ACADIA

First Quarter 2022 Earnings Call

May 4, 2022

1Q22 Earnings Call Agenda

Introduction	**Mark Johnson** | Vice President, Investor Relations
CEO Opening Remarks	**Steve Davis** | Chief Executive Officer
Commercial Update	**Brendan Teehan** | Chief Operating Officer, Head of Commercial
R&D Update	**Serge Stankovic, M.D., M.S.P.H** | President
Financial Update	**Mark Schneyer** | Chief Financial Officer
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 Alzheimer's disease 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, Alzheimer'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

Drive Growth of NUPLAZID® Franchise

3 Advance Three Late-Stage Opportunities

Develop the Next Wave of Breakthroughs

Building a Leading CNS Company

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Drive Growth of NUPLAZID® in PDP

1Q22

- Delivered net sales of $115.5M, increase of 8% YoY
- Similar rate of demand growth to what we experienced in 2021

Looking Ahead

- NUPLAZID has continued its strong outperformance
- NUPLAZID growth to accelerate when Parkinson's disease (PD) market growth rates return to historic levels
- PD market dynamics to normalize as pandemic abates

Continue to grow the brand as we execute on delivering the long-term potential of NUPLAZID for PDP

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Resubmitted sNDA of Pimavanserin for ADP

Advisory Committee on June 17, 2022 | Target Action Date of August 4, 2022

1 **Efficacy:** Pimavanserin has shown consistent and clinically meaningful improvement in the symptoms of psychosis and a reduction of relapse risk in Alzheimer's disease patients[1]

2 **Safety:** Pimavanserin was not associated with worsening of cognition or motor function compared to placebo in this frail and elderly patient population[2]

3 **Unmet Need:** ~900K patients treated in the U.S., majority of which use off-label multi-receptor acting antipsychotics, with no proven efficacy and safety issues

Prepared to make our case at the upcoming Advisory Committee that pimavanserin should be the first FDA-approved treatment for ADP patients

ADP = Alzheimer's Disease Psychosis.
[1]Based on Study 019 (6-weeks analysis) and subgroup analysis from 045 (26-week double-blind phase).
[2]As measured by MMSE, and ESRS-A scale, respectively, during the 26-week double-blind phase of Study 045.
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Advancing Late-Stage Opportunities

NDA for Rett syndrome (Trofinetide)

- FDA aligned with contents of NDA submission based on pivotal Lavender study
- NDA submission expected mid-22
- Expect priority review; action date expected 1Q23

Phase 3 NSS Program (Pimavanserin)

- Positive pivotal study, ADVANCE-1, already complete
- Evaluating 34 mg dose of pimavanserin in second pivotal study, ADVANCE-2
- Top-line results from ADVANCE-2 expected 2023

NSS = Negative Symptoms of Schizophrenia.
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Develop the Next Wave of Breakthroughs

Program	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Marketed
NUPLAZID® (pimavanserin)[1]	Parkinson's Disease Psychosis					
Pimavanserin[2]	Alzheimer's Disease Psychosis					
Trofinetide[3]	Rett Syndrome					
Pimavanserin	Negative Symptoms of Schizophrenia					
ACP-044	Postoperative and Osteoarthritis Pain					
ACP-319[4]	Schizophrenia and Cognition in Alzheimer's					
Stoke Therapeutics Collaboration[5]	Multiple ASO Programs *(SYNGAP1, Rett, other)*					
Additional Preclinical Programs *(undisclosed)*						

[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 received a CRL for its sNDA for pimavanserin for the treatment of DRP. Acadia has resubmitted the sNDA for the treatment of hallucinations and delusions associated with Alzheimer's disease psychosis.
[3]Acadia has an exclusive license to develop and commercialize trofinetide in North America from Neuren Pharmaceuticals.
[4]Acadia has an exclusive worldwide license to develop and commercialize ACP-319 and other M1 PAM program compounds from Vanderbilt University.
[5]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.
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Commercial Update

Brendan Teehan

Chief Operating Officer, Head of Commercial

NUPLAZID Growth and PD Market Dynamics

NUPLAZID

- **Delivered net sales of $115.5M, increase of 8% YoY**
  - Driven by 4% demand growth, in-line with FY22 net sales guidance
  - Recent HCP and patient/caregiver campaigns generated demand growth
  - Focus on top prescribers and top LTC facilities

PD Market Growth[1]

- **PD Market grew only ~3% total since March 2020 vs. expectation of ~9%**
  - LTC was hardest hit by the pandemic and many patients stayed at home
- **Starting to see signs of stabilization and return to growth in overall PD market**

NUPLAZID Outperformance[2]

Office-based Channel

1Q22 over 2019 TRx Monthly Average

NUPLAZID	**+19%**
Carbidopa/Levodopa	-6%
Avg. Top 10 PD Meds	-12%
Avg. Top 15 Neuro Brands	+5%

Long-term Care Channel

1Q22 over 2019 TRx Monthly Average

NUPLAZID	**+2%**
Carbidopa/Levodopa	-9%
Avg. Top 15 LTC Brands	-13%

[1]IQVIA National Prescription Audit (Carbidopa-Levodopa EUTRX QTY; pre-pandemic: MAT Mar 2018, MAT Mar 2019 and MAT Mar 2020; post-pandemic: MAT Mar 2021 and MAT Mar 2022).
[2]IQVIA National Prescription Audit (monthly NPA).
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Alzheimer's Disease Psychosis (ADP)

ADP represents a significant unmet medical need

- ADP market ~7X the size of PDP market size

No approved treatments, with marginal efficacy and known safety issues with currently used off-label, multi-receptor acting antipsychotics

Well-prepared to execute commercially with NUPLAZID®

- Strong brand recognition as *first and only* FDA approved drug for PDP
- Similar commercial preparation to dementia-related psychosis

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Trofinetide for Rett Syndrome

Significant Unmet Need:

- No FDA-approved treatment
- 6,000 to 9,000 patients in the U.S.[1]

- **NDA Submission Planned for mid-22;**
- **Potential PDUFA in 1Q23**

Market Preparation:

HCP Feedback	Caregiver Feedback	Patients and Physicians
Very high percentage of physicians would be excited to prescribe first FDA-approved treatment for Rett syndrome for their patients	Would actively ask their physicians for trofinetide, if approved, for their child	Focus on patient and HCP identification; including genetic testing

[1]U.S. prevalence estimate based on incidence rates from the National Institutes of Health – National Institute of Neurological Disorders and Stroke.
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R&D Update

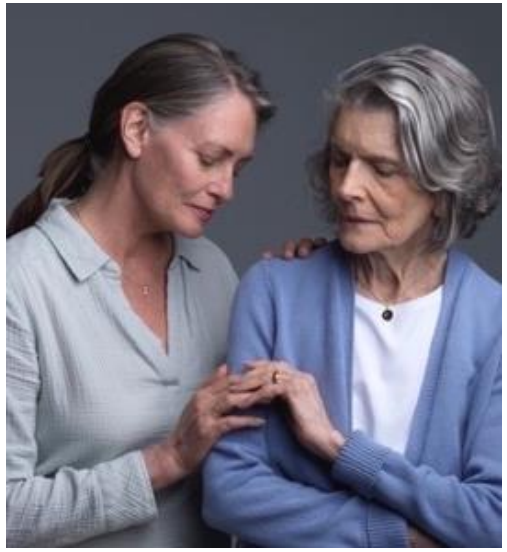
Serge Stankovic

President

Pimavanserin for the Treatment of ADP

High Unmet Need[1]:

- No FDA-approved treatment
- **~900K** ADP patients treated w/ off-label drugs in the U.S.



Concerns of Off-label Drugs[2]:

Off-label use of multi-receptor acting antipsychotics associated with no/limited efficacy and potential serious toxicity, including:

- Accelerate cognitive decline
- Extrapyramidal symptoms

Pimavanserin for ADP in Clinical Studies

- **HARMONY Study[3]:** Clinically meaningful reduction in risk of relapse of psychosis in ADP subgroup (n=123; ~40% reduction; HR=0.62). Results in context of overall positive DRP study (*p=0.0023*)
- **Study -019[4]:** Statistically significant and meaningful reduction in the severity and frequency of symptoms of psychosis in ADP patients (n=181; *p=0.045*)
- Pimavanserin did not negatively impact cognition or extrapyramidal symptoms compared to placebo[3,4,5]

sNDA Resubmission

- Advisory Committee meeting on June 17, 2022
- Target Action Date of August 4, 2022

[1]2021 Alzheimer's Disease Facts and Figures and Acadia market research.[2]US Food and Drug Administration. FDA Public Health Advisory. April 11, 2005; Schneider LS, et al. N Engl J Med. 2006;355:1525-1538.
[3]Tariot PN, et al. N Engl J Med. 2021; 385(4):309-319. [4]Ballard C, et al. Lancet Neurol. 2018;17(3):213-222. Ballard C, et al. J Prev Alzheimers Dis. 2019;6(1):27-33.
[5]As measured by MMSE (Mini-Mental State Examination) and ESRS-A (Extrapyramidal Symptom Rating Scale A) scores.
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Trofinetide for Treatment of Rett Syndrome

Proposed Mechanism of Action:

- Novel synthetic analog of amino-terminal tripeptide of IGF-1
- Potential to reduce neuroinflammation and support synaptic function

High Unmet Need:

- No FDA-approved treatment
- 6,000 to 9,000 patients in the U.S.[1]

Debilitating Symptoms[2]:

- Severe cognitive, emotional, sensory, and motor impairment
- Loss of spoken communication, and purposeful hand use
- Loss of independence

Pivotal Lavender Study Results

- **Co-Primary Endpoints:**
  Statistically significant separation from placebo; RSBQ *(p=0.0175)*, CGI-I *(p=0.0030)*
- **Key Secondary Endpoint:**
  Statistically significant separation from placebo; CSBS-DP-IT–Social *(p=0.0064)*
- **Consistent efficacy observed across age ranges and severity of disease**

NDA Timeline

- Plan to submit NDA mid-22
- Expect priority review with action date in 1Q23
- To seek rare pediatric disease priority review voucher

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.

[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 and https://www.rettsyndrome.org/about-rett-syndrome/what-is-rett-syndrome/.

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Pimavanserin for the Treatment of the Negative Symptoms of Schizophrenia

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High Unmet Need[1]:

- No FDA-approved treatment
- **>700K** patients receiving treatment in the U.S. have persistent negative symptoms

Negative Symptoms[1]:

- Social withdrawal
- Lack of emotion
- Restricted speech
- Blunted affect

This Can Lead to[1]:

- Long-term disability
- Significant caregiver burden

ADVANCE-1 Results[2]

- **Primary endpoint:** Improvement in NSA-16 compared to placebo at 26 weeks (*p=0.043*)
- **Patients on 34 mg** (n=107) had greatest improvement in NSA-16 (*unadjusted p=0.0065*)
- Positive results published in *The Lancet Psychiatry*

Phase 3 ADVANCE-2 Study

- 26-week pivotal study in ~386 patients[3]
- Evaluating **34 mg dose** of pimavanserin
- **Top-line results expected in 2023**

NSA = Negative Symptoms Assessment-16.

[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. According to National Institute of Mental Health; Martin Lepage et al. The Prevalence of Negative Symptoms Across the Stages of the Psychosis Continuum, Schizophrenia Bulletin. Mar 2017, Vol 43 and Acadia market research.

[2] 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.

[3]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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Early-Stage Pipeline Opportunities

	ACP-044 program with ongoing chronic osteoarthritis pain study	Phase 2
WARREN CENTER FOR NEUROSCIENCE DRUG DISCOVERY at Vanderbilt University	ACP-319 lead compound from M1 PAM program licensed from Vanderbilt	Phase 1
STOKE THERAPEUTICS	Collaboration with Stoke Therapeutics focused on development of ASO preclinical programs for SYNGAP1, Rett, and another undisclosed target	Preclinical
	• Programs targeted at leveraging the learnings of pimavanserin • Additional undisclosed CNS targets	Preclinical

Develop the next wave of breakthroughs in CNS

ASO = Antisense oligonucleotide.
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Finance Update

Mark Schneyer

Chief Financial Officer

1Q22 Financial Highlights

Millions, Except EPS	1Q22 (GAAP)	1Q21 (GAAP)	YoY Change
Total Revenue	$115.5	$106.6	+8%
R&D	$128.9	$57.0	+126%
SG&A	$96.7	$111.7	-13%
Net Loss	$113.1	$66.4	+70%
EPS	($0.70)	($0.42)	-67%
Cash Balance[1]	$446.0		

[1]Cash balance includes cash, cash equivalents and investments as of 3/31/2022.
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FY22 Financial Guidance - Reiterated

	FY22 Guidance	Commentary
NUPLAZID® Net Sales	$510 to $560M	• Midpoint reflects similar demand growth rate to 2021 • PDP related revenue only
GAAP R&D Expense	$355 to $375M	• ~$60M related to Stoke collaboration in 1Q22 • ~$25M of stock-based compensation expense
GAAP SG&A Expense	$360 to $380M	• ~$45M of stock-based compensation expense
YE Cash Balance[1]	$355 to $405M	• Does not include incremental Business Development

[1]YE cash balance guidance range based on revenue guidance range and assumes midpoint of expense guidance ranges.
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CEO Closing Remarks

Steve Davis

CEO

Significant Growth Opportunities

PDP Commercial	Significant opportunity for accelerated long-term growth	**FY22 Guidance = $510 - $560M**
ADP Resubmission	Action date for pimavanserin sNDA resubmission	**August 4, 2022**
Trofinetide for Rett Syndrome	Trofinetide NDA submission for Rett syndrome	**Mid-22**
Negative Symptoms of Schizophrenia	Phase 3 ADVANCE-2 top-line results	**2023**

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Q&A Session