



# Steve Davis, CEO

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Healthcare Conference

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# 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 or regulatory timelines for, 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.

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.

DAYBUE (trofinetide) is only approved in the U.S. by the FDA for the treatment of Rett syndrome in adults and pediatric patients two years of age and older.

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# ACADIA® Investment Thesis



**Two successful commercial franchises driving record revenues**



**Three late-stage assets with strong early-stage pipeline**



**Cash flow positive**







# Successful Launch of DAYBUE™ for Rett Syndrome





# DAYBUE Real World Experience



“It was her engagement level with the world outside of her – to me and to friends in school; it just blossomed, and it was like a light was turned on.”

“Her verbalization definitely improved, and she started saying more things.”

“Picking up things a lot more (mostly her cup), happens daily and she is now trying to drink by herself.”



“Improved cognitive ability, and [the parents] are hearing new words or words they have not heard in a while.”

“She knows that she can get her answers out quicker and that she’s answering accurately, and she’s getting more reciprocation from peers... People around her are able to communicate with her more effectively.”

“Better at following directions and listening to what someone tells her, better with "receptive" language.”

# Successful DAYBUE Launch



- Current demand tracking to typical rare disease launch trajectory
- Early surge in demand from centers of excellence



~5,000 diagnosed Rett syndrome patients

- >800 patients on DAYBUE, as of end of 3Q23



Expect **\$170 to \$177.5 million** in FY 2023 product sales (first 8½ months of launch)<sup>1</sup>

## Continuing to expand breadth and depth in Rett community leveraging:

- Real world benefits
- Physician experience
- Caregiver familiarity
- Established broad payor access

<sup>1</sup>Based on guidance range provided on November 2, 2023 combined with YTD actual results through September 30, 2023.

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# DAYBUE Performance Metrics



## 6-month real world persistency vs. clinical trial experience

**76%**

Based on confirmed discontinuations only

**68%**

Based on confirmed discontinuations and patients who were 60 days past their scheduled refill

**58%**

LILAC-1 persistency at month 6

**Compliance to dose estimated 75-80%**

**Formal payor policies in place for ~80% of Rett covered lives**

# Worldwide DAYBUE Opportunity



Expanding globally beginning in 2024

## CANADA

- NDS filing 1Q24
- Potential approval around YE24

### *Prevalence*

- Estimated 600 to 900 patients

## EUROPE

- Engaging with EMA in 1Q24
- MAA filing in 1H25

### *Prevalence*

- Estimated 9,000 to 14,000 patients (Europe and UK)

## JAPAN

- Engaging Japanese regulatory agency (PMDA) in 2024

### *Prevalence*

- Estimated 1,000 to 2,000 patients

NDS: New Drug Submission; EMA: European Medical Authority; MAA: Marketing Authorization Application; PMDA: Pharmaceuticals and Medical Devices Agency

Prevalence numbers estimated by Acadia based on information available.

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# NUPLAZID<sup>®</sup> Provides Strong Foundation



# NUPLAZID Strategy: Optimize Cash Flow

Real world evidence has grown new patient starts and net sales



Reduced NUPLAZID SG&A spend by >\$100M on an annualized basis ('21 vs. '23)

Franchise generates >\$300 million in annual cash flow





# Positioning Acadia for Further Growth



# Deep CNS Pipeline

Program	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Marketed	
<b>NUPLAZID® (pimavanserin)</b>	Parkinson's Disease Psychosis	[Progress bar spanning Preclinical, Phase 1, Phase 2, and Phase 3]					
<b>DAYBUE™ (trofinetide)</b>	Rett Syndrome	[Progress bar spanning Preclinical, Phase 1, Phase 2, and Phase 3]					
<b>Pimavanserin<sup>1</sup></b>	Negative Symptoms of Schizophrenia	[Progress bar spanning Preclinical, Phase 1, and Phase 2]					
<b>ACP-101<sup>2,3</sup></b>	Hyperphagia in Prader-Willi Syndrome	[Progress bar spanning Preclinical, Phase 1, and Phase 2]					
<b>ACP-204<sup>3</sup></b>	Alzheimer's Disease Psychosis	[Progress bar spanning Preclinical and Phase 1]					
<b>ACP-2591<sup>3</sup></b>	Rett Syndrome; Fragile X Syndrome	[Progress bar spanning Preclinical and Phase 1]					
<b>ASO Programs<sup>3</sup></b>	SYNGAP1; Rett; Undisclosed	[Progress bar in Preclinical]					
<b>Multiple Undisclosed Programs</b>	Neuropsychiatric and Rare Disorders	[Progress bar in Preclinical]					

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<sup>1</sup> Safety and efficacy of pimavanserin for the treatment of negative symptoms of schizophrenia have not been established or approved by the FDA. <sup>2</sup> Acadia acquired Levo Therapeutics and its rights/licenses to ACP-101.

<sup>3</sup> The safety and efficacy of these investigational agents have not been established. There is no guarantee these investigational agents will be filed with or approved by any regulatory agency.

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# Negative Symptoms of Schizophrenia

# Negative Symptoms of Schizophrenia



No FDA-approved treatment



>700,000 patients in the U.S. have persistent negative symptoms<sup>1</sup>

**Chronic, persistent negative symptoms include social withdrawal, restricted speech, lack of emotion, loss of motivation, and blunted affect and can lead to:**

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



<sup>1</sup>Studies suggest that ~40-50% of schizophrenia patients experience predominant negative symptoms; Patel et al. 2015, Haro et al., 2015, Bobes et al. 2010, and Chue and Lalonde, 2014. Provided January 9, 2024 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



# Addressing Unmet Need in Predominant, Chronic Negative Symptoms of Schizophrenia



**Topline results  
from ADVANCE-2  
Phase 3 study of  
pimavanserin  
expected 1Q24**



- ✓ Completed one positive pivotal study, ADVANCE-1
- ✓ ADVANCE-2 leverages optimal therapeutic dose of 34 mg
- ✓ 6-month study designed to evaluate impact on persistent negative symptoms beyond acute psychosis period
- ✓ Designed to treat patients whose positive psychotic symptoms are adequately controlled, but still suffer from predominant and uncontrolled negative symptoms, inhibiting their ability to live a normal, productive life



**ACP-101 for  
the Treatment  
of Prader-Willi  
Syndrome  
(PWS)**



# Prader-Willi Syndrome Opportunity



## Significant Unmet Need

- ✓ ~8,000-10,000 patients in the U.S.
- ✓ No FDA approved medicine to treat hyperphagia in PWS

- Rare and complex neurobehavioral genetic disorder that often leads to social isolation
- Hyperphagia is a defining characteristic of PWS and commonly begins between the ages of 3-8
- Hyperphagia is characterized by unrelenting hunger
  - Often leads to obesity and behavioral challenges including anxiety and aggression
  - Extremely distressing for patients, parents and caregivers
- 30 years average life expectancy<sup>1</sup>

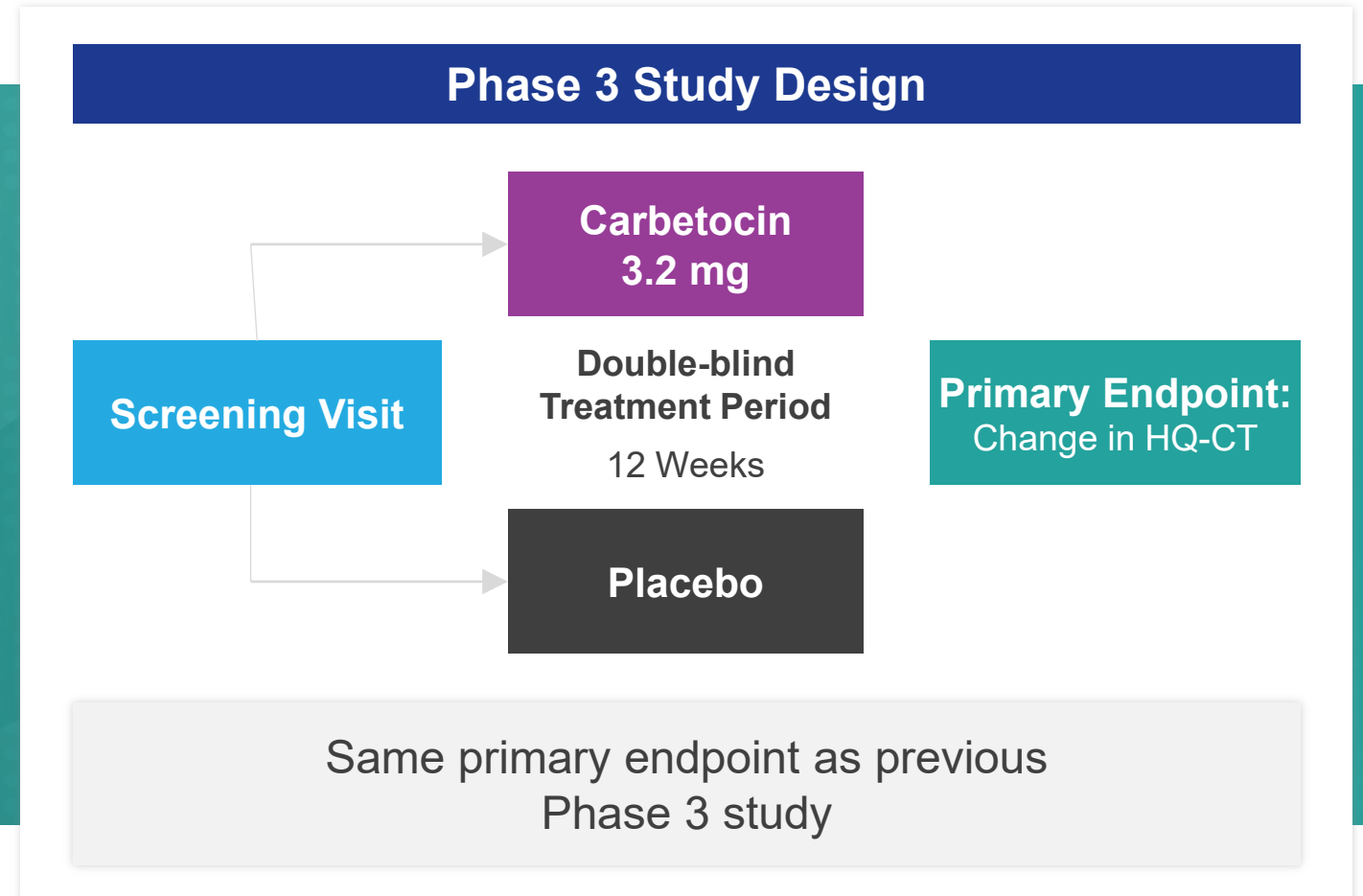
<sup>1</sup>Causes of Death in Prader-Willi Syndrome: Prader-Willi Syndrome Association (USA) 40-Year Mortality Survey. Genet Med. 2017 June ; 19(6): 635–642. Provided January 9, 2024 as part of an oral presentation and is qualified by such; contains forward-looking statements; actual results may vary materially; Acadia disclaims any duty to update.

# Initiated Phase 3 Study of ACP-101 for the Treatment of Hyperphagia in PWS



**Trial builds on previous Phase 3 clinical trial experience**

3.2 mg dose was observed to significantly reduce hyperphagia-related behaviors







**ACP-204 for  
the Treatment  
of Alzheimer's  
Disease  
Psychosis  
(ADP)**

# ACP-204 in ADP

ACP-204 is a next generation 5HT<sub>2A</sub> blocker that builds on the learnings of pimavanserin



## Target Product Profile

Mitigate or eliminate QT prolongation

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Explore doses higher than pimavanserin 34 mg equivalent

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Improved time to onset of action

## Phase 1 Results

- ✓ No sign of QT prolongation
- ✓ Wide dose range established supporting potential for ~2x pimavanserin 34 mg equivalent
- ✓ Steady state PK achieved in less than half the time of pimavanserin

# Phase 2 / Phase 3 Program for the Treatment of ADP

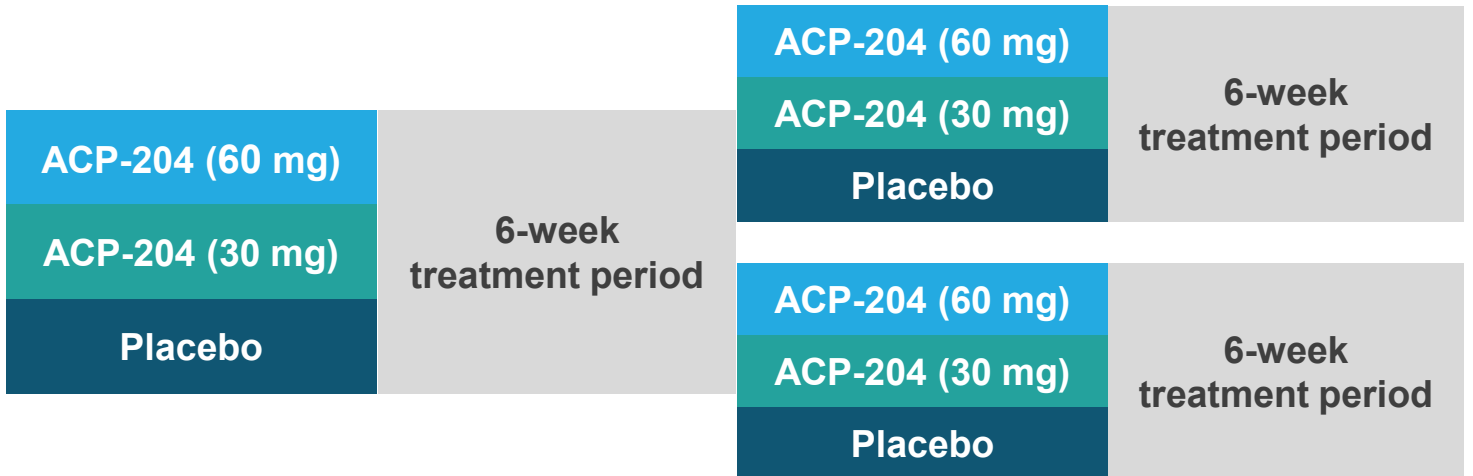


Our experience with pimavanserin supports seamless P2 / P3 program

**Phase 2**  
N=318, double-blind,  
randomized 1:1:1

**Two Phase 3 Studies**  
Each study sized ~equivalent to  
Phase 2 double-blind,  
randomized 1:1:1

Seamless Enrollment





# Building On Our Success



## 2023 Recap

- Launched second commercial drug, DAYBUE
- 38% revenue growth from two commercial franchises, DAYBUE and NUPLAZID<sup>1</sup>
- Completed enrollment in ADVANCE-2
- Acquired worldwide rights to trofinetide
- Initiated Phase 3 trial of ACP-101
- Initiated seamless Phase 2 / Phase 3 of ACP-204
- Reached cash flow positivity<sup>2</sup>

## 2024 and Beyond

- Capitalize on successful DAYBUE launch
- Strong revenue streams from DAYBUE and NUPLAZID franchises
- Topline results from ADVANCE-2 in 1Q24
- Global expansion of trofinetide into Canada, Europe and Japan
- Potential new therapy for Prader-Willi syndrome
- Potential new therapy for Alzheimer's disease psychosis
- Sustainable and growing cash flow from operations

<sup>1</sup>Based on mid-point of guidance ranges for 4Q23 sales of DAYBUE and FY23 sales of NUPLAZID provided on November 2, 2023. <sup>2</sup> Excluding one-time payment of \$100 million to Neuren to secure worldwide rights to trofinetide. 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. DAYBUE (trofinetide) is only approved in the U.S. by the FDA for the treatment of Rett syndrome in adults and pediatric patients two years of age and older. Provided January 9, 2024 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.