NUPLAZID® for hallucinations and delusions associated with Parkinson's disease psychosis:

LATEST FINDINGS OF A POST HOC ANALYSIS

SEE INSIDE FOR DATA ON:

- The primary endpoint of the pivotal trial, measuring changes in the frequency and/or severity of hallucinations and delusions associated with Parkinson's disease (PD) psychosis
- The proportion of patients with changes in SAPS-PD scores
- Safety outcomes in patients with PD psychosis
- Post hoc analysis of NUPLAZID's treatment response based on duration of symptoms
- Information on the SAPS-PD scale

SAPS-PD=Scale for the Assessment of Positive Symptoms adapted for Parkinson's disease.

Actor Portrayals

Indication

NUPLAZID is indicated for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis.

Important Safety Information

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

- **Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.**
- **NUPLAZID is not approved for the treatment of patients with dementia who experience psychosis unless their hallucinations and delusions are related to Parkinson's disease.**

See additional Important Safety Information throughout. Please read the full Prescribing Information, including **Boxed WARNING**, also available at NUPLAZIDhcp.com.

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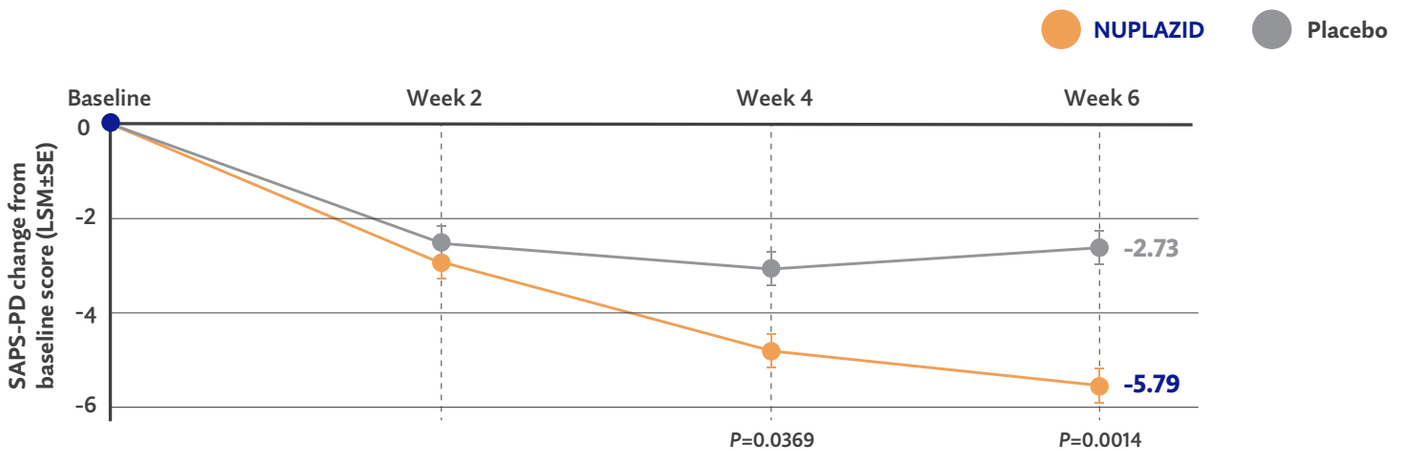
(pimavanserin) 34mg capsules

NUPLAZID® significantly reduced the frequency and/or severity of hallucinations and delusions associated with PD psychosis[1]

SAPS-PD CHANGE FROM BASELINE THROUGH WEEK 6 vs PLACEBO (PRIMARY ENDPOINT)[1,2]



NUPLAZID has been studied in patients with PD-related hallucinations and/or delusions with or without dementia[1]

Study design

A Phase 3, randomized, double-blind, placebo-controlled, parallel-group study of patients with hallucinations and delusions associated with PD psychosis (N=199).[1] Primary efficacy was evaluated based on change from baseline to Week 6 in the 9-item SAPS-PD total score.[1,2]* The mean age of patients enrolled in the clinical study with NUPLAZID was 72 years and patients had MMSE scores ≥21.[2] At screening, 20% of patients (40/198) had a history of dementia per medical history, and 37% of patients (69/185) were taking anti-dementia medications at baseline.[3,4] The mean (SD) SAPS-PD baseline score was 15.9 (6.12) for NUPLAZID and 14.7 (5.55) for placebo.[1,2] The majority of patients were on PD medications at entry; these medications were required to be stable for at least 30 days prior to study start and throughout the study.[1]

Study results

The LSM change from baseline (SE) for NUPLAZID was -5.79 (0.66) and -2.73 (0.67) for placebo; placebo-subtracted difference (drug minus placebo) for NUPLAZID was -3.06 (95% CI: -4.91, -1.20).[1,2]

NUPLAZID worked without impacting motor function or activities of daily living vs placebo at Week 6 (Key Secondary Endpoint)[1,2]

The mean change from baseline was -1.4 for NUPLAZID (n=92) and -1.7 for placebo (n=88) as measured by the UPDRS Parts II+III.† The placebo-subtracted difference was 0.3 [95% CI: -2.1, 2.7]).[1,2‡§]

*SAPS-PD is a 9-item scale derived from SAPS that evaluates hallucinations and delusions in patients with PD psychosis. Each item is scored on a scale of 0 (none) to 5 (severe and frequent symptoms), for a maximum score of 45.[1,5]

†The mean UPDRS II+III baseline score in the secondary endpoint was 51.5 for NUPLAZID and 52.6 for placebo.[2]

‡Difference (drug minus placebo) in LSM.[1]

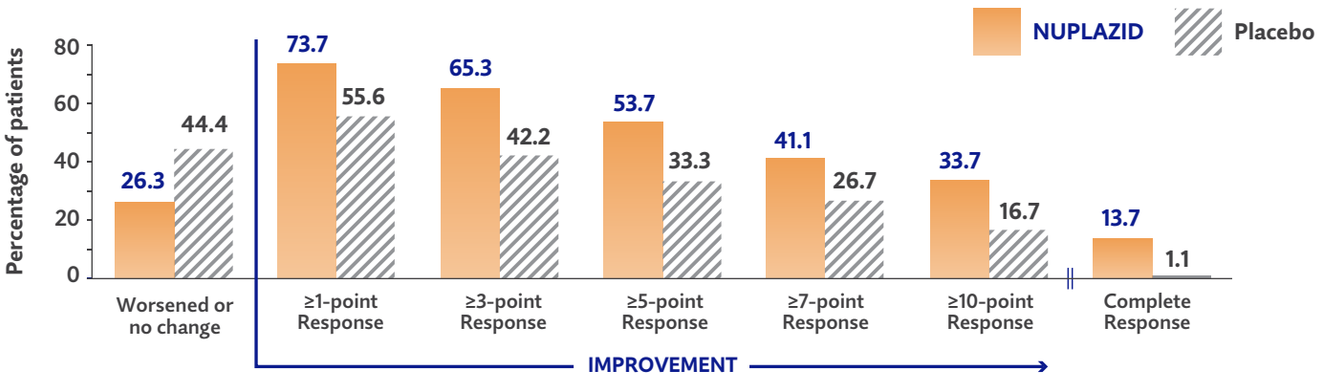
§Noninferiority criteria required that the upper bound of the 95% CI not exceed 5.[2]

CI=confidence interval; **LSM**=least squares mean; **SAPS-PD**=Scale for the Assessment of Positive Symptoms adapted for Parkinson's disease; **SD**=standard deviation; **SE**=standard error; **UPDRS II+III**=Unified Parkinson's Disease Rating Scale Parts II and III.

Real improvement for the majority of your PD psychosis patients

About 65% of NUPLAZID-treated patients experienced a clinically meaningful ≥3-point response vs 42.2% placebo[1]*

PROPORTION OF PATIENTS (RESPONDERS) WITH SAPS-PD SCORE IMPROVEMENT AT END OF WEEK 6 (N=185)[1]



13.7% of NUPLAZID-treated patients experienced complete resolution of symptoms (SAPS-PD score reduced to 0 from baseline) vs. 1.1% for placebo.[1]

26.3% of NUPLAZID-treated patients experienced a worsening of, or no change in, their SAPS-PD scores vs 44.4% placebo.[1]

A 2.33-point change in the SAPS-PD is associated with clinically meaningful improvement—equivalent to a 1-point change in CGI-I[5]

Note: Complete response=SAPS-PD scores reduced to 0 from baseline value. Patients with missing values were counted as nonresponders.[1]

*Based on regression analysis, a clinically meaningful 1-unit change in the CGI-I scale was associated with a 2.33-point change in SAPS-PD.[5]

Important Safety Information (cont'd)

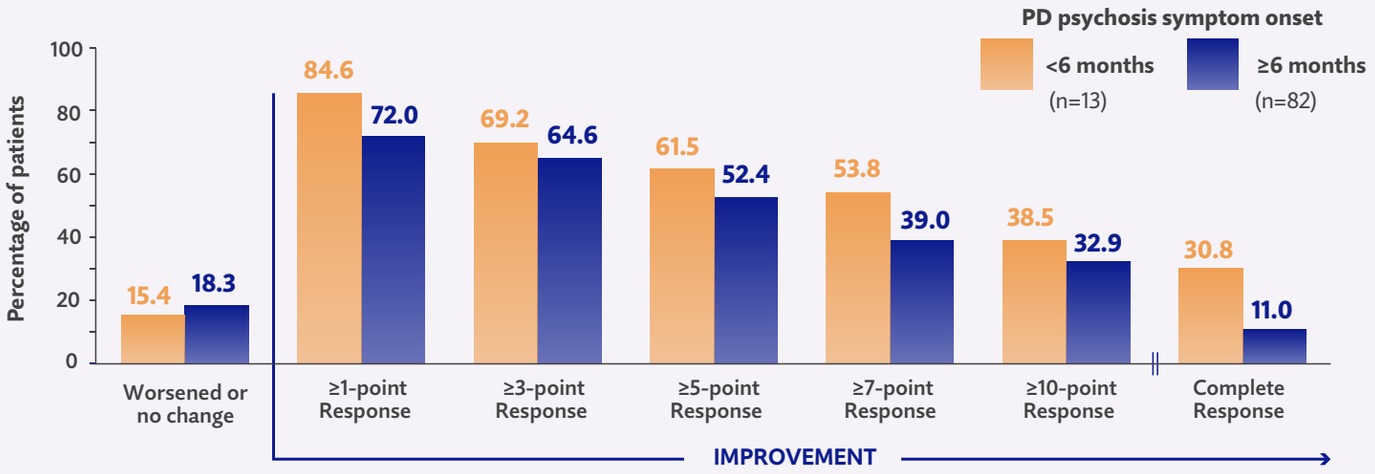
Contraindication: NUPLAZID is contraindicated in patients with a history of a hypersensitivity reaction to pimavanserin or any of its components. Rash, urticaria, and reactions consistent with angioedema (e.g., tongue swelling, circumoral edema, throat tightness, and dyspnea) have been reported.

See additional Important Safety Information throughout. Please read the full Prescribing Information, including **Boxed WARNING**, also available at NUPLAZIDhcp.com.

Post hoc analysis of pivotal trial: treatment response based on duration of symptoms

This post hoc responder analysis was designed to assess SAPS-PD score change in patients who started on NUPLAZID within 6 months of PD psychosis symptom onset vs patients that started NUPLAZID 6 months or later. The results of this post hoc analysis come from the pivotal Phase 3, randomized, double-blind, placebo-controlled clinical trial. A total of 95 patients who received active treatment with NUPLAZID were included in this analysis.[6]

PROPORTION OF PATIENTS (RESPONDERS) WITH SAPS-PD SCORE IMPROVEMENT BY TIME OF NUPLAZID TREATMENT INITIATION (N=95)[7]



Across all defined response thresholds, patients who started NUPLAZID within 6 months of PD psychosis symptom onset had numerically higher response rates than those who were treated later.[7]

Earlier vs later treatment initiation

- 30.8% of patients who started NUPLAZID within 6 months of PD psychosis symptom onset had a complete response on the SAPS-PD scale, compared to 11% of patients who initiated treatment after ≥6 months[7]
- **"No change or worsening"** in SAPS-PD was 15.4% for early treatment vs 18.3% for later treatment[7]

Limitations of the post hoc analysis:

- These analyses were not prespecified endpoints, they are descriptive and supportive of the clinical information related to the FDA-approved indication for the treatment of hallucinations and delusions associated with PD psychosis[8]
- These results should be interpreted cautiously since this study was not designed or powered to draw clinical conclusions, and treatment differences cannot be regarded as statistically significant[8]

Important Safety Information (cont'd)

Warnings and Precautions: QT Interval Prolongation

- NUPLAZID prolongs the QT interval. The use of NUPLAZID should be avoided in patients with known QT prolongation or in combination with other drugs known to prolong QT interval (e.g., Class 1A antiarrhythmics, Class 3 antiarrhythmics, certain antipsychotics or antibiotics).
- NUPLAZID should also be avoided in patients with a history of cardiac arrhythmias, as well as other circumstances that may increase the risk of the occurrence of torsade de pointes and/or sudden death, including symptomatic bradycardia, hypokalemia or hypomagnesemia, and presence of congenital prolongation of the QT interval.

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Demonstrated safety in patients with PD psychosis[1]

ADVERSE DRUG REACTIONS REPORTED IN ≥2% AND GREATER THAN PLACEBO IN 6-WEEK PLACEBO-CONTROLLED STUDIES[1]

	NUPLAZID® n=202	Placebo n=231
GASTROINTESTINAL DISORDERS		
Nausea	**7%**	**4%**
Constipation	**4%**	**3%**
GENERAL DISORDERS		
Peripheral edema	**7%**	**2%**
Gait disturbance	**2%**	**<1%**
PSYCHIATRIC DISORDERS		
Hallucination	**5%**	**3%**
Confusional state	**6%**	**3%**

Low rates of discontinuation due to adverse reactions[1]

In the 6-week placebo-controlled studies, 8% (n=16) of patients treated with NUPLAZID discontinued due to adverse reactions vs 4% (n=10) with placebo.[1] The adverse reactions that occurred in more than 1 patient and with an incidence at least twice that of placebo were hallucination (2% NUPLAZID vs <1% placebo), urinary tract infection (1% NUPLAZID vs <1% placebo), and fatigue (1% NUPLAZID vs 0% placebo).[1]

SEDATION-RELATED AND ORTHOSTATIC HYPOTENSION–RELATED EVENTS[9]

	NUPLAZID n=202	Placebo n=231
Sedation-related events	**6.4%**	**5.2%**
Orthostatic hypotension-related events	**6.9%**	**10.4%**

- There are no warnings or precautions in the Prescribing Information for sedation or orthostatic hypotension[1]
- Sedation-related events included sedation, somnolence, fatigue, asthenia, lethargy, and hypersomnia[9]
- Orthostatic hypotension–related events included dizziness, hypotension, orthostatic hypotension, orthostatic intolerance, syncope, vertigo positional, postural orthostatic tachycardia syndrome, and vertigo[9]

Important Safety Information (cont'd)

Warnings and Precautions: QT Interval Prolongation

- NUPLAZID should also be avoided in patients with a history of cardiac arrhythmias, as well as other circumstances that may increase the risk of the occurrence of torsade de pointes and/or sudden death, including symptomatic bradycardia, hypokalemia or hypomagnesemia, and presence of congenital prolongation of the QT interval.

Drug Interactions:

- Coadministration with strong CYP3A4 inhibitors increases NUPLAZID exposure. Reduce NUPLAZID dose to 10 mg taken orally as one tablet once daily.
- Coadministration with strong or moderate CYP3A4 inducers reduces NUPLAZID exposure. Avoid concomitant use of strong or moderate CYP3A4 inducers with NUPLAZID.

See additional Important Safety Information throughout. Please read the full Prescribing Information, including **Boxed WARNING**, also available at NUPLAZIDhcp.com.

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About the SAPS-PD efficacy assessment

The SAPS-PD scale

SAPS-PD is a 9-item scale derived from SAPS that evaluates hallucinations and delusions in patients with PD psychosis.[5] The types of hallucinations measured were auditory, voices conversing, somatic or tactile, and visual as well as a global rating of severity.[5] The types of delusions measured were persecutory, jealousy, and reference as well as a global rating of severity.[5] Each item is scored on a scale of 0 (none) to 5 (severe and frequent symptoms), for a maximum score of 45.[1] Below is a representation of one item of the full SAPS-PD scale.

EXAMPLE SAPS ITEM: GLOBAL HALLUCINATIONS[10]

Scale	Severity	Patient response
0	None	
1	Questionable	
2	Mild	Hallucinations definitely present, but occur infrequently; at times, the patient may question their existence
3	Moderate	Hallucinations are vivid and occur occasionally; they may bother the patient to some extent
4	Marked	Hallucinations are quite vivid, occur frequently, and pervade the patient's life
5	Severe	Hallucinations are almost daily and are sometimes unusual or bizarre; they are very vivid and extremely troubling

Important Safety Information (cont'd)

Adverse Reactions: The adverse reactions (≥2% for NUPLAZID® and greater than placebo) were peripheral edema (7% vs 2%), nausea (7% vs 4%), confusional state (6% vs 3%), hallucination (5% vs 3%), constipation (4% vs 3%), and gait disturbance (2% vs <1%).

Drug Interactions:

- Coadministration with strong CYP3A4 inhibitors increases NUPLAZID exposure. Reduce NUPLAZID dose to 10 mg taken orally as one tablet once daily.
- Coadministration with strong or moderate CYP3A4 inducers reduces NUPLAZID exposure. Avoid concomitant use of strong or moderate CYP3A4 inducers with NUPLAZID.

Dosage and Administration

Recommended dose: 34 mg capsule taken orally once daily, without titration, with or without food.

NUPLAZID is available as 34 mg capsules and 10 mg tablets.

See additional Important Safety Information throughout. Please read the full Prescribing Information, including **Boxed WARNING**, also available at NUPLAZIDhcp.com.

References: 1. Acadia Pharmaceuticals Inc. NUPLAZID® [package insert]. San Diego, CA; 2023. **2.** Cummings J, Isaacson S, Mills R, et al. Pimavanserin for patients with Parkinson's disease psychosis: a randomised, placebo-controlled phase 3 trial. *Lancet*. 2014;383(9916):533-540. **3.** Data on file_ACP-103-020 posthoc demographics_July2020. **4.** Espay AJ, Guskey MT, Norton C, et al. Pimavanserin for Parkinson's Disease psychosis: Effects stratified by baseline cognition and use of cognitive-enhancing medications. *Mov Disord*. 2018;33(11):1769-1776. **5.** Voss T, Bahr D, Cummings J, Mills R, Ravina B, Williams H. Performance of a shortened scale for assessment of positive symptoms for Parkinson's disease psychosis. *Parkinsonism Relat Disord*. 2013;19(3):295-299. **6.** Data on file. 2025. **7.** Data on file. ACP-103-045_PDD 34 mg subgroup_Sep2021. **8.** Data on File. Post-hoc analysis limitations. 2025. **9.** Acadia Pharmaceuticals Inc. NUPLAZID Advisory Committee Briefing Document. San Diego, CA: Sponsor Background Information for a Meeting of the Psychopharmacologic Drugs Advisory Committee; March 29, 2016. **10.** Andreasen NC. Scale for the Assessment of Positive Symptoms (SAPS). Iowa City, IA: University of Iowa; 1984.

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