



**Neuren (NEU) - ASX Announcement**

**21 September 2018**

## **FDA Issues Statement Reaffirming the Positive Benefit-Risk Profile of ACADIA'S NUPLAZID® (pimavanserin) for Patients with Hallucinations and Delusions Associated with Parkinson's Disease Psychosis**

**Melbourne, Australia, 21 September 2018:** Neuren Pharmaceuticals (ASX: NEU) today reported that the US Food and Drug Administration (FDA) has completed a postmarketing review and issued a clear statement reaffirming the positive benefit-risk profile of NUPLAZID (pimavanserin) for patients with Parkinson's disease psychosis. NUPLAZID was developed and commercialized by Neuren's partner for trofinetide in North America, ACADIA Pharmaceuticals. The announcement issued by ACADIA is attached.

### **About Neuren**

Neuren Pharmaceuticals Limited (Neuren) is a biopharmaceutical company developing new therapies for neurodevelopmental and neurodegenerative disorders and brain injury. Neuren has completed Phase 2 development of trofinetide for Rett syndrome and has completed a Phase 2 clinical trial in Fragile X syndrome. The programs in Rett syndrome and Fragile X syndrome have each been granted Fast Track designation by the US Food and Drug Administration and Orphan Drug designation in both the United States and the European Union. Neuren has granted an exclusive license to ACADIA Pharmaceuticals Inc. for the development and commercialization of trofinetide in North America, whilst retaining all rights to trofinetide outside North America. Neuren is also advancing the pre-clinical development of its second drug candidate NNZ-2591.

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### *Forward-looking Statements*

*This ASX-announcement contains forward-looking statements that are subject to risks and uncertainties. Such statements involve known and unknown risks and important factors that may cause the actual results, performance or achievements of Neuren to be materially different from the statements in this announcement.*

Sept. 20, 2018

## **FDA Issues Statement Reaffirming the Positive Benefit-Risk Profile of NUPLAZID<sup>®</sup> (pimavanserin) for Patients with Hallucinations and Delusions Associated with Parkinson's Disease Psychosis**

- FDA analysis finds no new or unexpected safety risks associated with NUPLAZID
- Patients taking NUPLAZID for Parkinson's disease psychosis should continue to use it as prescribed by their health care provider
- FDA also reminds health care providers that no other antipsychotic medication is approved for the treatment of Parkinson's disease psychosis

SAN DIEGO--([BUSINESS WIRE](#))-- ACADIA Pharmaceuticals Inc. (NASDAQ: ACAD) today announced that the FDA has completed a postmarketing review and issued a clear statement reaffirming the positive benefit-risk profile of NUPLAZID (pimavanserin) for patients with Parkinson's disease psychosis. NUPLAZID is the only medicine approved in the United States to treat hallucinations and delusions associated with Parkinson's disease psychosis (PDP). NUPLAZID was approved by the FDA based on a pivotal Phase 3 study that demonstrated clinically robust and highly statistically significant efficacy, combined with other supportive studies.

Following the FDA's review, the FDA concluded, "The U.S. FDA has completed a review of all postmarketing reports of deaths and serious adverse events (SAEs) reported with the use of NUPLAZID. Based on an analysis of all available data, FDA did not identify any new or unexpected safety findings with NUPLAZID, or findings that are inconsistent with the established safety profile currently described in the drug label. After a thorough review, FDA's conclusion remains unchanged that the drug's benefits outweigh its risks for patients with hallucinations and delusions of Parkinson's disease psychosis." In addition, the FDA stated that, "patients taking NUPLAZID for Parkinson's disease psychosis should continue to use it as prescribed by their health care providers. Based on this observation, FDA reminds health care providers to be aware of the risks described in the prescribing information. FDA also reminds health care providers that none of the other antipsychotic medications are approved for the treatment of Parkinson's disease psychosis."

"Nothing is more important to ACADIA than the wellbeing of the patients who use NUPLAZID. We are very pleased with the FDA's clear statement reaffirming NUPLAZID's positive benefit-risk profile," said Steve Davis, ACADIA's President and Chief Executive Officer. "We are also pleased with the FDA's conclusion that patients taking NUPLAZID for Parkinson's disease psychosis should continue to use it as prescribed by their health care provider and its reminder that no other antipsychotic medication is approved for the treatment of PDP."

### **FDA Full Statement**

**FDA analysis finds no new or unexpected safety risks associated with NUPLAZID (pimavanserin), a medication to treat the hallucinations and delusions of Parkinson's disease psychosis ([Link](#))**

*Health care providers reminded to follow prescribing information*

[09-20-2018] The U.S. Food and Drug Administration (FDA) has completed a review of all postmarketing reports of deaths and serious adverse events (SAEs) reported with the use of NUPLAZID (pimavanserin). Based on an analysis of all available data, FDA did not identify any new or unexpected safety findings with NUPLAZID, or findings that are inconsistent with the established safety profile currently described in the [drug label](#). After a thorough review, FDA's conclusion remains unchanged that the drug's benefits outweigh its risks for patients with hallucinations and delusions of Parkinson's disease psychosis.

NUPLAZID and other antipsychotics have a Boxed Warning regarding the increased risk of death in elderly patients with dementia-related psychosis associated with the use of these drugs. In view of the numbers of reports of death and other serious adverse events, FDA conducted a comprehensive analysis of all available information. This analysis included information submitted to the FDA Adverse Event Reporting System (FAERS), drug utilization data, safety data from the NUPLAZID new drug application, the sponsor's Periodic Adverse Drug Experience Reports, the sponsor's analysis of fatal adverse event reports with NUPLAZID and published medical literature.

In assessing the reports of deaths, FDA considered that patients with Parkinson's disease psychosis, for whom NUPLAZID is indicated, have a higher mortality (death) rate due to their older age, advanced Parkinson's disease, and other medical conditions. Moreover, NUPLAZID is primarily distributed through a patient support program and a specialty pharmacy network, which increases the likelihood that deaths will be reported to the manufacturer. In FAERS reports that included a cause of death (many reports did not provide sufficient information to assess drug cause and effect), there was no evident pattern to suggest a drug effect. Overall, the postmarketing data were consistent with the safety data obtained from the premarketing controlled clinical trials of NUPLAZID for Parkinson's disease psychosis.

Although FDA did not identify any new or unexpected safety risks, some potentially concerning prescribing patterns were observed, such as the concomitant use of other antipsychotic drugs or drugs that can cause QT prolongation, a potential cause of heart rhythm disorder. The risk of QT prolongation and serious arrhythmia (abnormal heart rhythm) associated with NUPLAZID is noted in the Warnings and Precautions section of the drug label, which warns of the increased risks associated with using NUPLAZID together with other drugs known to cause QT interval prolongation. Based on this observation, FDA reminds health care providers to be aware of the risks described in the prescribing information. FDA also reminds health care providers that none of the other antipsychotic medications are approved for the treatment of Parkinson's disease psychosis.

Patients taking NUPLAZID for Parkinson's disease psychosis should continue to use it as prescribed by their health care provider. FDA continues to monitor reports of adverse events associated with NUPLAZID. The agency will communicate any updates to the public as necessary. To help FDA assess potential medication safety issues, we urge health care providers and patients to report suspected side effects involving NUPLAZID and other drugs to the [FDA MedWatch program](#).

## **End of FDA Full Statement**

### *About Parkinson's Disease Psychosis*

According to the Parkinson's Foundation, about one million people in the United States and from four to six million people worldwide suffer from Parkinson's disease. More than 50 percent of people with Parkinson's will experience symptoms of psychosis over the course of their disease. PD Psychosis is characterized by hallucinations and delusions, is associated with significant caregiver burden, and is a major reason for nursing home placement among Parkinson's patients.

### *About NUPLAZID<sup>®</sup> (pimavanserin)*

NUPLAZID is the first FDA-approved treatment for hallucinations and delusions associated with Parkinson's disease psychosis. NUPLAZID is a non-dopaminergic, selective serotonin inverse agonist preferentially targeting 5-HT<sub>2A</sub> receptors that are thought to play an important role in Parkinson's disease psychosis. NUPLAZID is an oral medicine taken once a day with a recommended dose of 34 mg. ACADIA discovered and developed this new chemical entity and holds worldwide rights to develop and commercialize NUPLAZID.

### *About ACADIA Pharmaceuticals*

ACADIA is a biopharmaceutical company focused on the development and commercialization of innovative medicines to address unmet medical needs in central nervous system disorders. ACADIA has developed and is commercializing the first and only medicine approved for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis. In addition, ACADIA has ongoing clinical development efforts in additional areas with significant unmet need, including dementia-related psychosis, schizophrenia inadequate response, schizophrenia-negative symptoms, major depressive disorder and Rett syndrome. This press release and further information about ACADIA can be found at: [www.acadia-pharm.com](http://www.acadia-pharm.com).

### *Forward-Looking Statements*

Statements in this press release that are not strictly historical in nature are forward-looking statements. These statements include but are not limited to statements related to the benefits to be derived from NUPLAZID. These statements are only predictions based on current information and expectations and involve a number of risks and uncertainties. Actual events or results may differ materially from those projected in any of such statements due to various factors, including the risks and uncertainties inherent in drug discovery, development, approval and commercialization, and the fact that past results of clinical trials may not be indicative of future trial results. For a discussion of these and other factors, please refer to ACADIA's annual report on Form 10-K for the year ended December 31, 2017 as well as ACADIA's subsequent filings with the Securities and Exchange Commission. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All forward-looking statements are qualified in their entirety by this cautionary statement and ACADIA undertakes no obligation to revise or update this press release to reflect events or circumstances after the date hereof, except as required by law.

## **Important Safety Information and Indication for NUPLAZID (pimavanserin)**

**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-related psychosis unrelated to the hallucinations and delusions associated with Parkinson's disease psychosis.

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

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.

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 including Class 1A antiarrhythmics or Class 3 antiarrhythmics, certain antipsychotic medications, and certain 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.

Adverse Reactions: The most common adverse reactions ( $\geq 2\%$  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 (e.g., ketoconazole) increases NUPLAZID exposure. Reduce NUPLAZID dose to 10 mg taken orally as one tablet once daily. Coadministration with strong CYP3A4 inducers may reduce NUPLAZID exposure. Monitor patients for reduced efficacy and an increase in NUPLAZID dosage may be needed.

Pediatric Use: Safety and efficacy have not been established in pediatric patients.

Dosage and Administration: Recommended dose: 34 mg taken orally once daily, without titration.

NUPLAZID is available as 34 mg capsules, 17 mg tablets and 10 mg tablets.

For additional Important Safety Information, including Boxed WARNING, please see the full Prescribing Information for NUPLAZID at [https://www.NUPLAZID.com/pdf/NUPLAZID\\_Prescribing\\_Information.pdf](https://www.NUPLAZID.com/pdf/NUPLAZID_Prescribing_Information.pdf).

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