Fourth Quarter and Full Year 2022 Earnings Call

February 27, 2023
# 4Q and Full Year 2022 Earnings Call Agenda

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<th>Mark Johnson</th>
<th>Vice President, Investor Relations</th>
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<td>Steve Davis</td>
<td>Chief Executive Officer</td>
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<td>Mark Schneyer</td>
<td>Chief Financial Officer</td>
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<td>NUPLAZID Update</td>
<td>Brendan Teehan</td>
<td>Chief Operating Officer, Head of Commercial</td>
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<td>Trofinetide Update</td>
<td>Kathie Bishop Ph.D.</td>
<td>Chief Scientific Officer, Head of Rare Disease and External Innovation</td>
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<td></td>
<td>Brendan Teehan</td>
<td>Chief Operating Officer, Head of Commercial</td>
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<td>R&amp;D Update</td>
<td>Doug Williamson M.D.</td>
<td>Head of Research and Development</td>
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<td>CEO Closing Remarks</td>
<td>Steve Davis</td>
<td>Chief Executive Officer</td>
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</table>

**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
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.

Four Strategic Priorities for Acadia

NUPLAZID for Parkinson’s Disease Psychosis
- $517.2M net sales in FY22
- Cash flow positive since 2019

Trofinetide for Rett Syndrome
- PDUFA Date: 3/12/2023
- Potential first FDA-approved drug specifically for Rett

Negative Symptoms of Schizophrenia
- Positive pivotal results: ADVANCE-1
- ADVANCE-2 ongoing, TLR expected early 2024

Alzheimer’s Disease Psychosis
- ACP-204 Phase 1 program ongoing
- Plan to initiate Phase 2 in ADP patients in 2023

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

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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

Net Sales (in millions)

<table>
<thead>
<tr>
<th>Year</th>
<th>Net Sales (in millions)</th>
</tr>
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<tbody>
<tr>
<td>2016</td>
<td>$100</td>
</tr>
<tr>
<td>2017</td>
<td>$100</td>
</tr>
<tr>
<td>2018</td>
<td>$200</td>
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<tr>
<td>2019</td>
<td>$300</td>
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<tr>
<td>2020</td>
<td>$400</td>
</tr>
<tr>
<td>2021</td>
<td>$500</td>
</tr>
<tr>
<td>2022</td>
<td>$550</td>
</tr>
</tbody>
</table>

PDP = Parkinson's disease psychosis; RWE = Real-world evidence; HCP = Healthcare provider; LTC = Long-term care
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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

RSBQ = Rett Syndrome Behavioural Questionnaire (caregiver assessment); CGI-I = Clinical Global Impression Scale-Improvement (physician assessment)
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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
# 4Q22 and FY22 Financial Highlights

<table>
<thead>
<tr>
<th>Millions, Except EPS</th>
<th>4Q22 (GAAP)</th>
<th>4Q21 (GAAP)</th>
<th>YoY Change</th>
<th>FY22 (GAAP)</th>
<th>FY21 (GAAP)</th>
<th>YoY Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Revenue</td>
<td>$136.5</td>
<td>$130.8</td>
<td>4%</td>
<td>$517.2</td>
<td>$484.1</td>
<td>7%</td>
</tr>
<tr>
<td>R&amp;D</td>
<td>$75.7</td>
<td>$67.1</td>
<td>13%</td>
<td>$361.6¹</td>
<td>$239.4</td>
<td>51%</td>
</tr>
<tr>
<td>SG&amp;A</td>
<td>$104.4</td>
<td>$105.8</td>
<td>-1%</td>
<td>$369.1</td>
<td>$396.0</td>
<td>-7%</td>
</tr>
<tr>
<td>Net Income (Loss)</td>
<td>($41.7)</td>
<td>($43.1)</td>
<td></td>
<td>($216.0)</td>
<td>($167.9)</td>
<td></td>
</tr>
<tr>
<td>EPS</td>
<td>($0.26)</td>
<td>($0.27)</td>
<td></td>
<td>($1.34)</td>
<td>($1.05)</td>
<td></td>
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<tr>
<td>Cash Balance</td>
<td>$416.8</td>
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</table>

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

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## FY23 Financial Guidance

<table>
<thead>
<tr>
<th>FY23 Guidance</th>
<th>Commentary</th>
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<tbody>
<tr>
<td>NUPLAZID® Net Sales</td>
<td>• Midpoint of the range reflects ~1% growth volume YoY and includes ~2.5% net price growth YoY</td>
</tr>
<tr>
<td></td>
<td>• Parkinson’s disease psychosis (PDP) guidance only</td>
</tr>
<tr>
<td></td>
<td>• No sales guidance for Trofinetide</td>
</tr>
<tr>
<td>Gross-to-Net</td>
<td>• Increased due to IRA inflation cap rebate accruals</td>
</tr>
<tr>
<td></td>
<td>• Incorporates various scenarios including inflation rates and changes in 340b volumes</td>
</tr>
<tr>
<td>GAAP R&amp;D Expense</td>
<td>• ~$20M of stock-based compensation expense</td>
</tr>
<tr>
<td>GAAP SG&amp;A Expense</td>
<td>• Reflects continued optimization of PDP commercial spend</td>
</tr>
<tr>
<td></td>
<td>• Supports investment in trofinetide launch</td>
</tr>
<tr>
<td></td>
<td>• ~$45M of stock-based compensation expense</td>
</tr>
</tbody>
</table>

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NUPLAZID® for the Treatment of PDP
New Real-World Evidence

Safety Publications: Retrospective Analyses\textsuperscript{1,2}:

\textbf{Moshholder et al. Publication (PD Patients)}

Overall analysis 360 days: \textit{23\% lower} mortality risk
- Hazard Ratio = 0.77; 95\% CI 0.66-0.90

Interval analysis 1-180 days: \textit{35\% lower} mortality risk
- Hazard Ratio = 0.65; 95\% CI 0.53-0.79

Interval analysis 181+ days:
- No additional mortality advantage observed

\textbf{Layton et al. Publication (PDP Patients)}

Overall cumulative mortality: \textit{22\% lower} mortality risk
- Hazard Ratio = 0.78; 95\% CI 0.67-0.91

The first 180 days of treatment: \textit{34\% lower} mortality risk
- Hazard Ratio = 0.66; 95\% CI 0.54-0.82

Cumulative mortality at 1 year: \textit{23\% lower} mortality risk
- Hazard Ratio = 0.77; 95\% CI 0.64-0.91

Healthcare Utilization Presentation\textsuperscript{3}:

\textbf{Kumar et al. Publication (PDP Patients)}

Patients treated with NUPLAZID had:
- \textit{Lower} all-cause hospitalizations, ER visits, and shorter length of stays vs. atypical antipsychotics

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\textsuperscript{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
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.rettsyndrome.org/about-rett-syndrome/what-is-rett-syndrome/. 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.
Phase 3 Lavender Study Design

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

187 young females (5–20 years) with Rett Syndrome

Pre-treatment baseline

Double-Blind Treatment Period (12 weeks)

Trofinetide*

Placebo

End of Treatment

Co-primary efficacy endpoints
1. RSBQ
2. CGI-I

Key secondary efficacy endpoint
1. CSBS-DP-IT

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

RSBQ = Rett Syndrome Behavioural 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

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Positive Phase 3 Lavender Study Results

Rett Syndrome Behavioural Questionnaire (RSBQ)

<table>
<thead>
<tr>
<th>Change from Baseline</th>
<th>Placebo</th>
<th>Trofinetide*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>-1.7</td>
<td>-5.1</td>
</tr>
<tr>
<td>p-value</td>
<td>0.0175</td>
<td></td>
</tr>
<tr>
<td>Effect size</td>
<td>0.37</td>
<td></td>
</tr>
</tbody>
</table>

Clinical Global Impression – Improvement (CGI-I)

<table>
<thead>
<tr>
<th>Week 12 Score</th>
<th>Placebo</th>
<th>Trofinetide*</th>
</tr>
</thead>
<tbody>
<tr>
<td>CGI-I</td>
<td>3.8</td>
<td>3.5</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td>0.0030</td>
</tr>
<tr>
<td>Effect size</td>
<td></td>
<td>0.47</td>
</tr>
</tbody>
</table>

*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

154 young females from Lavender Study

Open-Label Treatment Period (40 weeks)

- Pre-treatment baseline
- Trofinetide*
- End of Treatment

Primary objective to assess safety
Also includes the same efficacy endpoints as Lavender (e.g. RSBQ and CGI-I)

Patients may continue to receive treatment in Lilac-2

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Lilac Top-Line Results: Efficacy Assessments

RSBQ

<table>
<thead>
<tr>
<th>Baseline</th>
<th>LAVENDER (12 weeks)</th>
<th>Placebo-controlled</th>
<th>LILAC (40 weeks)</th>
<th>Open-label extension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose Group</td>
<td>RSBQ mean change (12 wks)</td>
<td>Dose Group</td>
<td>RSBQ mean change from Lavender baseline to end of Lilac (52 wks)</td>
<td></td>
</tr>
<tr>
<td>Trofinetide</td>
<td>-5.1</td>
<td>Trofinetide</td>
<td>-7.3</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>-1.7</td>
<td>Placebo</td>
<td>n/a</td>
<td></td>
</tr>
</tbody>
</table>

Lilac change score calculated from Lavender baseline

- Observed sustained and continued improvement in RSBQ over 52 weeks

RSBQ scores improved ≥7 points from Lavender baseline

RSBQ: n=161 for Lavender at 12 weeks; n=88 for Lilac at 40 weeks.
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### Lilac Top-Line Results: Efficacy Assessments

**CGI-I**

**LAVENDER**
(12 weeks)
Placebo-controlled

<table>
<thead>
<tr>
<th>Dose Group</th>
<th>CGI-I score (at 12 wks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trofinetide</td>
<td>3.5</td>
</tr>
<tr>
<td>Placebo</td>
<td>3.8</td>
</tr>
</tbody>
</table>

**LILAC**
(40 weeks)
Open-label extension

<table>
<thead>
<tr>
<th>Dose Group</th>
<th>CGI-I score (at 40 wks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trofinetide</td>
<td>3.1</td>
</tr>
<tr>
<td>Trofinetide</td>
<td>3.2</td>
</tr>
<tr>
<td>Placebo</td>
<td>n/a</td>
</tr>
</tbody>
</table>

**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

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

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# Addressing Significant Unmet Needs in CNS

<table>
<thead>
<tr>
<th>Program</th>
<th>Indication</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Registration</th>
<th>Marketed</th>
</tr>
</thead>
<tbody>
<tr>
<td>NUPLAZID®</td>
<td>Parkinson’s Disease Psychosis</td>
<td></td>
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<tr>
<td>(pimavanserin)¹</td>
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</tr>
<tr>
<td>Trofinetide²</td>
<td>Rett Syndrome</td>
<td></td>
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<tr>
<td>Pimavanserin</td>
<td>Negative Symptoms of Schizophrenia</td>
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<tr>
<td>ACP-204</td>
<td>Alzheimer’s Disease Psychosis</td>
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<tr>
<td>ASO Programs³</td>
<td>SYNGAP1; Rett Syndrome; Undisclosed</td>
<td></td>
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<tr>
<td>Other Programs</td>
<td>Neuropsychiatric Symptoms</td>
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</table>

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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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

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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Clinical Development Program for the Negative Symptoms of Schizophrenia

34 MG Dose\textsuperscript{1,2}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{34_mg_graph.png}
\caption{At Week 26: \( p=0.0065 \) (unadjusted)}
\end{figure}

ADVANCE-1 Results

<table>
<thead>
<tr>
<th>Primary Endpoint (Overall – all 3 doses tested)</th>
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<tbody>
<tr>
<td>Improvement in NSA-16 vs. placebo at 26 weeks</td>
</tr>
<tr>
<td>Two-sided p-value = ( p=0.043 )</td>
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<table>
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<tr>
<th>Patients on 34 mg vs. placebo</th>
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<tbody>
<tr>
<td>Two-sided p-value = 0.0065 (unadjusted)</td>
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</tbody>
</table>

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

\textsuperscript{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

\textsuperscript{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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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

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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

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.
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Q&A Session