ACADIA

Second Quarter 2022 Earnings Call

August 8, 2022

2Q22 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
Commercial Update	**Brendan Teehan** | Chief Operating Officer, Head of Commercial
Trofinetide Update	**Kathie M. Bishop, Ph.D.** | Chief Scientific Officer and Head of Rare Disease
R&D Update	**Serge Stankovic, M.D., M.S.P.H** | President
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 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, 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 2022 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.

CEO Opening Remarks

Steve Davis

CEO

Acadia's Growth Strategy

Grow and Maximize Value of NUPLAZID® Franchise

Deliver Trofinetide to Rett Community

Develop the Next Wave of Breakthroughs

Building a Leading CNS Company

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 August 8, 2022 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.

Drive Growth of NUPLAZID® in PDP

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Net Sales

Delivered net sales of $134.6M in 2Q22, increase of 17% YoY

- NUPLAZID continues to outperform in the neurology and PD markets and in LTC facilities

PD Market Recovery Slow

PD market dynamics remained constrained vs. pre-pandemic levels:

- PD patient visits are down double-digits (~15%)[1]
- LTC occupancy rates are down double-digits (~11-12%)[2]
- Staffing levels are down double-digits (~11-12%)[1]

Looking Ahead

- Optimizing efficient commercial spend to grow cash flow
- Composition of Matter patent with pediatric exclusivity out to 4Q, 2030[1]
  - *Additional method of use and formulation patents that protect currently marketed tablets and capsules of NUPLAZID out to 2037 and 2038 respectively*

[1]Acadia internal numbers and IQVIA raw data as of end of April 2022. [2]CMS Data Source: https://www.nic.org/snf-covid-tracker. Monthly 2021 census figures reflect occupancy level at the end of each month.
[3]Composition of matter in the Orange book includes patent term extension and expires 4/29/2030. Anticipated pediatric exclusivity would extend out expiry an additional 6 months.
PD = Parkinson's disease; **PDP** = Parkinson's disease psychosis; **LTC** = Long-term care.
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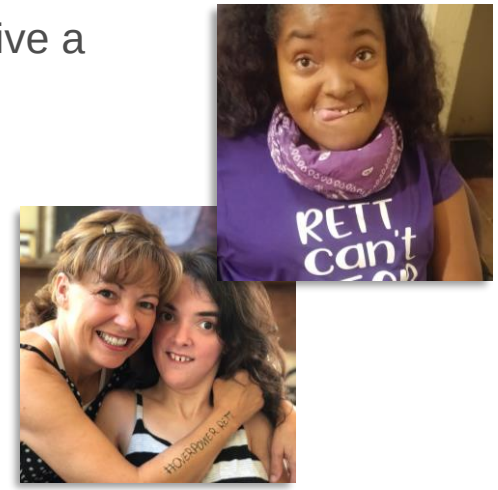
Advancing Late-Stage Opportunities

Rett syndrome
NDA Submitted (Trofinetide)

- NDA submitted in July 2022
- Expect priority review; action date in 1Q23
- Fast Track Status, Orphan Drug Designation and Rare Pediatric Disease designation
  - If approved, should receive a rare pediatric disease priority review voucher
- Method of use patent with patent term extension provides exclusivity out to early 2036; *Additional patents pending*



Negative Symptoms of Schizophrenia
Phase 3 Program (Pimavanserin)

- Positive pivotal study, ADVANCE-1
- Evaluating 34 mg dose of pimavanserin in second pivotal study, ADVANCE-2
- Completion of enrollment of ADVANCE-2 expected mid-year 2023 due to Ukraine/Russia impact

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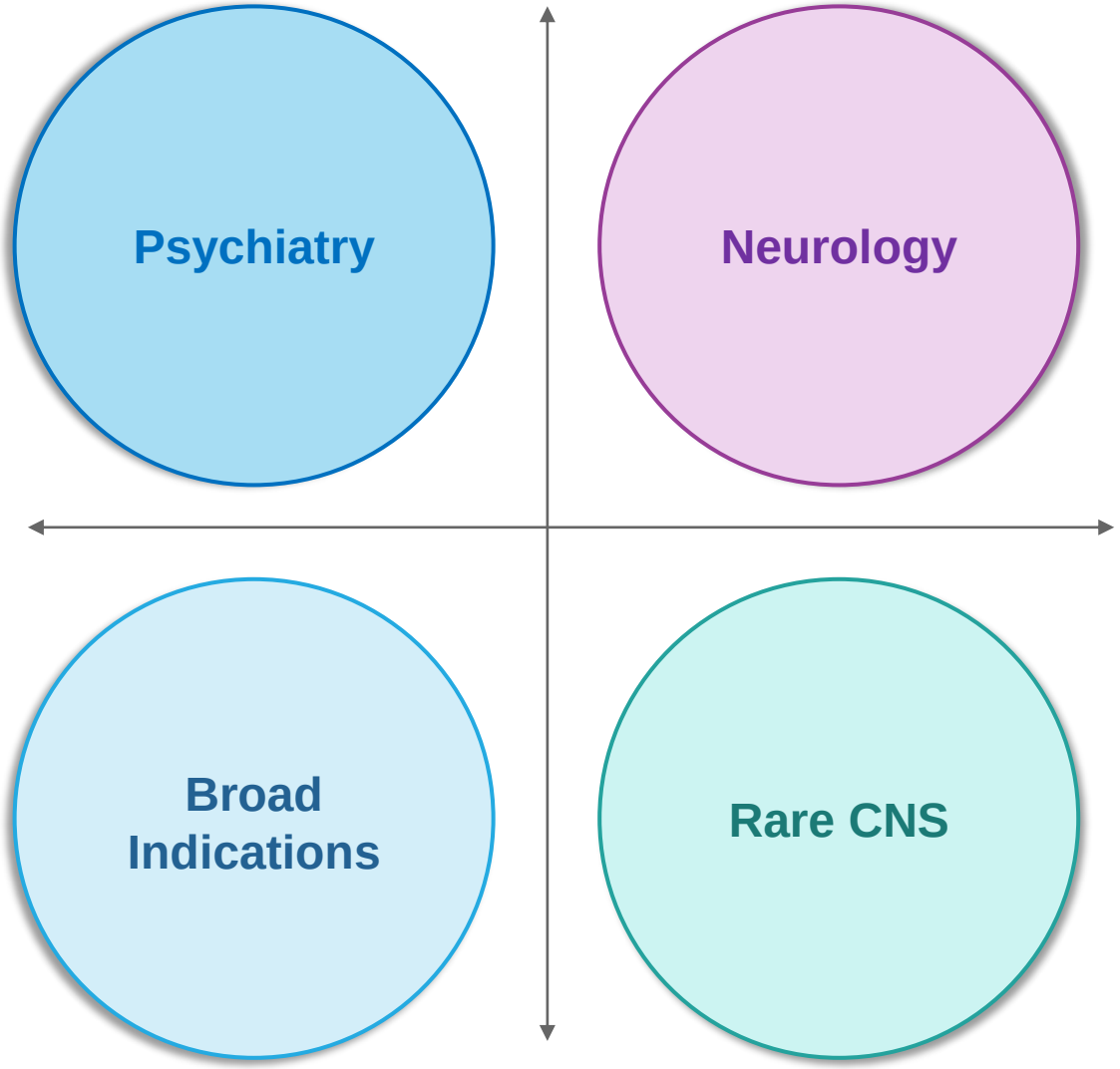
Evolution of CNS Portfolio

Continual Optimization of R&D Portfolio

- **Investing** in a new molecule ACP-204
  - ACP-204 builds upon learnings of pimavanserin; currently in Phase 1 development
- **Discontinuing** ACP-044 and ACP-319 candidates

Investing in Future Growth Opportunities

- **Established infrastructure** of commercial and R&D operations in all four quadrants
- **Evolving BD landscape** favors companies with established infrastructure, growing revenues and strong cash reserves
- **Build upon trofinetide success,** investing in "Neurology" and "Rare" quadrants, including Stoke collaboration



Finance Update

Mark Schneyer

Chief Financial Officer

Optimizing Business for Long-term Growth

1. **Focused investments in PDP commercial to efficiently grow the brand**
2. **Optimized SG&A spend enables successful launch of trofinetide without increasing SG&A expense next year**
3. **Prioritization of R&D portfolio**

Continual optimization of our business enables us to generate sustainable growth with existing cash resources

Current business can turn cash flow positive without a need for additional financing

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2Q22 Financial Highlights

Millions, Except EPS	2Q22 (GAAP)	2Q21 (GAAP)	YoY Change
Total Revenue	$134.6	$115.2	+17%
R&D	$75.6	$56.9	+33%
SG&A	$89.9	$96.8	-7%
Net Loss	$34.0	$43.9	
EPS	($0.21)	($0.27)	
Cash Balance[1]	$436.4		

[1]Cash balance includes cash, cash equivalents and investments as of 6/30/2022.
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FY22 Financial Guidance

	Previous FY22 Guidance *(5/4/2022)*	Updated FY22 Guidance *(8/8/2022)*	Commentary
NUPLAZID® Net Sales	$510 to $560M	$510 to $540M	• Top end of net sales removed as significant PD market recovery not yet seen
GAAP R&D Expense	$355 to $375M	$340 to $360M	• R&D program spend trending lower • ~$25M of stock-based compensation
GAAP SG&A Expense	$360 to $380M	$360 to $380M	• Unchanged • ~$45M of stock-based compensation
YE Cash Balance[1]	$355 to $405M	$375 to $405M	• Strong cash balance • Raised lower end of range

[1]YE cash balance guidance range based on revenue guidance range and assumes midpoint of expense guidance ranges.
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Commercial Update

Brendan Teehan

Chief Operating Officer, Head of Commercial

NUPLAZID® Growth and PD Market Dynamics

Net Sales & Volume Growth

Delivered net sales of $134.6M, increase of 17% YoY

- Demand volume up 1H22 vs. 1H21

NUPLAZID continued to gain market share during pandemic

- Market share increased ~15% since 2019

NUPLAZID Outperformance[1]

Office-based Channel

2Q22 over 2Q19 TRx Monthly Average[1]

NUPLAZID	**+26%**
Carbidopa/Levodopa	-5%
Avg. Top 10 PD Meds	-11%
Avg. Top 15 Neuro Brands	+9%

Long-term Care Channel

2Q22 over 2Q19 TRx Monthly Average[1]

NUPLAZID	**+6%**
Carbidopa/Levodopa	-10%
Avg. Top 15 LTC Brands	-13%

Growing Body of Evidence for PDP

Real-world data from additional studies adds to growing body of evidence of safety of pimavanserin in the treatment of Parkinson's disease psychosis

[1]IQVIA National Prescription Audit (monthly NPA).
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Trofinetide Pre-Launch Activities Ongoing

Developing the Market with Rett Caregivers & Patients at the Center

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Rett Syndrome Stakeholders and Objectives

Patients/Caregivers

Build awareness of Acadia and treatment expectations for trofinetide experience.

HCPs

Increase disease education and community resources.

Payors

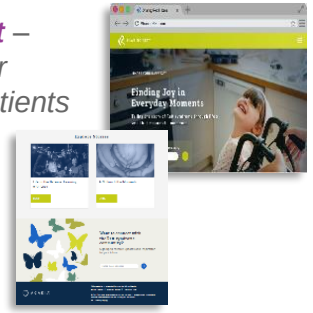
Educate payor ecosystem on Rett syndrome and trofinetide's clinical profile.

Market Development:

Engage the Community & Build Patient Support Services

Support Services & Engagement **–**

- *Building database of hand raiser caregivers of diagnosed Rett patients*



International Rett Syndrome Foundation
www.rettsyndrome.org

Partnering with KOLs and Advocacy groups to best understand care team needs and perspectives; and enhance communication with the Rett community

Increase Disease Education and Establish Trofinetide's Clinical Impact

KOL Engagement **–**

- *Disease state education; establish the unmet need, including clinical meaningfulness of trofinetide clinical data and GI management*

AAN 2022 Annual Meeting

ASCEND 2022

Launch Objective: Establish trofinetide as foundational treatment, ensuring quick access and superior product experience for rapid adoption and long-term treatment

Trofinetide Update

Kathie Bishop

CSO and Head of Rare Disease

Rett Syndrome

High Unmet Need

No FDA-approved drug for the treatment of Rett syndrome

Estimated 6,000 to 9,000 patients in the U.S.[1]

Debilitating Symptoms[2]:

- Fine and gross motor impairment
- Loss of verbal and nonverbal communication
- Hand stereotypies
- Seizures
- Gastrointestinal 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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Trofinetide for the Treatment of Rett Syndrome:
Positive Phase 3 Lavender Study Results

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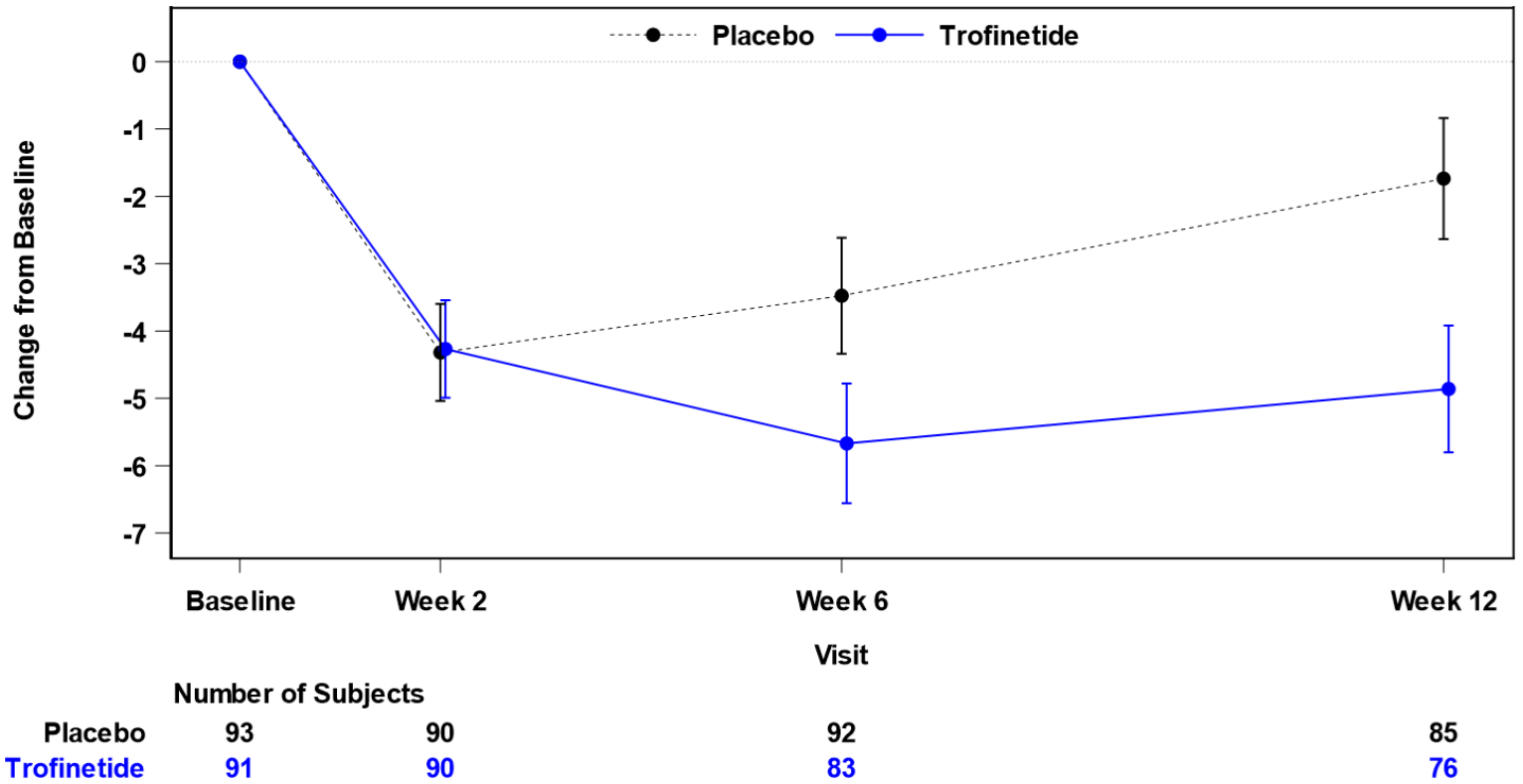
RSBQ Change from Baseline by Visit



Number of Subjects				
Placebo	93	90	92	85
Trofinetide	91	90	83	76

Co-Primary Endpoints:

RSBQ
(Change from baseline to week 12)

Two-sided p-value = 0.0175

Effect Size; Cohen's d = 0.37

CGI-I
(Score at week 12)

Two-sided p-value = 0.0030

Effect Size; Cohen's d = 0.47

Key Secondary Endpoint:

CSBS-DP-IT Social Composite Score
(Change from baseline to week 12)

Two-sided p-value = 0.0064

Effect Size; Cohen's d = 0.43

RSBQ = Rett Syndrome Behaviour Questionnaire (caregiver assessment); **CGI-I** = Clinical Global Impression Scale-Improvement (physician assessment); **CSBS-DP-IT-Social** = Communication and Symbolic Behavior Scales. Developmental Profile™ Infant-Toddler Checklist–Social composite score.

R&D Update

Serge Stankovic

President

Develop the Next Wave of Breakthroughs

ACADIA

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

[1]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.
[2]Acadia has an exclusive license to develop and commercialize trofinetide in North America from Neuren Pharmaceuticals.
[3]Acadia 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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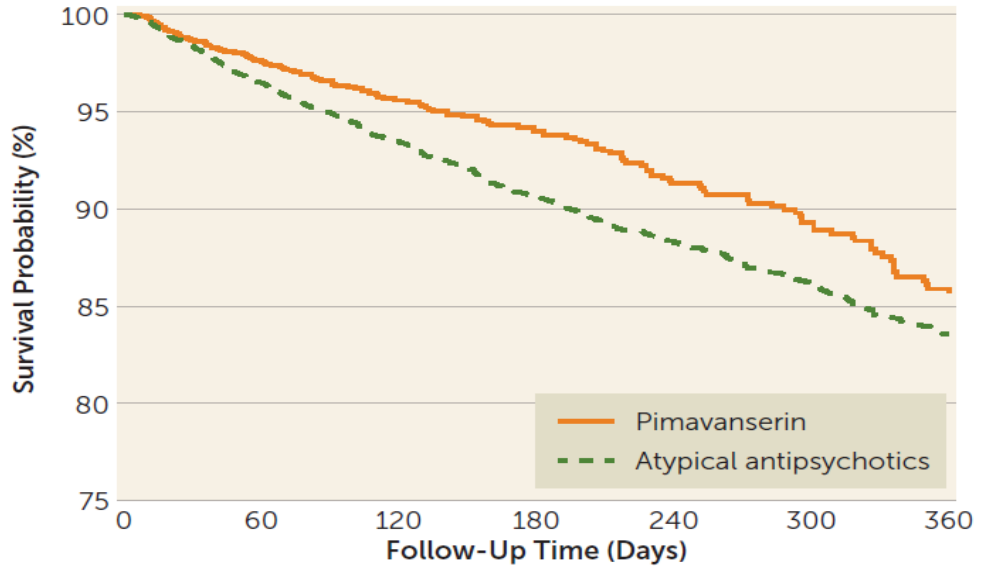
Growing Body of Evidence of Pimavanserin Compared to Multi-receptor Antipsychotics

Published in *Journal of Psychiatry:* June 2022[1]

FIGURE 1. Kaplan-Meier plot of weighted cumulative survival probability among patients with Parkinson's disease treated with pimavanserin or atypical antipsychotics

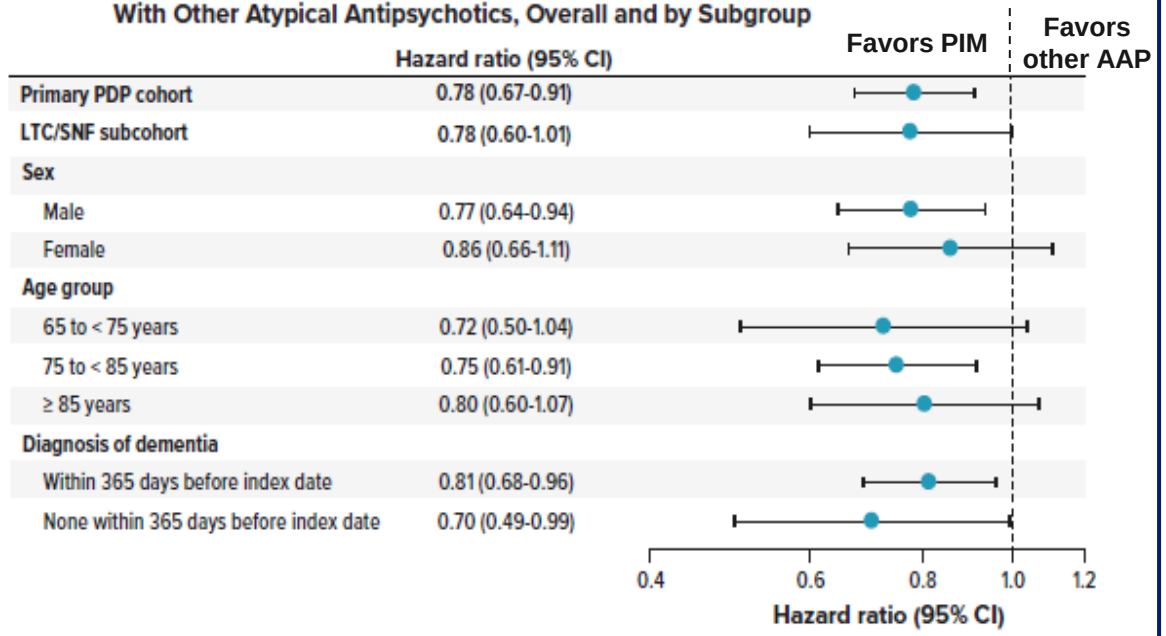


Pimavanserin associated with lower mortality than other atypical antipsychotics during the first 180 days of use, while the risk was similar thereafter.

Retrospective new-user cohort study of Medicare beneficiaries with Parkinson's disease initiating pimavanserin (N=3,227) or atypical antipsychotics (N=18,442) for psychosis treatment from April 2016 to March 2019.

Presented *at ASCP Conference* in June 2022[2]

Figure 1. Matched Hazard Ratios for Mortality in Patients With Parkinson's Disease Psychosis Who Initiated Treatment With Pimavanserin Compared With Those Initiating Treatment With Other Atypical Antipsychotics, Overall and by Subgroup



The largest differences in mortality risk between treatment groups were observed in the first 180 days of follow-up.

Retrospective new-user cohort study of Medicare beneficiaries with PDP initiating pimavanserin (N=2,892) or atypical antipsychotics (N=19,083) from April 2016 to December 2019.

[1,2]Definitive conclusions of differences in mortality between pimavanserin and other atypical antipsychotics or direct causation of mortality cannot be inferred due to limitations of observational studies. LTC = Long-term Care Facility; SNF = Skilled Nursing Facility.

[1]Mosholder AD et al., Mortality Among Parkinson's Disease Patients Treated With Pimavanserin or Atypical Antipsychotics: An Observational Study in Medicare Beneficiaries. Am J Psychiatry. 2022 Aug;179(8):553-561.
[2]Layton et al., Mortality Associated With Pimavanserin Compared With Atypical Antipsychotics in Patients With Parkinson's Disease–Related Psychosis: RTI Health Solutions. 2022 May.

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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

Potential U.S. addressable population:
>1M patients diagnosed[1]

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

[1]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.
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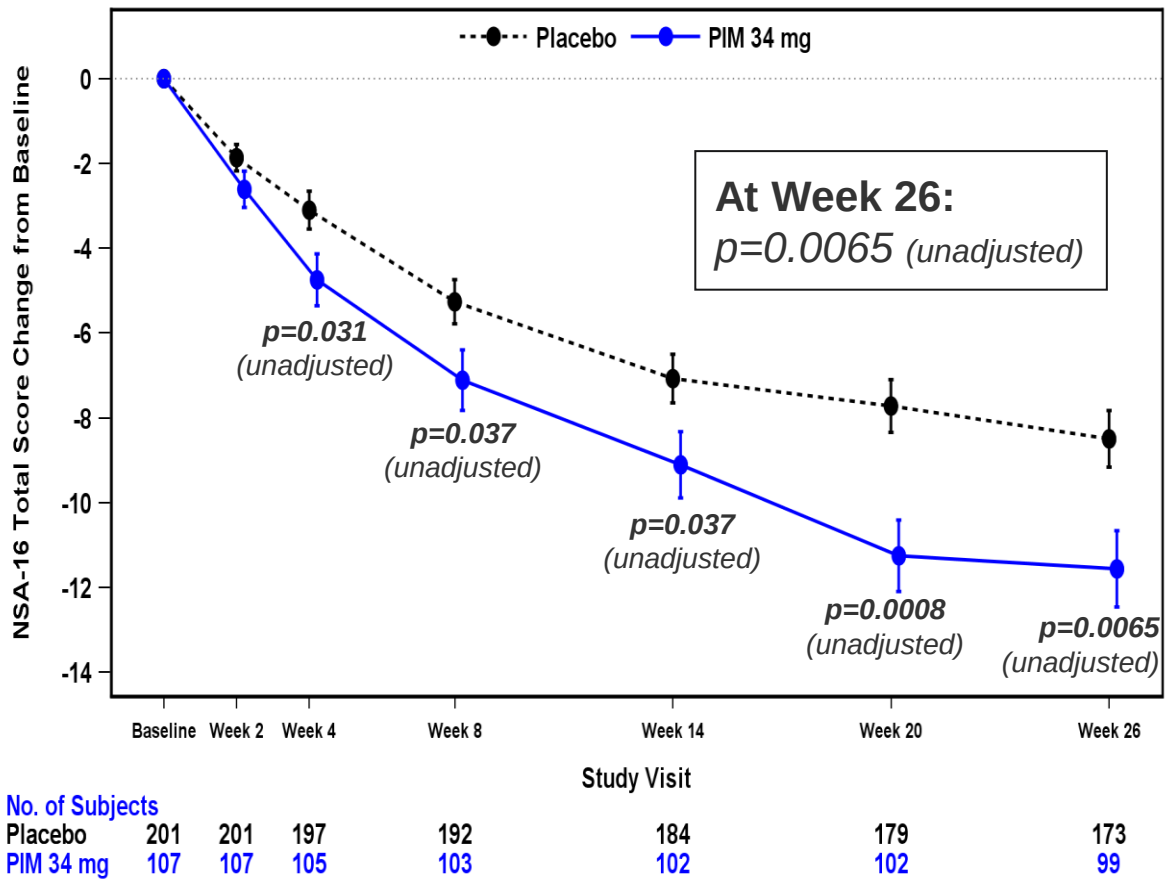
Positive Pivotal Study, ADVANCE-1; Optimal Dose 34mg

34 MG DOSE[1,2]



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.

[1]Pimavanserin 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
[2]Prespecified 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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CEO Closing Remarks

Steve Davis

CEO

Building a Leading CNS Company

Advance Late-Stage and Early-Stage Pipeline

Execute Business Development

Launch Potential 2nd Commercial Product

Trofinetide for Rett Syndrome

Drive NUPLAZID® Growth in PDP

$510 - $540M

FY22 Net Sales Guidance

Key Strengths:

- Established infrastructure, commercial teams, clinical development
- Committed to investing in high-value CNS opportunities
- Optimized spend with focus on positive cash flow
- Strong balance sheet allowing execution without need for additional capital

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Q&A Session