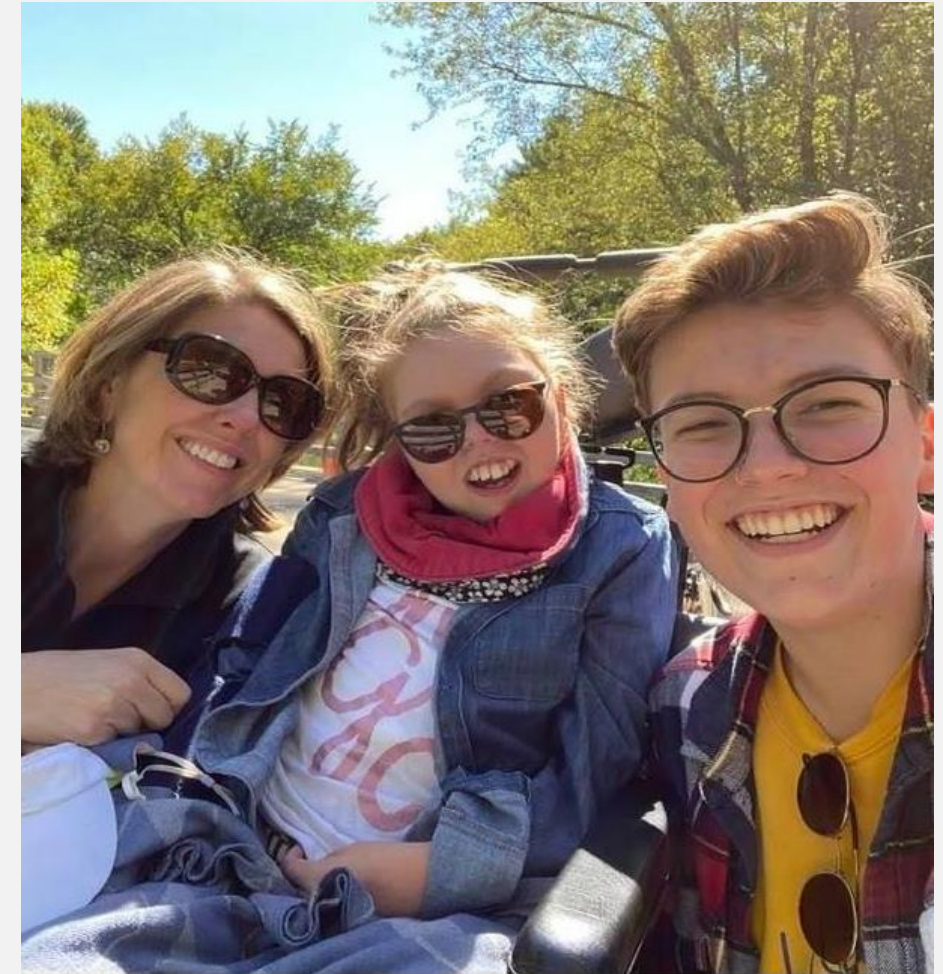
Trofinetide for the Treatment of Rett Syndrome



PDUFA: March 12, 2023

Promise of Trofinetide

- No FDA approved therapies specifically for Rett
 - A rare and severe neurodevelopmental disorder
- Positive Phase 3 Lavender study results achieved on co-primary endpoints and key secondary endpoint
 - Improvement on both caregiver (RSBQ) and physician (CGI-I) assessments of the core symptoms of Rett syndrome
- Trofinetide demonstrated potential to treat all populations and severities of Rett patients
- Acadia prepared to support families every step of the way in their trofinetide patient experience



Next Wave of Breakthroughs in CNS

Negative Symptoms of Schizophrenia

- Positive ADVANCE-1 study complete
- ADVANCE-2 study expect to complete enrollment mid-year with TLR in early 2024



Alzheimer's Disease Psychosis

- ACP-204 Phase 1 program ongoing
- Plan to evaluate in Phase 2 trials in patients with Alzheimer's disease psychosis later this year



TLR = Top-line results.

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Finance Update

4Q22 and FY22 Financial Highlights



Millions, Except EPS	4Q22 (GAAP)	4Q21 (GAAP)	YoY Change	FY22 (GAAP)	FY21 (GAAP)	YoY Change
Total Revenue	\$136.5	\$130.8	4%	\$517.2	\$484.1	7%
R&D	\$75.7	\$67.1	13%	\$361.6 ¹	\$239.4	51%
SG&A	\$104.4	\$105.8	-1%	\$369.1	\$396.0	-7%
Net Income (Loss)	(\$41.7)	(\$43.1)		(\$216.0)	(\$167.9)	
EPS	(\$0.26)	(\$0.27)		(\$1.34)	(\$1.05)	
Cash Balance	\$416.8					

¹ Includes \$60M Stoke Therapeutics upfront payment, \$10M Neuren Pharmaceuticals milestone, ~\$23M in additional business development and ~\$30M trofinetide commercial supply build.

FY23 Financial Guidance



	FY23 Guidance	Commentary
NUPLAZID[®] Net Sales	\$520 to \$550M	<ul style="list-style-type: none"> • Midpoint of the range reflects ~1% growth volume YoY and includes ~2.5% net price growth YoY • Parkinson's disease psychosis (PDP) guidance only • No sales guidance for Trofinetide
Gross-to-Net	22% to 25%	<ul style="list-style-type: none"> • Increased due to IRA inflation cap rebate accruals • Incorporates various scenarios including inflation rates and changes in 340b volumes
GAAP R&D Expense	\$235 to \$255M	<ul style="list-style-type: none"> • ~\$20M of stock-based compensation expense
GAAP SG&A Expense	\$360 to \$380M	<ul style="list-style-type: none"> • Reflects continued optimization of PDP commercial spend • Supports investment in trofinetide launch • ~\$45M of stock-based compensation expense

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NUPLAZID® for the Treatment of PDP

New Real-World Evidence

Safety Publications: Retrospective Analyses^{1,2}:

COMPARED TO ATYPICAL ANTIPSYCHOTICS*, PATIENTS TREATED WITH NUPLAZID HAD LOWER ALL-CAUSE MORTALITY

MOSHOLDER ET AL. PUBLICATION (PD PATIENTS)

Overall analysis 360 days: **23% lower mortality risk**

- Hazard Ratio = 0.77; 95% CI 0.66-0.90

Interval analysis 1-180 days: **35% lower mortality risk**

- Hazard Ratio = 0.65; 95% CI 0.53-0.79

Interval analysis 181+ days:

- No additional mortality advantage observed

LAYTON ET AL. PUBLICATION (PDP PATIENTS)

Overall cumulative mortality: **22% lower mortality risk**

- Hazard Ratio = 0.78; 95% CI 0.67-0.91

The first 180 days of treatment: **34% lower mortality risk**

- Hazard Ratio = 0.66; 95% CI 0.54-0.82

Cumulative mortality at 1 year: **23% lower mortality risk**

- Hazard Ratio = 0.77; 95% CI 0.64-0.91

Healthcare Utilization Presentation³:



HIGHLIGHTS IMPORTANT DATA
FOR LTC and Community Channels

KUMAR ET AL. PUBLICATION (PDP PATIENTS)

Patients treated with NUPLAZID had:

- **Lower** all-cause hospitalizations, ER visits, and shorter length of stays vs. atypical antipsychotics



¹ Mosholder AD, et al. *Am J Psychiatry*. 2022;179(8):553-561. Medicare beneficiaries (Parts A,B,D) – Apr.'16-Mar.'19 ² Layton JB, et al. *Drug Safety*. Published online 14 Dec 22. Medicare beneficiaries (Parts A,B,D) MDS 3.0 assessment – Apr. '16-Dec.'19

³ Kumar S. et al., *Journal of Medical Economics* 2023 Vol. 26 No.1,34-42. Retrospective cohort analysis of Parts A, B, and D claims from 100% Medicare sample from Jan.'13-Dec.'19

*Comparator atypical antipsychotics included quetiapine, risperidone, olanzapine, and aripiprazole.

Important note: The findings from the retrospective analyses presented here are descriptive and should be interpreted with caution as the study was not designed or powered to make direct safety comparisons between antipsychotics. Findings are limited to patients in the community setting.

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Trofinetide for Rett Syndrome

Rett Syndrome

HIGH UNMET NEED

No FDA-approved drug for the treatment of Rett syndrome

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

Debilitating Symptoms²:

- 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



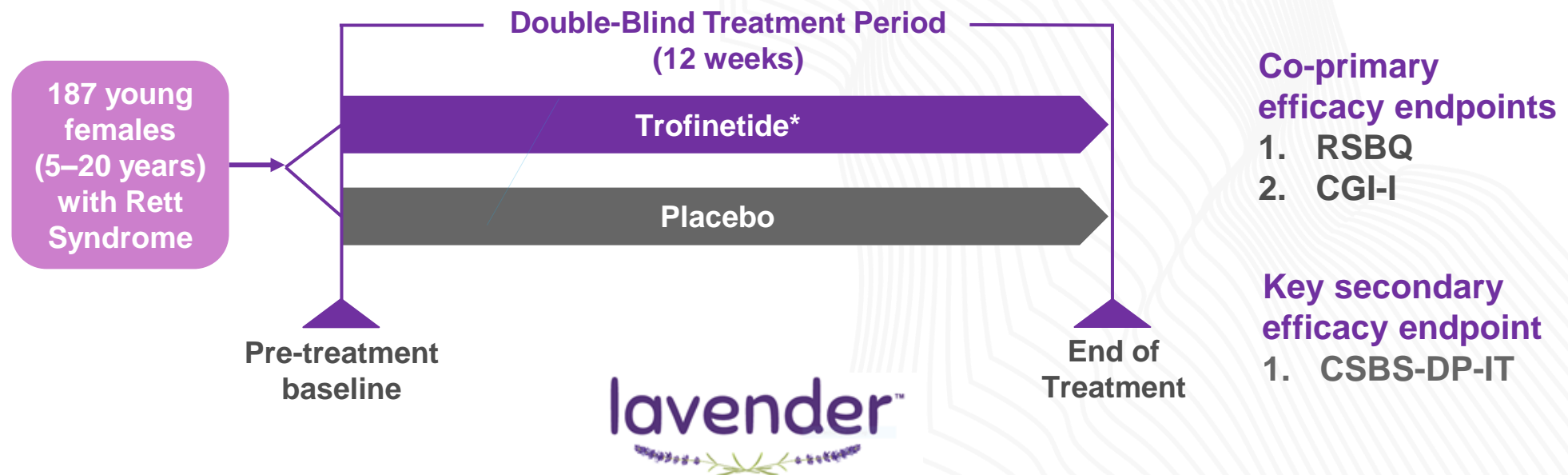
¹U.S. prevalence estimate based on incidence rates from the National Institutes of Health – National Institute of Neurological Disorders and Stroke.

²Acadia market research, Neul JL et al, Annal Neurol. 2010;68;944-50 and <https://www.rett syndrome.org/about-rett-syndrome/what-is-rett-syndrome/>.

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Phase 3 Lavender Study Design

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

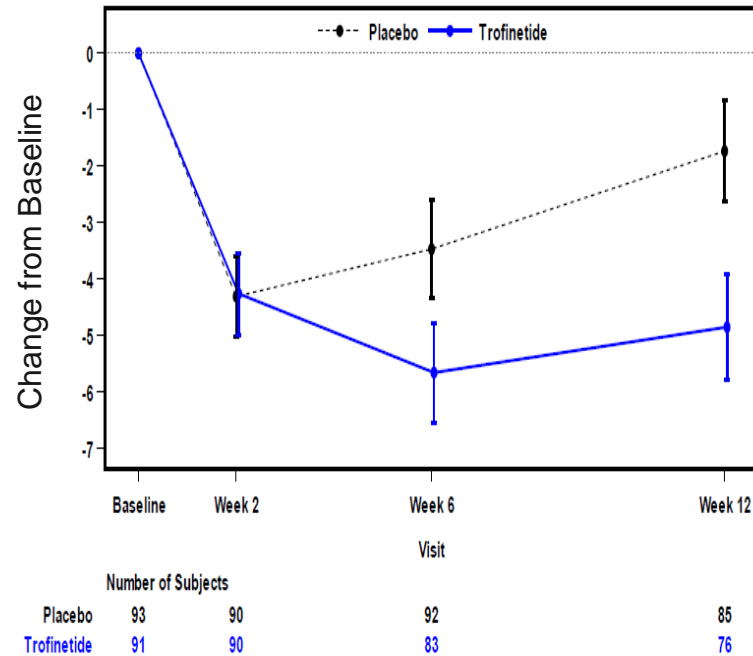


Patients may continue into open-label extension studies: Lilac and Lilac-2

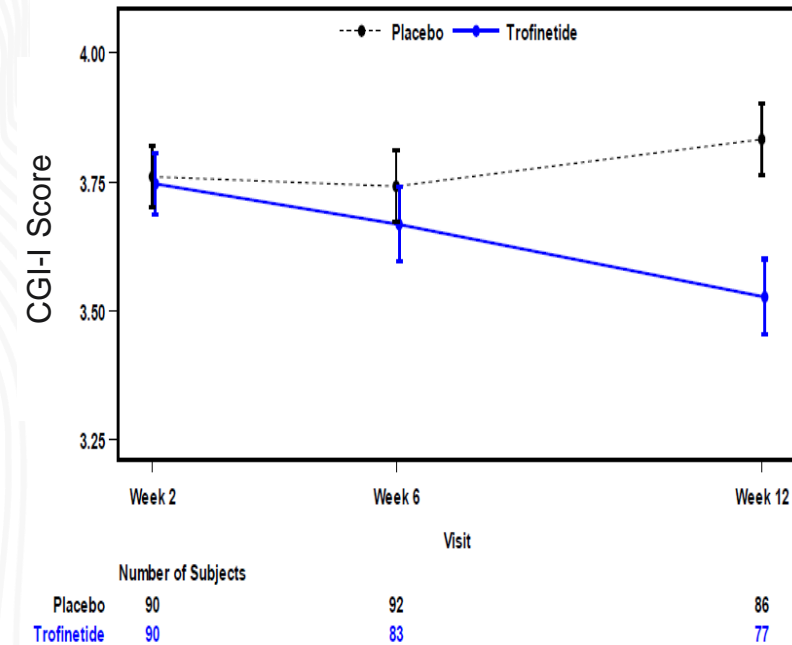
Positive Phase 3 Lavender Study Results



Rett Syndrome Behavioural Questionnaire (RSBQ)



Clinical Global Impression – Improvement (CGI-I)

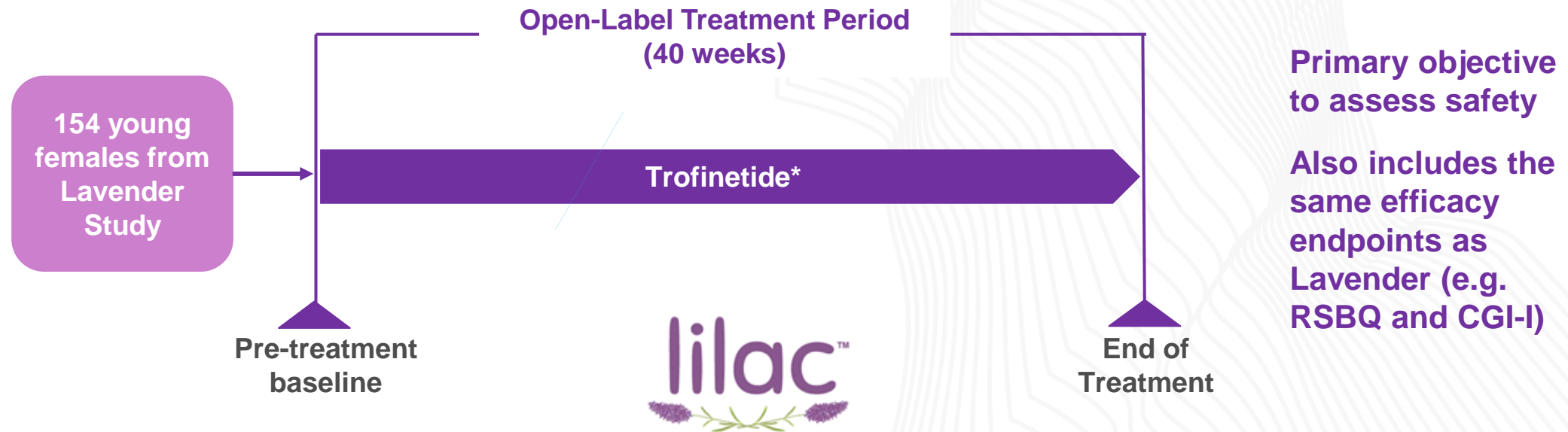


Change from Baseline	Placebo	Trofinetide*
Mean	-1.7	-5.1
<i>p-value</i>		0.0175
<i>Effect size</i>		0.37

Week 12 Score	Placebo	Trofinetide*
CGI-I	3.8	3.5
<i>p-value</i>		0.0030
<i>Effect size</i>		0.47

*RSBQ mean (SE) baseline score placebo = 44.5 (1.26) and trofinetide = 43.7 (1.21). CGI-I no baseline score. CGI-I uses a 7-point Likert scale; with a score of 4 = no improvement; >4 = worsening and <4 = improvement. *p-values* based on least squares mean from the mixed-effects model for repeated measures analysis. Provided February 27, 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.

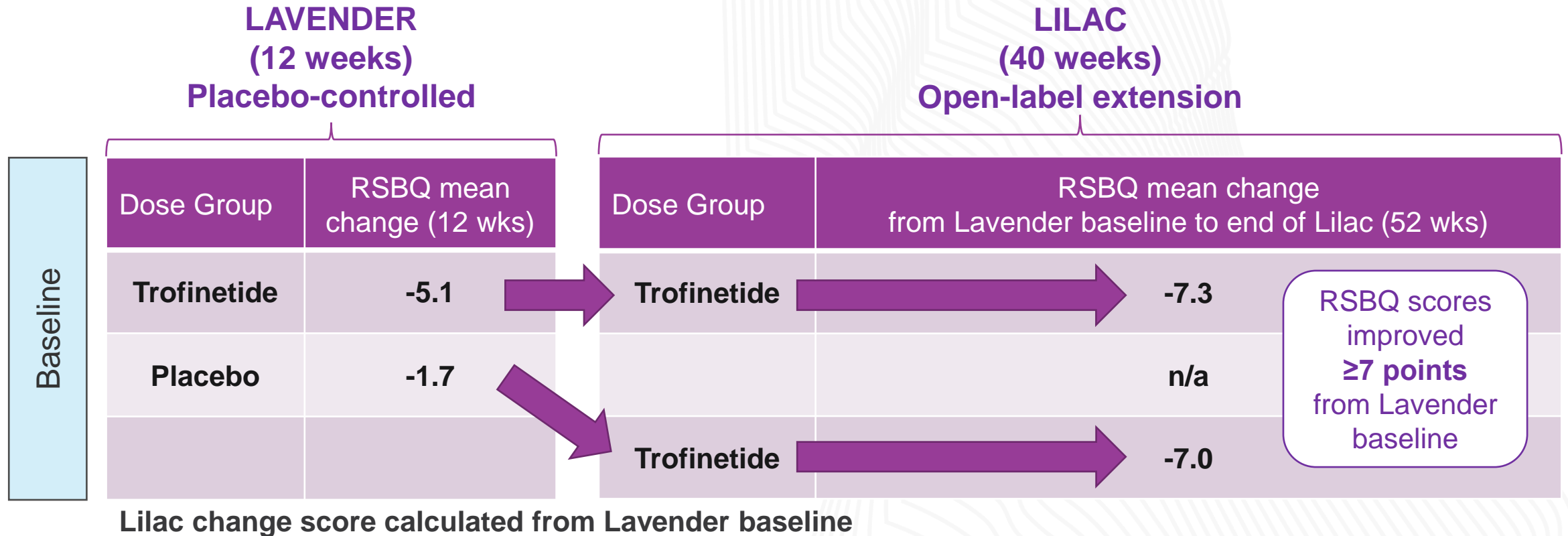
Lilac: Open-Label Extension Study



Patients may continue to receive treatment in Lilac-2

Lilac Top-Line Results: Efficacy Assessments

RSBQ



Observed sustained and continued improvement in RSBQ over 52 weeks

Lilac Top-Line Results: Efficacy Assessments

CGI-I

LAVENDER
(12 weeks)
Placebo-controlled

LILAC
(40 weeks)
Open-label extension

Lilac Baseline	LAVENDER (12 weeks) Placebo-controlled		New Baseline for Lilac	LILAC (40 weeks) Open-label extension	
	Dose Group	CGI-I score (at 12 wks)		Dose Group	CGI-I score (at 40 wks)
Lavender Baseline	Trofinetide	3.5	New Baseline for Lilac	Trofinetide	3.1
	Placebo	3.8		n/a	
				Trofinetide	3.2

CGI-I improvements:

- Trofinetide group: 0.5 improvement in Lavender, then 0.9 improvement in Lilac
- Trofinetide crossovers: 0.8 improvement in Lilac

Lilac score assessed from Lilac baseline

CGI-I uses a 7-point Likert scale; a score of 4 = no improvement; >4 = worsening and <4 = improvement.

Observed meaningful improvements in CGI-I over 40 weeks

Lilac Top-Line Results: Safety and Tolerability



Adverse Event (AE) Summary

Adverse Events >10% observed:

- Diarrhea (74.7%);
 - 96% were mild-to-moderate
- Vomiting (28.6%);
 - 100% were mild-to-moderate
- COVID-19 (11%)

Discontinuations

- Discontinuations due to AE of diarrhea was 21%
- Overall 46% of patients discontinued

AEs were consistent with Lavender; no new safety or tolerability findings

Key Launch Initiatives for Trofinetide

1

Drive Disease State Awareness and Education

- Understand Rett syndrome and the unmet needs of core symptoms, such as hand wringing, lack of purposeful eye gaze and communication



RettDialogue

2

Hire Rare Disease Commercial Team and Patient Identification

- Hiring seasoned leadership team w/ rare disease expertise
- ~4,500 Rett patients diagnosed in U.S. and cared for at Centers of Excellence, non-COE academic institutions and other neurology practices



3

Build Support Services for Rett Community

- Our Acadia Connect hub provide patients, caregivers, and HCPs with personalized support and resources
- Helps care teams navigate any issues that may arise



Well-Positioned for a Successful Launch if Approved

R&D Update

Addressing Significant Unmet Needs in CNS



Program	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Registration	Marketed
NUPLAZID® (pimavanserin)¹	Parkinson's Disease Psychosis						
Trofinetide²	Rett Syndrome						
Pimavanserin	Negative Symptoms of Schizophrenia						
ACP-204	Alzheimer's Disease Psychosis						
ASO Programs³	SYNGAP1; Rett Syndrome; Undisclosed						
Other Programs	Neuropsychiatric Symptoms						

¹NUPLAZID (pimavanserin) is only approved in the U.S. by the FDA for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis.

²Acadia has an exclusive license to develop and commercialize trofinetide in North America from Neuren Pharmaceuticals.

³Acadia entered into a collaboration with Stoke Therapeutics to discover, develop and commercialize novel RNA-based medicines for the potential treatment of severe and rare genetic neurodevelopmental diseases.

ASO = Antisense oligonucleotide.

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Negative Symptoms of Schizophrenia

HIGH UNMET NEED

No FDA-approved treatment for the negative symptoms of schizophrenia

>700K patients receiving treatment in the U.S. have persistent negative symptoms

Negative symptoms include apathy, lack of emotion, social withdrawal, restricted speech, and blunted affect and can lead to:

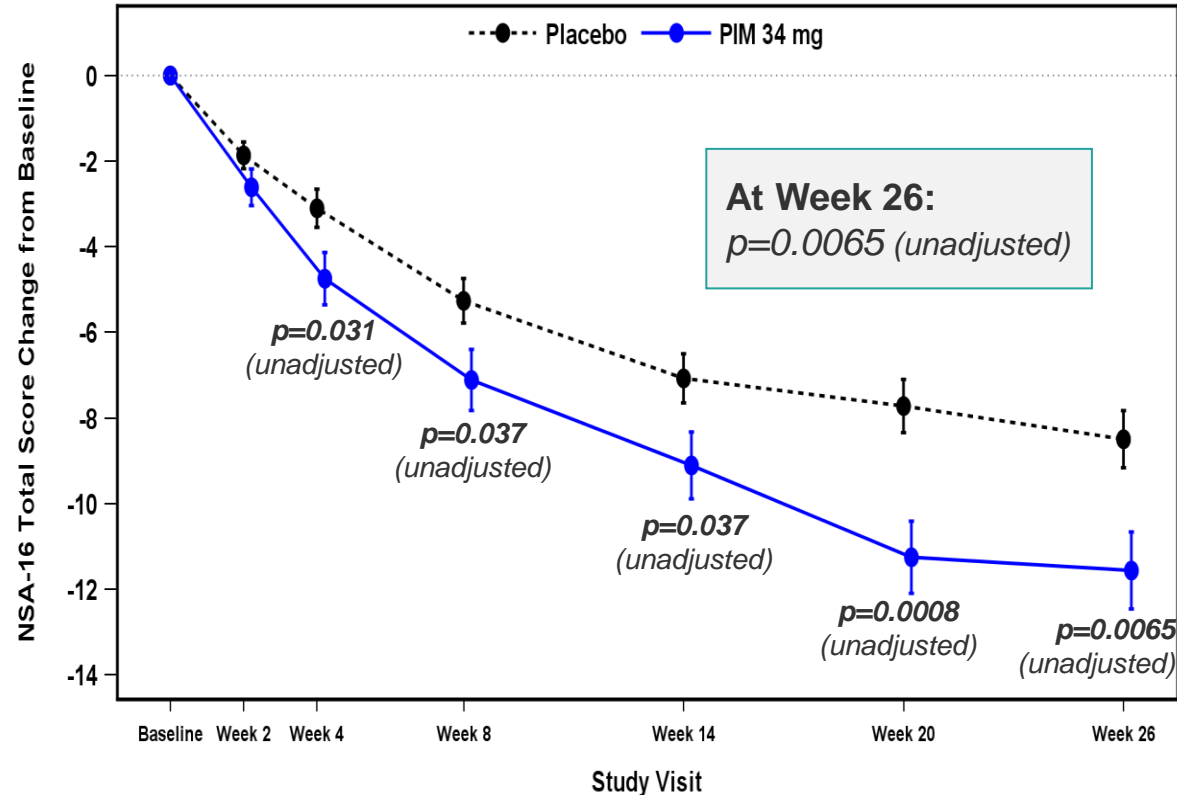
- Low social functioning
- Long-term disability
- Significant caregiver burden



Clinical Development Program for the Negative Symptoms of Schizophrenia



34 MG Dose^{1,2}



No. of Subjects

Placebo	201	201	197	192	184	179	173
PIM 34 mg	107	107	105	103	102	102	99

ADVANCE-1 Results

Primary Endpoint (Overall – all 3 doses tested)

Improvement in NSA-16 vs. placebo at 26 weeks

Two-sided p-value = $p=0.043$

Patients on 34 mg vs. placebo

Two-sided p-value = 0.0065 (unadjusted)

Based on the results of ADVANCE-1, Acadia is pursuing the optimal 34 mg dose in its second pivotal study: ADVANCE-2.

¹Pimavanserin for negative symptoms of schizophrenia: results from the ADVANCE phase 2 randomised, placebo-controlled trial in North America and Europe, Bugarski-Kirola, Dragana et al. The Lancet Psychiatry, Volume 9, Issue 1, 46 – 58

²Prespecified subgroup with p-values calculated post-hoc. Patients in the ADVANCE-2 study are on either 34mg of pimavanserin or placebo in addition to a stable background antipsychotic to control their positive symptoms.

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Investing in New Opportunities in Alzheimer's Disease Psychosis: ACP-204



Program Objectives

- Leverage 5HT_{2A} benefits and favorable safety/tolerability profile
- Reduce risk of QT prolongation
- Optimize the efficacy profile
- Potentially improve onset of action

Clinical Development

- Phase 1 program ongoing
- Plan to meet with FDA to discuss development plan
- Plan to initiate Phase 2 studies in patients with Alzheimer's disease psychosis later this year



Closing Remarks

Upcoming Development Milestones

Rett Syndrome

Trofinetide

PDUFA Date
3/12/2023

Negative Symptoms of Schizophrenia

Pimavanserin

Phase 3
ADVANCE-2 Study
Complete Enrollment:
Mid-2023

TLR: 1H24

Alzheimer's Disease Psychosis

ACP-204

Phase 1 Results:
1H23

Initiate ADP Study:
2023

Profitable PDP franchise enables ACAD to execute on its strategic priorities with existing cash balance

Q&A Session