Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes Meeting of the Psychopharmacologic Drugs Advisory Committee
March 29, 2016

Location: FDA White Oak Campus, Building 31, the Great Room (Rm. 1503), White Oak Conference Center, Silver Spring, Maryland.

Topic: The committee discussed the specific risk-benefit profile for new drug application (NDA) 207318, NUPLAZID (pimavanserin) 17 milligram (mg) immediate-release, film-coated oral tablets, submitted by Acadia Pharmaceuticals Inc., for the proposed treatment of psychosis associated with Parkinson's disease.

These summary minutes for the March 29, 2016 meeting of the Psychopharmacologic Drugs Advisory Committee of the Food and Drug Administration were approved on April 3, 2016.

I certify that I attended the March 29, 2016 meeting of the Psychopharmacologic Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/
Kalyani Bhatt, BS, MS
Designated Federal Officer
Psychopharmacologic Drugs Advisory Committee (PDAC)

/s/
David Brent, MD
Chairperson, PDAC

Meeting of the Psychopharmacologic Drugs Advisory Committee
March 29, 2016

The Psychopharmacologic Drugs Advisory Committee (PDAC) of the FDA, Center for Drug Evaluation and Research, met on March 29, 2016, at the FDA White Oak Campus, Building 31 Conference Center, The Great Room (Rm. 1503), Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided briefing materials from FDA and Acadia Pharmaceuticals, Inc. The meeting was called to order by David Brent, MD (Chairperson). The conflict of interest statement was read into the record by Kalyani Bhatt, BS, MS (Designated Federal Officer). There were approximately160 people in attendance. There were 15 Open Public Hearing speakers.

Issues: The committee discussed the specific risk-benefit profile for new drug application (NDA) 207318, NUPLAZID (pimavanserin) 17 milligram (mg) immediate-release, film-coated oral tablets, submitted by Acadia Pharmaceuticals Inc., for the proposed treatment of psychosis associated with Parkinson's disease.

Attendance:
Psychopharmacologic Drugs Advisory Committee Members Present (Voting): David Brent, MD (Chairperson); Thomas Grieger, MD; Dawn Ionescu, MD; Rajesh Narendran, MD; David Pickar, MD; Kim Olsen Wictzak (Consumer Representative)

Psychopharmacologic Drugs Advisory Committee Member Not Present: Murray Stein, MD, MPH

Temporary Members (Voting): John Duda, MD; Susan Elmore, DVM, MS; Stanley Fahn, MD; Tobias Gerhard, PhD, RPH; Linda Morgan, MBA, RPh (Patient Representative); Urmimala Sarkar, MD, MPH; Christopher Schmid, PhD; Almut Winterstein, RPh, PhD, FISPE;

Acting Industry Representative to the Committee (Non-Voting): Mark Forrest Gordon, MD

FDA Participants (Non-Voting): Robert Temple, MD; Mitchell Mathis, MD; Tiffany R. Farchione, MD; Marc Stone, MD; Paul Andreason, MD

Designated Federal Officer (Non-Voting): Kalyani Bhatt, BS, MS

Open Public Hearing Speakers : Peter Schmidt, PhD, (Sr. Vice President and Chief Mission Officer, National Parkinson Foundation); Elaine Casavant, RN; Mary Ann Conway; David Kreitzman, MD (video presented by Ted Thompson); Brittmarie Janson Perez, PhD; Dr. Jamie Eberling (Director, The Michael J Fox Foundation for Parkinson's Research); Stephanie Fox-Rawlings, PhD (Senior Fellow, National Center for Health Research); Ted Thompson (Parkinson's Action Network); Francis Philibert (video presented by Ted Thompson); Neal Hermanowicz, MD (Director, University of California Irvine Parkinson's Disease & Movement Disorders Program); Zoey Wade; Jody Wade; Brendan Tyne; Daniel E. Kremens MD, JD; (Co-

Director, Parkinson's Disease & Movement Disorders Division, Thomas Jefferson University); Drew Bourrut (video presented by Ted Thompson)

The agenda proceeded as follows:

8:00 a.m.	Call to Order and Introduction of Committee	**David A. Brent, MD** Chairperson, PDAC
	Conflict of Interest Statement	**Kalyani Bhatt, BS, MS** Designated Federal Officer, PDAC
8:10 a.m.	FDA Opening Remarks	**Mitchell Mathis, MD** Director Division of Psychiatry Products (DPP) Office of Drug Evaluation I (ODE-I) Office of New Drugs (OND), CDER, FDA
8:15 a.m.	**APPLICANT PRESENTATIONS**	**ACADIA Pharmaceuticals Inc.**
	Introduction	**Michael Monahan, MBA, RAC** Director, Regulatory Affairs ACADIA Pharmaceuticals Inc.
	Burden of PD Psychosis and Need for Additional Treatment Options	**Stuart Isaacson, MD** Director, Parkinson's Disease and Movement Disorders Center of Boca Raton Boca Raton, Florida
	Efficacy of Pimavanserin	**Serge Stankovic, MD, MSPH** Executive Vice President, Research and Development ACADIA Pharmaceuticals Inc.
	Safety of Pimavanserin	**George Demos, MD** Executive Director, Drug Safety and Pharmacovigilance ACADIA Pharmaceuticals Inc.
	Benefit/Risk Profile	**Serge Stankovic, MD, MSPH**
	Clinician Perspective	**Clive Ballard, MD** Institute of Psychiatry King's College London London, United Kingdom
9:45 a.m.	Clarifying Questions to Applicant	
10:15 a.m.	**FDA PRESENTATIONS**	
	Clinical Review of Pimavanserin for the Treatment of Psychosis Associated with	**Paul Andreason, MD** Clinical Reviewer

	Parkinson's Disease	DPP, ODE-I, OND, CDER, FDA
	Mortality and Antipsychotic Drug Use in Dementia	**Marc Stone, MD** Deputy Director of Safety DPP, ODE-I, OND, CDER, FDA
11:45 a.m.	Clarifying Questions to FDA	
1:00 p.m.	**OPEN PUBLIC HEARING**	
2:00 p.m.	Questions to the Committee/Committee Discussion	
3:45 p.m.	Questions to the Committee/Committee Discussion	
5:00 p.m.	**ADJOURNMENT**	

Questions to the Committee:

1. **VOTE:** Has the applicant provided substantial evidence of the effectiveness for pimavanserin for the treatment of psychosis associated with Parkinson's disease?

   Yes: 12 No: 2 Abstain: 0

Committee Discussion: *Overall, the committee agreed that there was evidence for the effectiveness for pimavanserin vs. placebo for the treatment of psychosis associated with Parkinson's disease. The panel members noted although statistically significant, the effects were modest. In addition, there was a consensus among the panel members that there is no other effective agent for this very serious condition. Please see the transcript for details of the committee's discussion.*

2. **VOTE:** Has the applicant adequately characterized the safety profile of pimavanserin?

   Yes: 11 No: 3 Abstain: 0

Committee Discussion: *The majority of the panel members agreed that the applicant had adequately characterized the safety profile of pimavanserin. There was evidence of an increased risk of serious adverse events and death relative to placebo when pooling the results from several studies, although there was no clear explanatory pattern. Moreover, unlike agents currently used for the treatment of Parkinson's related psychosis, pimavanserin did not worsen motor symptoms. The panel members who voted "No" commented on the limited data. Some of the panel members also commented that, if*

approved, there should be information included in the labeling, such a boxed warning that warns about possible increased risk of serious adverse events and death while other members stated there is not enough data to support the recommendation of a boxed warning. In addition, the committee noted that additional long-term surveillance was essential to more fully characterize the risks of this agent. Please see the transcript for details of the committee's discussion.

3. **VOTE:** Do the benefits of pimavanserin for the treatment of psychosis associated with Parkinson's disease outweigh the risk of treatment?

Yes: 12 **No: 2** **Abstain: 0**

Committee Discussion: *The majority of the panel members agreed that the benefits outweighed the risks of treatment. The panel members who voted "Yes" noted that the benefits of the agent outweighed the risks due to the possible improvement of quality of life associated with Parkinson's related psychosis. The committee noted that as long as the risks were made clear that individual patients and physicians could make their own determination, but that given that this is the only effective agent for a very serious condition that did not worsen motor symptoms, the benefits outweighed the risks. The panel members who voted "No" commented on the safety concerns with pimavanserin. Please see the transcript for details of the committee's discussion.*

The meeting was adjourned at approximately 3:50 p.m.