ACADIA

Second Quarter 2021 Earnings Call

August 4, 2021

2Q21 Earnings Call Agenda

Introduction	**Mark Johnson** | Vice President, Investor Relations
CEO Opening Remarks	**Steve Davis** | Chief Executive Officer
Commercial Update	**Amanda Morgan** | Chief Revenue and Customer Officer **Charmaine Lykins** | Global Product Planning and Chief Marketing Officer
R&D Update	**Serge Stankovic, M.D., M.S.P.H** | President
Financial Update	**Elena Ridloff** | 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 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 2021 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, 2020 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

Drive Growth of NUPLAZID® in PDP

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2Q21

- Delivered net sales of $115.2M, increase of 5% YoY
- Driven by YoY and sequential volume growth
- PD office visits and LTC occupancy below pre-pandemic levels

FY21

- Revised FY21 sales guidance to $480M to $515M
- Slower pace of recovery due to continued impact of pandemic
- Gross-to-net anticipated to be ~20% for FY21 due to shift in payer mix

Long-term

- Strong relative performance throughout the pandemic across all channels
- Pandemic headwinds expected to abate over time
- Significant opportunity for long-term growth

PD = Parkinson's Disease; LTC = Long-term Care
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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Deliver on the DRP Opportunity: Key Takeaways from FDA Type A Meeting

Key Takeaways:

- FDA reiterated their stated position in the CRL that pimavanserin should be studied by individual subgroups of dementia
- FDA advised that the best path forward is to conduct an additional clinical study in each of the subgroups for which we seek approval
- FDA also indicated an openness to meeting later this year to further discuss additional analyses from the HARMONY and -019 studies in support of a potential resubmission without an additional clinical study

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Develop Next Wave of Breakthroughs

Program	Indication	Phase 1	Phase 2	Phase 3	Marketed
NUPLAZID® (pimavanserin)[1]	Parkinson's Disease Psychosis				
Pimavanserin[2]	Dementia-Related Psychosis				
Pimavanserin	Negative Symptoms of Schizophrenia				
Trofinetide[3]	Rett Syndrome				
ACP-044	Postoperative Pain				
ACP-044	Osteoarthritis Pain				
ACP-319[4]	Schizophrenia and Cognition in Alzheimer's				

[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 is in an ongoing discussion with FDA to align on next steps.
[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.
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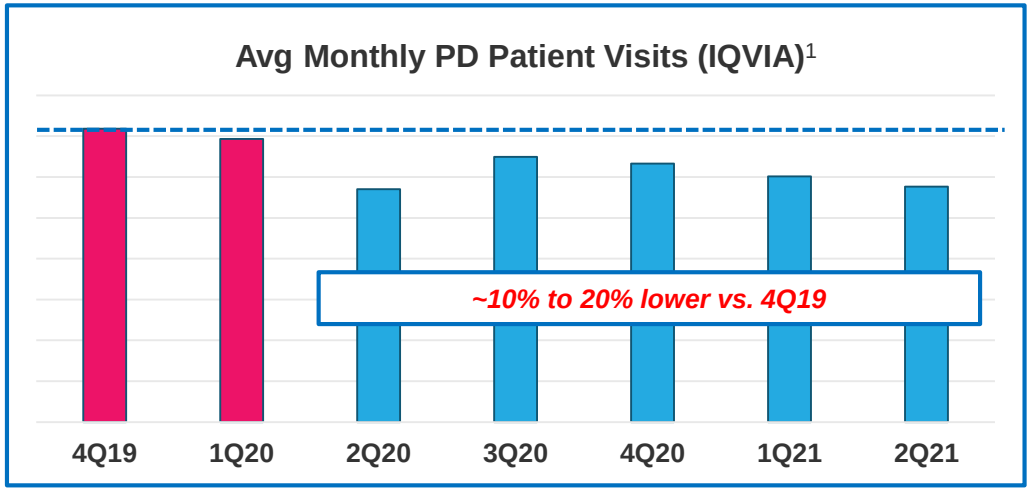
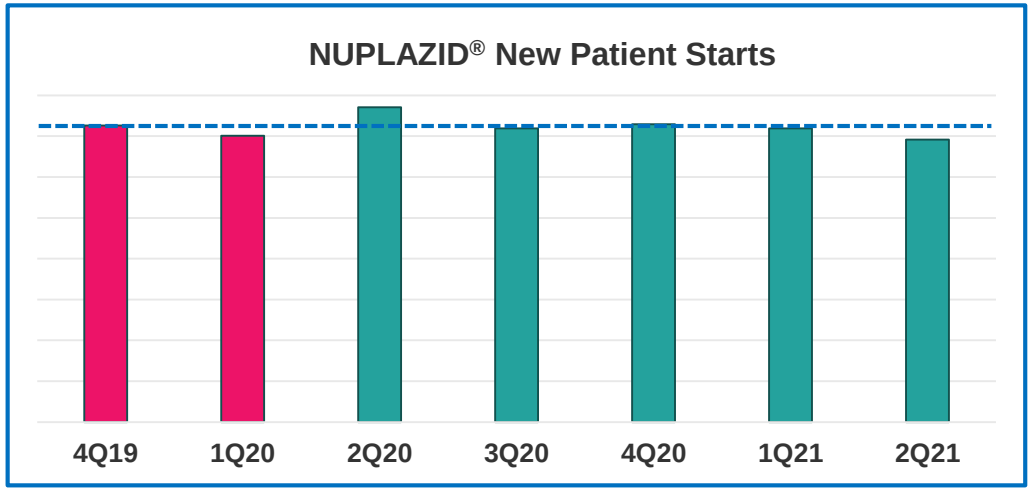
Commercial Update

Amanda Morgan
Chief Revenue and Customer Officer

Charmaine Lykins
Global Product Planning and
Chief Marketing Officer

Office-based Channel Growth Dynamics





Office-Based Channel:

- Continuing patients maintained high fulfillment rates
- PD patient office visits ~20% below pre-pandemic levels in 2Q[1]
- New patient starts at pre-pandemic levels despite reduced office visits
  - High correlation between increased office visits and growth in new patient starts
- **When patients return to physician offices, expect new patient starts to accelerate**

[1]According to IQVIA data;
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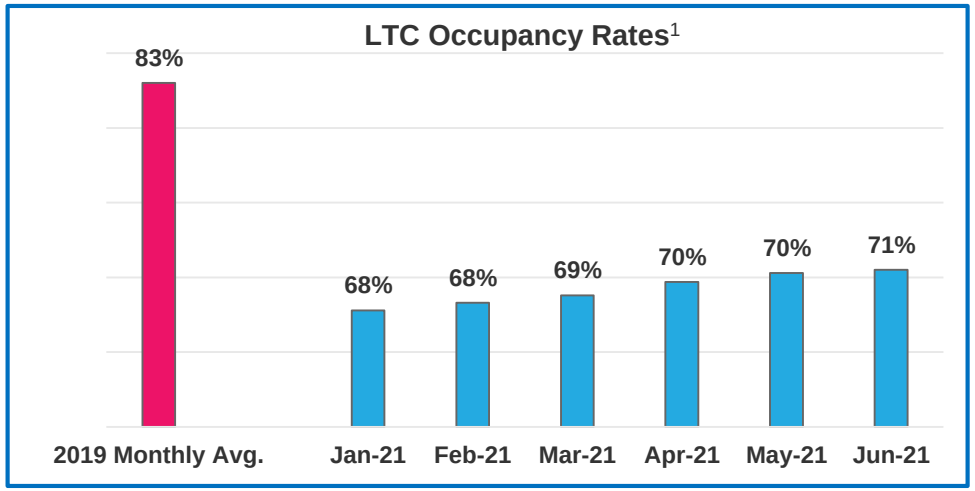
Long-Term Care Channel Growth Dynamics

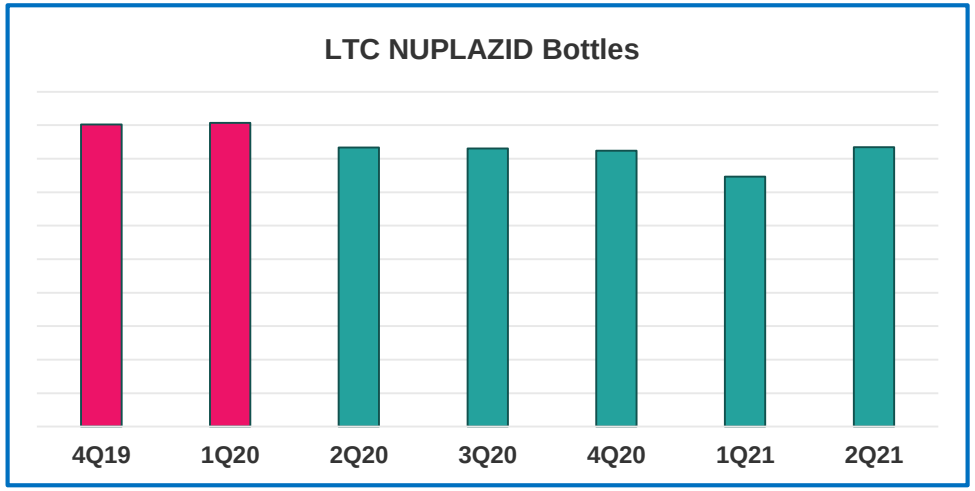
Long-Term Care Channel:

- New admission rates and LTC occupancy levels slowly improving (*0.5% to 1% per month*)[1]
- Occupancy and new admissions rates still below pre-pandemic levels

➢ **Strong relative performance gives confidence that as patients return to LTC facilities, growth in new patients will continue to accelerate:**

Product(s) in LTC[2]	Q2 vs. Q1
NUPLAZID®	+8%
Levodopa / Carbidopa	+1%
Avg. Across Top 15 Brands	0%





[1]According to CMS (https://www.nic.org/snf-covid-tracker); Monthly 2021 figures reflect occupancy level at the end of each month
[2]According to IQVIA data as of end of June 2021.
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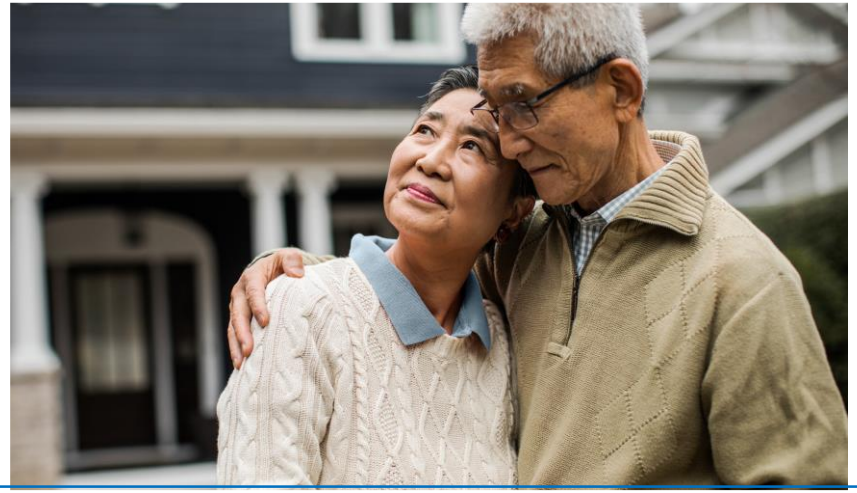
NUPLAZID® Message Platform

Less than **50%** of patients with PD Psychosis patients receive treatment

37% of physicians say they delay treating PD Psychosis due to safety concerns of atypical antipsychotics



"Real improvement without impacting motor function"

- *Relevant messaging to the challenges of psychosis in Parkinson's patients motivates HCPs to treat*

77% of physicians are now more likely to prescribe NUPLAZID to their patients earlier

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Driving Long-term Growth in PDP

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Marketing	➢ Drive new patient identification and new patient starts ➢ Promotional messaging prioritizes efficacy and safety of NUPLAZID®, symptom identification, and the urgency to treat early
Medical Congresses	**>2,000** HCPs attended a branded NUPLAZID program in 2Q Neuroscience Education Institute AMERICAN ACADEMY OF NEUROLOGY® Psych Congress
Patients / Caregivers	➢ DTC, digital, and social media promotions to activate patients and caregivers to engage their HCPs regarding their symptoms and treatment with NUPLAZID

Well-positioned to drive long-term prescription and prescriber growth of NUPLAZID in PDP

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R&D Update

Serge Stankovic

President

Key Takeaways from FDA Type A Meeting

Key Takeaways:

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Publication of Positive HARMONY Results in The *New England Journal of Medicine*[1]

HARMONY Study Results:

- In the 12-week open-label portion, pimavanserin treatment showed a sustained reduction of psychotic symptoms
- In 26-week double-blind portion, continuation of pimavanserin treatment significantly reduced the risk of relapse of psychosis by 2.8 fold compared to placebo
- Importantly, pimavanserin was not associated with a decline in cognition or motor symptoms[2]
- Pimavanserin was well-tolerated in an elderly patient population with dementia

[1]Tariot, Pierre N. *Trial of Pimavanserin in Dementia-Related Psychosis*. N Engl J Med 2021; 385:309-319.
[2]Decline in cognition as measured by Mini-Mental State Examination (MMSE); Worsening of motor symptoms as measured by Extrapyramidal Symptom Rating Scale A (ESRS-A)
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Trofinetide for the Treatment of Rett Syndrome

Trofinetide MOA:

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

High Unmet Need:

- No FDA-approved treatment for Rett syndrome
- 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

Phase 2 Study Results[3]

- 6-week, placebo-controlled dose ranging study in 82 young females (ages 5 – 15)
- Statistically significant and clinically meaningful improvements in 3 core efficacy endpoints including RSBQ and CGI-I
- Positive Phase 2 study published in ***Neurology***®[3]

Phase 3 LAVENDER Study

- 12-week, placebo-controlled study in ~180 females (ages 5 – 20) with trofinetide
- Enrollment completed in 3Q21
- **Co-primary endpoints:** RSBQ and CGI-I
- **Top-line results expected:** 4Q21

RSBQ = Rett Syndrome Behaviour Questionnaire (caregiver assessment) and CGI-I = Clinical Global Impression Scale-Improvement (physician assessment).
[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/.
[3]Glaze D, et al. *Neurology*. Apr 2019, 92 (16) e1912-e1925.
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Pimavanserin for the Treatment of the Negative Symptoms of Schizophrenia

High Unmet Need[1]:

- 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[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]

- 26-week pivotal study in 403 patients with predominant negative symptoms[3]
- **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)***
- Pimavanserin was well-tolerated

Phase 3 ADVANCE-2 Study

- 26-week pivotal study in ~386 patients with predominant negative symptoms[3]
- Evaluating **34 mg dose** of pimavanserin
- **Primary endpoint:** Improvement in NSA-16 compared to placebo at 26 weeks
- Study initiated in 3Q20

[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]Bugarski-Kirola D. et al. ADVANCE: Phase 2, Randomised, Double-Blind, Placebo-Controlled Study of Adjunctive Pimavanserin in Patients With Negative Symptoms of Schizophrenia. Presented at SIRS 2020 Congress. ADVANCE-1 patients were on either 34mg, 20 mg, or 10mg of pimvanserin or placebo in addition to a stable background antipsychotic to control their positive symptoms.
[3]Patients in the ADVANCE-2 study are on either 34mg of pimavansserin or placebo in addition to a stable background antipsychotic to control their positive symptoms.
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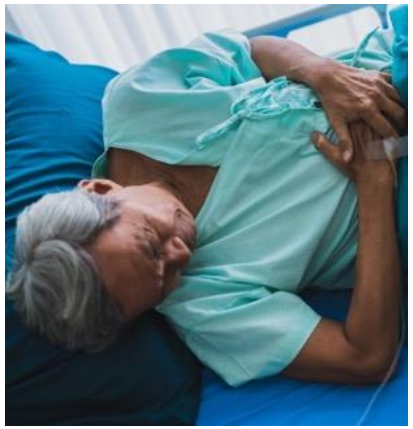
ACP-044 for the Treatment of Acute and Chronic Pain

ACP-044 Mechanism of Action:

- A novel, first-in-class, orally administered, ***non-opioid*** analgesic
- Interrupts multiple pain pathways and sensitization of neurons to pain, by accelerating the decomposition of peroxynitrite, a nitroxidative agent elevated following tissue injury

High Unmet Need for more effective, safe, non-opioid and non-addictive treatments for pain management

Opioid epidemic in the U.S. leading to average of 128 overdose deaths each day[1]



Acute Postoperative Pain:

- >13 million ambulatory surgeries in hospital-owned facilities annually in the U.S.[2]
- ~75% of patients report postoperative pain as moderate to extreme[3]
- Opioids mainstay treatment for pain with significant risks of abuse and addiction

Chronic Pain:

- >30 million patients suffer from osteoarthritis in the U.S.[4] (~25% prescribed opioids[5])
- Other treatments (NSAIDs) associated with GI bleeding and other complications[6]

Phase 2 Program

- Phase 2 study in postoperative pain following bunionectomy surgery ongoing
  - Top-line results expected by 4Q21
- Initiated a Phase 2 study in pain associated with osteoarthritis in 2Q21

Additional Molecules

- Portfolio of preclinical molecules, including brain penetrant molecules, with potential for symptomatic and disease modifying treatments

[1]Wilson N, Kariisa M, Seth P, Smith H IV, Davis NL. *Drug and Opioid-Involved Overdose Deaths — United States, 2017–2018.* MMWRWkly Rep 2020;69:290–297. [2] Karaca Z, McDermott KW. *High-volume invasive, therapeutic ambulatory surgeries performed in hospital-owned facilities. 2016.* Statistical brief #252. September 2019; [3]Chou R, Gordon et al *Management of Postoperative Pain: A Clinical Practice Guideline* J Pain. 2016 Feb;17(2):131-57. doi: 10.1016/j.jpain.2015.12.008.
[4]https://www.cdc.gov/arthritis/basics/osteoarthritis.htm. [5]Alamanda VK et al. Arthritis Care Res (Hoboken). 2019. doi: 10.1002/acr.23933.
[6]Laufer S. *Osteoarthritis therapy--are there still unmet needs?* Rheumatology (Oxford). 2004 Feb;43 Suppl 1:i9-15. doi: 10.1093/rheumatology/keh103.
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ACP-319 for the Treatment of Schizophrenia and Cognitive Impairment in Alzheimer's Disease

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ACP-319 Mechanism of Action:

- Positive Allosteric Modulator of the M1 receptor (M1 PAM)
  - Targets muscarinic (M1) receptors
  - Challenge with targeting the muscarinic system has been tolerability; associated with cholinergic side effects
- Allosteric modulation of the M1 receptor may achieve the potential therapeutic benefits without these side effects

Preclinical Evidence:

- Animal studies demonstrate activity in models of cognition and schizophrenia without cholinergic side effects

ACP-319 Development Status

- Plan to initiate Phase 1 multiple ascending dose (MAD) study in 4Q21

Research Collaboration

- Research collaboration with **Warren Center for Neuroscience Drug Discovery** at Vanderbilt University
- Collaboration focused on additional M1 PAM in preclinical development and discovery

WARREN CENTER
FOR NEUROSCIENCE DRUG DISCOVERY
at Vanderbilt University

Development Timelines

Compound	Indication	Milestone	Expected Timing
ACP-044	Chronic Pain *(Osteoarthritis)*	✓ Initiated Phase 2 Study	2Q21
ACP-044	Acute Pain *(Bunionectomy)*	Top-line Results: Phase 2 Study	4Q21
Trofinetide	Rett Syndrome	Top-line Results: Phase 3 LAVENDER Study	4Q21
ACP-319	Schizophrenia and Cognition in Alzheimer's	Initiate Phase 1 MAD Study	4Q21
Pimavanserin	Negative Symptoms of Schizophrenia	Phase 3 ADVANCE-2 Study	Ongoing

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Finance Update

Elena Ridloff

Chief Financial Officer

2Q21 Financial Highlights

Millions, Except EPS	2Q21 (GAAP)	2Q20 (GAAP)	YoY Change
Total Revenue	$115.2	$110.1	+5%
Cost of Product Sales, License Fees and Royalties	$5.2	$5.5	-5%
R&D	$56.9	$64.3	-11%
SG&A	$96.8	$84.3	+15%
Net Loss	$43.9	$42.1	+4%
EPS	($0.27)	($0.27)	-
Cash Balance[1]	$556.9		

[1]Cash balance includes cash, cash equivalents and investments as of 6/30/2021.
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FY2021 Financial Guidance

FY 2021	Previous Guidance *(5/5/2021)*	Updated Guidance *(8/4/2021)*	Commentary
NUPLAZID® Net Sales	$510 to $550M	$480M - $515M	Reduced guidance due to continued impacts of the COVID-19 pandemic and gross-to-net of ~20% vs. prior expectations of high teens
GAAP R&D Expense	$280 to $300M	$250 to $270M	Includes ~$25M of SBC expense
GAAP SG&A Expense	$385 to $415M	$385 to $415M	Includes ~$50M of SBC expense

SBC = Stock-based compensation.
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CEO Closing Remarks

Steve Davis

CEO

Building a Leading CNS Company

1 Significant long-term opportunity to grow NUPLAZID® in PDP

2 Ongoing discussions with FDA regarding pimavanserin for DRP

3 Near-term clinical data read-outs in the second half of 2021

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Q&A Session