

**Testimony Before FDA's Psychopharmacologic Drugs Advisory  
Committee  
regarding pimavanserin**

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**I have no financial conflicts of interest.**

# Serious Problems with Phase 2 Study 019

**From 2018 Ballard, Banister study: “Pimavanserin showed efficacy in patients with Alzheimer's disease psychosis at the primary endpoint (week 6) with an acceptable tolerability profile and without negative effect on cognition. Further follow-up to week 12 did not show significant advantage for pimavanserin versus placebo.”**

**From FDA Brief: “OSI had concerns about the reliability of Study 019 data because of the number of protocol deviations (Table 3). These violations principally involved subjects who did not have clear documentation that psychotic symptoms developed after AD diagnosis had been established or subjects who received exclusionary medications at the time of randomization.”**

# Serious Problems with Phase 3 Study 045

**From 2021 NEJM Tariot, et al: “Longer and larger trials are required to Determine the effects of pimavanserin in dementia-related psychosis. ....approximately 15% of the patients in the trial had Parkinson’s disease, which may have skewed the results in favor of pimavanserin.”**

**From FDA Brief: “overall significance appears driven primarily by results in the PDD subgroup (HR=0.251, 95% CI: 0.086, 0.733), with a relatively wide confidence interval that includes 1 in the AD subgroup (HR=0.658, 95% CI: 0.326, 1.329)...The apparent differential effects of pimavanserin in the PDD subgroup relative to the other dementia subgroups was the primary reason for the complete response action in the first review cycle and the reason that a broad “dementia-related” psychosis indication is no longer being considered.”**

# Serious Problems with Phase 3 Study 045 (cont'd)

**From FDA Brief: “The sample size for the AD group would need to be increased in order to potentially obtain robust findings on the treatment effect for the AD group at the final analysis. Because the trial was terminated early at the IA, the conclusion for the AD population can only be based on the IA results; that is, the study failed to demonstrate a treatment effect in the AD population.”**

# The Voting question

**VOTE: Does the available evidence support a conclusion that pimavanserin is effective for the treatment of hallucinations and delusions in the ADP population?**

**Given the serious flaws in both studies, we would agree with the FDA's conclusion: "that is, the study failed to demonstrate a treatment effect in the AD population."**