ACADIA

Regulatory Update on sNDA for NUPLAZID® (pimavanserin)

December 20, 2021

Call Agenda

Introduction	**Mark Johnson** | Vice President, Investor Relations
CEO Opening Remarks	**Steve Davis** | Chief Executive Officer
Regulatory Update	**Serge Stankovic, M.D., M.S.P.H** | President
CEO Closing Remarks	**Steve Davis** | Chief Executive Officer
Q&A	Also available for Q&A: **Mark Schneyer** | Chief Financial Officer **Brendan Teehan** | Chief Operating Officer, Head of Commercial

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

sNDA Resubmission for Pimavanserin

Resubmission focused on Alzheimer's Disease Psychosis (ADP)

- ADP represents the majority of DRP patients and is the largest dementia subgroup

- Efficacy observed across multiple clinical studies and endpoints:
  - Improvement of psychosis symptoms and reduction of relapse risk

- Safety profile with pimavanserin, a selective serotonin $5HT_{2A}$ inverse agonist/antagonist includes:
  - No worsening of cognition (core dementia symptom)
  - No onset of worsening of extrapyramidal symptoms (EPS), including motor functioning
  - Supported by >6 years post-marketing data in patients with PDP

Acadia plans to resubmit sNDA specifically for ADP in 1Q22

DRP = Dementia-Related Psychosis; **PDP** = Parkinson's Disease Psychosis
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 December 20, 2021 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.

Timeline from CRL to Resubmission

2Q21: Complete Response Letter (CRL) regarding the sNDA in dementia-related psychosis

3Q21: Type A, End of Review Meeting

- FDA stated they would evaluate pimavanserin by individual subgroups of dementia
- Acadia presented additional analyses to demonstrate consistency of effect across subgroups
- FDA advised the best path forward is to conduct additional studies by subgroup
- FDA also advised that we could request another meeting to further discuss potential resubmission without additional clinical work

3Q21: Type B Meeting to Discuss Breakthrough Therapy Designation

- Brief discussion on breakthrough therapy designation
- Followed by more in-depth discussion on subgroup analyses

4Q21: Type B Meeting to Discuss ADP Resubmission

- Acadia presented additional analyses supporting efficacy in ADP from two positive, placebo-controlled studies:
  - Consistent effect observed in ADP patients in HARMONY study across multiple analyses
  - Analyses support validity of the -019 ADP study results to address FDA's concerns
- FDA restated their previous advice that the conduct of an additional study in ADP would appear to be the path capable of providing the strongest data in support of a resubmission. FDA also stated they are prepared to consider our arguments in support of ADP approval without additional clinical studies in a resubmission

1Q22: Resubmission of sNDA of NUPLAZID® (pimavanserin) focused on ADP

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Regulatory Update

Serge Stankovic

President

Alzheimer's Disease Psychosis

Alzheimer's Disease Psychosis (ADP)[1]:

- There are >6M Alzheimer's patients in the U.S., representing 60 – 80% of all dementia patients
  - ~30% (>1.8M patients in the U.S.) experience psychosis
  - ~50% of ADP patients diagnosed
  - No approved treatments for ADP

ADP represents a serious unmet medical need with no FDA-approved drugs

- Off-label use of multi-receptor acting antipsychotics associated with no/limited proven efficacy and potentially substantial toxicity (oftentimes leading to treatment discontinuation):
  - Seriously impacts patient's ability to function and increases caregiver burden
  - Higher risk to severe dementia and nursing home placement

[1]2021 Alzheimer's Disease Facts and Figures and Acadia market research.
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HARMONY Study: Alzheimer's Disease Subgroup

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HARMONY Study[1]

Pimavanserin showed consistent and clinically meaningful reduction in risk of psychosis relapse in AD subgroup (~40% reduction)

	Overall	AD Subgroup	
Open-label portion of study (12 weeks)			
Response Rate (Sustained at weeks 8 and 12)	**61.8%**	**59.8%**	
Complete Response Rates (Remission Rates)	**33.6%**	**32.1%**	
	Overall *N=194*	**AD Subgroup** *N=123*	**AD (34 mg)** *N=116*
Double-blind portion of study (26 weeks)			*Ad-hoc Analysis*:*
Relapse Rate (Placebo)	**28.3%**	**22.6%**	**23.7%**
Relapse Rate (Pimavanserin)	**12.6%**	**13.1%**	**10.5%**
Hazard Ratio (HR)	**0.35**	**0.62**	**0.47**

Examples of analyses for HARMONY supporting antipsychotic efficacy in AD patients:

- 34 mg relative performance
- Responder analyses
- Exposure-response relationship
- SAPS–H+D and CGI–I severity scores
- Additional analyses of consistency across dementia subgroups

Response Rate = Percentage of subjects who acheived ≥30% SAPS – H+D improvement and CGI – I much improved at both Weeks 8 and 12.
Complete Response Rate = Percentage of subjects who responded that acheived SAPS – H+D (score=0) prior to randomization.
SAPS – **H+D** = Scale for the Assessment of Positive Symptoms – Hallucinations + Delusions; **CGI** – **I** = Clinical Global Impression Scale – Improvement
[1]Tariot PN, et al. N Engl J Med. 2021; 385(4):309-319 and Acadia data on file.
*The 34 mg subgroup of the AD subgroup was a post-hoc/exploratory analysis.
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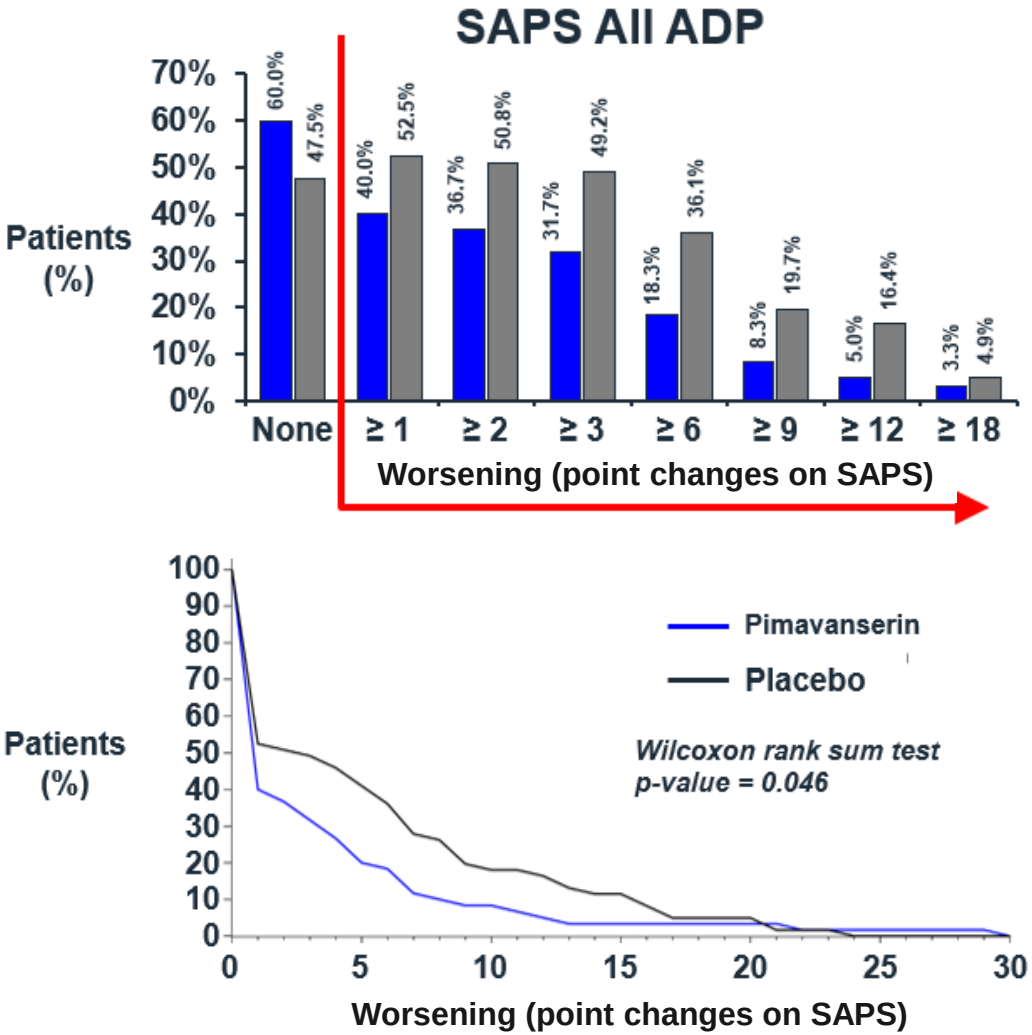
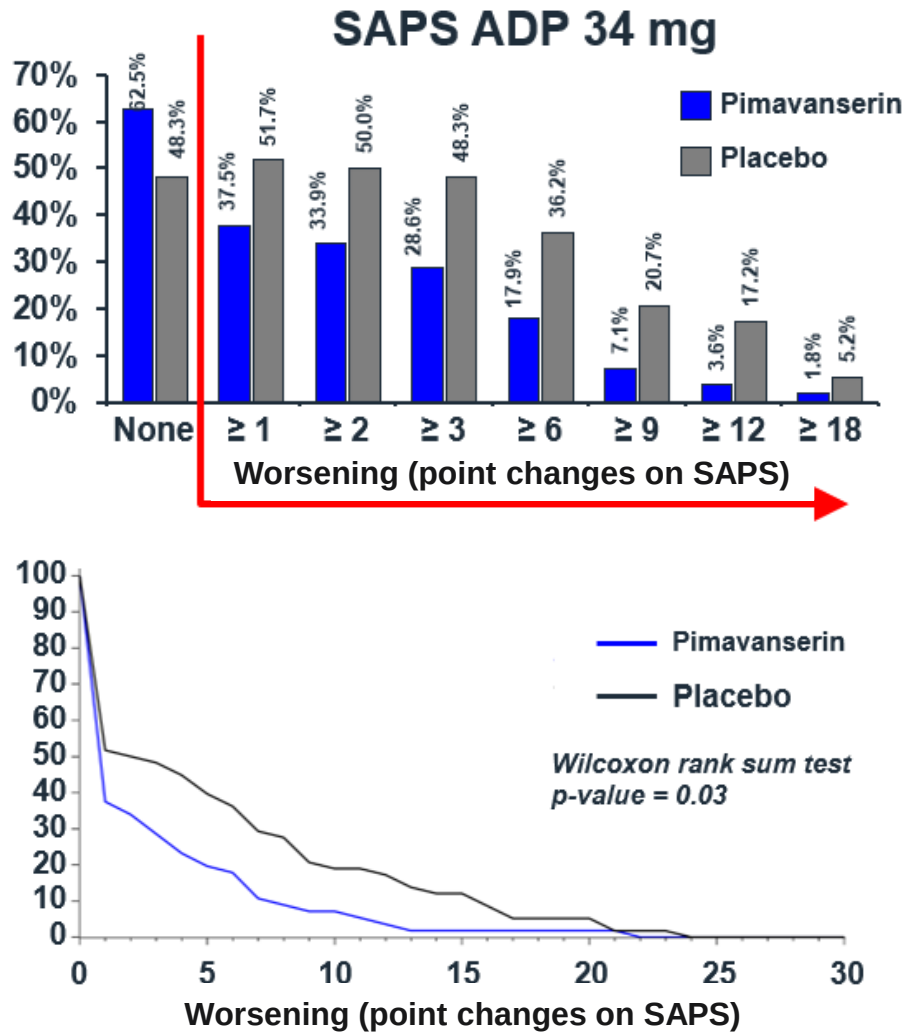
HARMONY Study: Responder Analysis





For subjects who never worsened from Baseline (i.e., improved during double-blind phase), their maximum worsening score was set to 0 for the purpose of evaluating maximum worsening of symptoms.
Subjects who do not have post=baseline SAPS H+D scores are not included in this analysis.
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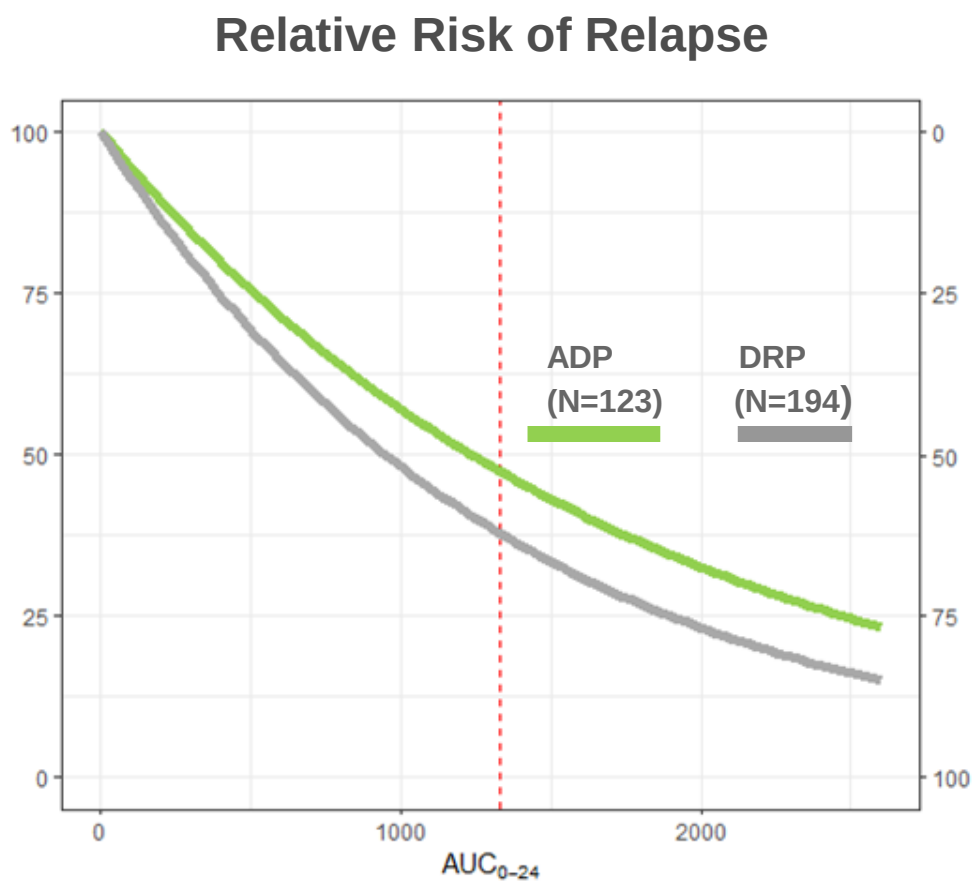
HARMONY Study: Exposure-Response Relationship



- Exposure-Response relationship indicator of true drug effect vs. spurious finding
- Higher pimavanserin exposure associated with decreased relapse rate
- Very consistent improvement in ADP subgroup, similar to overall DRP population

Cox proportional hazards model with pimavanserin AUC0-24 as a continuous variable.
Red line indicates median AUC0-24 of 1330 ng×hr/mL from a 34 mg daily dose.
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HARMONY Study: Consistent Efficacy Observed Across Dementia Subgroups

- Similar levels of efficacy observed across subgroups in the open-label period
- Observed consistently low relapse rates across subgroups in the double-blind randomized period
- PDD response only different in response of patients randomized to placebo:
  - Potential result of this subgroup being on concomitant dopaminergic agents
- Symptoms of psychosis present in a similar fashion regardless of dementia type

PDD = Parkinson's Disease Dementia.
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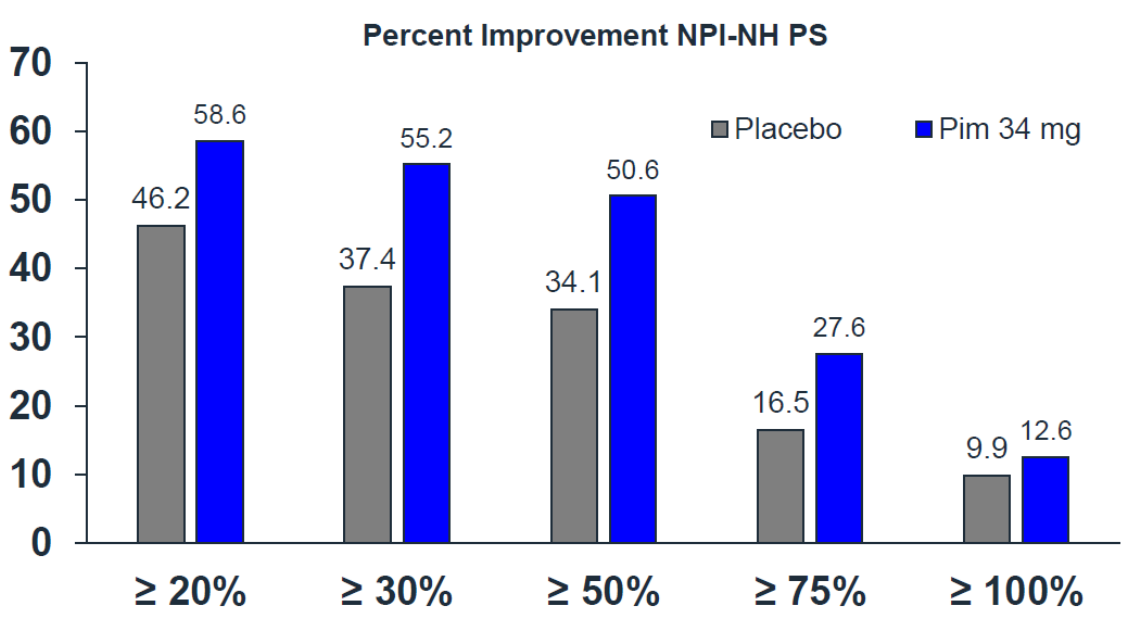
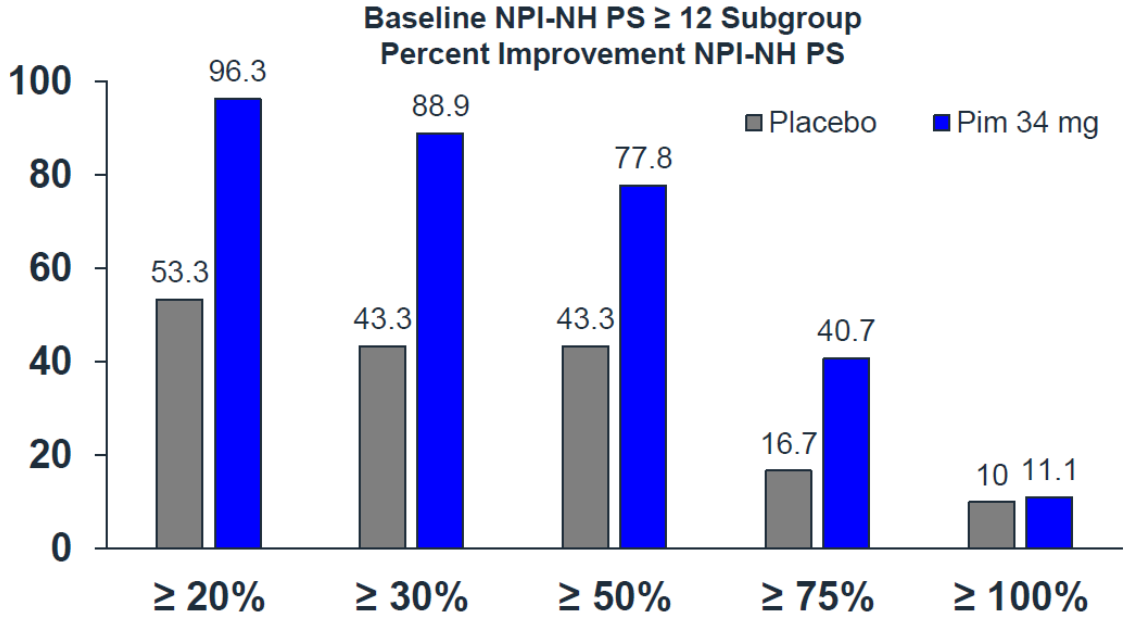
Study -019[1,2]: Primary Efficacy and Responder Analyses

NPI-NH PS at 6 Weeks (Primary Endpoint)	Placebo	Pim 34 mg	Delta	Effect size	P-value
MMRM LSM Change (N=178)	**-1.93**	**-3.76**	**-1.84**	**0.320**	**0.0451**
Baseline NPI-NH PS ≥12 Subgroup (N=57)	-5.72	-10.15	-4.43	0.734	0.0114





NPI – NH PS = Neuropsychiatric Inventory – Nursing Home Version Psychosis Score; **LSM** = least squares mean; **MMRM** = mixed – effect model repeated measures.
*Nominal p-value (exploratory).
[1]Ballard C, et al. Lancet Neurol. 2018;17(3):213-222. [2]Ballard C, et al. J Prev Alzheimers Dis. 2019;6(1):27-33.
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Study -019: Providing Independent Evidence of Efficacy in ADP

In the resubmission Acadia plans to address FDA's concerns outlined in CRL

- Study -019 contributes to substantial evidence of efficacy

Study -019 was a randomized, double-blind, placebo-controlled study that met its pre-specified, primary endpoint

- Single center (Clive Ballard, MD) included multiple care homes (N=133) and qualified raters (N=20)
- Protocol deviation sensitivity analyses suggest no impact on the conclusions of the primary outcome in the study

CEO Closing Remarks

Steve Davis

CEO

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Program Development Pipeline

Program	Indication	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 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 planning to resubmit the sNDA for the treatment of dementia focused on 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.
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Q&A Session