Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Oncologic Drugs Advisory Committee (ODAC) Meeting
December 18, 2019

Location: FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland

Topic: The committee discussed new drug application (NDA) 211723 for tazemetostat tablets, submitted by Epizyme, Inc. The proposed indication (use) for this product is for the treatment of patients with metastatic or locally advanced epithelioid sarcoma not eligible for curative surgery.

These summary minutes for the December 18, 2019 meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration were approved on January 14, 2020.

I certify that I attended the (DATE) meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/	**/s/**
Lauren Tesh Hotaki, PharmD, BCPS, BCIDP	Philip Hoffman, MD
Designated Federal Officer	*Chairperson*
ODAC	*ODAC*

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
December 18, 2019

The Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on December 18, 2019, at the FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and Epizyme, Inc. The meeting was called to order by Philip C. Hoffman, MD (Chairperson). The conflict of interest statement was read into the record by Lauren Tesh Hotaki, PharmD, BCPS, BCIDP (Designated Federal Officer). There were approximately 100 people in attendance. There were nine (9) Open Public Hearing (OPH) speaker presentations.

A verbatim transcript will be available, in most instances, at approximately ten to twelve weeks following the meeting date.

Agenda: The committee discussed new drug application (NDA) 211723 for tazemetostat tablets, submitted by Epizyme, Inc. The proposed indication (use) for this product is for the treatment of patients with metastatic or locally advanced epithelioid sarcoma not eligible for curative surgery.

Attendance:

Oncologic Drugs Advisory Committee Members Present (Voting): Massimo Cristofanilli, MD, FACP; Susan Halabi, PhD; Christian S. Hinrichs, MD; Philip Hoffman, MD (Chairperson); Heidi D. Klepin, MD, MS; Anthony D. Sung, MD; Thomas S. Uldrick, MD, MS

Oncologic Drugs Advisory Committee Members Not Present (Voting): Jaffer A. Ajani, MD; Jorge A. Garcia, MD; David E. Mitchell (Consumer Representative); Alberto S. Pappo, MD; Gregory J. Riely, MD, PhD

Oncologic Drugs Advisory Committee Member Present (Non-Voting): Jonathan D. Cheng, MD (Industry Representative)

Temporary Members (Voting): Randy W. Hawkins, MD (Acting Consumer Representative); Christian F. Meyer, MD, MS, PhD; Richard F. Riedel, MD; Kimberly A. Webb, MA (Patient Representative)

FDA Participants (Non-Voting): Richard Pazdur, MD; Marc Theoret, MD; Steven Lemery, MD; Ashley Ward, MD; Leslie Doros, MD

Designated Federal Officer (Non-Voting): Lauren Tesh Hotaki, PharmD, BCPS, BCIDP

Open Public Hearing Speakers: Jeff Nelson; Anita Nelson; Sandra Griego; Joshua Kerr; Brandi Felser (Sarcoma Foundation of America); Jon Trent MD, PhD (University of Miami, Sylvester Comprehensive Cancer Center); Denise Reinke, MS, NP, MBA (Sarcoma Alliance for Research through Collaboration); Siobhan A. Collins, BA, CCRC; Stephanie Fox-Rawlings, PhD (National Center for Health Research)

Call to Order and Introduction of Committee	**Philip C. Hoffman, MD** Chairperson, ODAC
Conflict of Interest Statement	**Lauren Tesh Hotaki, PharmD, BCPS, BCIDP** Designated Federal Officer, ODAC
FDA Opening Remarks	**Ashley Ward, MD** Cross-Discipline Team Leader Division of Oncology 3 (DO3) Office of Oncologic Diseases (OOD) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATIONS	**Epizyme, Inc.**
Introduction	**Shefali Agarwal, MD** Chief Medical Officer Epizyme, Inc.
Unmet Need	**Shreyaskumar R. Patel, MD** Center Medical Director Department of Sarcoma Medical Oncology Division of Cancer Medicine The University of Texas MD Anderson Cancer Center Houston, Texas
Tazemetostat Efficacy in Patients with Epithelioid Sarcoma	**Shefali Agarwal, MD**
Tazemetostat Safety	**George D. Demetri, MD** Professor, Medicine, Harvard Medical School Director, Center for Sarcoma and Bone Oncology, Dana-Farber Cancer Institute

APPLICANT PRESENTATIONS (CONT.)

Clinical Perspective	**Gary K. Schwartz, MD** Division of Hematology/Oncology Division Chief, Hematology/Oncology Deputy Director Herbert Irving Comprehensive Cancer Center Columbia University

FDA PRESENTATION

Efficacy & Safety Analyses and Issues	**Leslie Doros, MD** Clinical Reviewer DO3, OOD, OND, CDER, FDA

Clarifying Questions to Presenters

BREAK

OPEN PUBLIC HEARING

Questions to the Committee/Committee Discussion

ADJOURNMENT

Questions to the Committee:

1. **DISCUSSION:** Please discuss whether the evidence from Cohorts 5 and 6 of EZH-202 is sufficient to establish the benefit of tazemetostat in patients with epithelioid sarcoma.

   Committee Discussion: *The committee members discussed the evidence from Cohorts 5 and 6 of the EZH-202 study and generally agreed that the data were sufficient to establish a benefit of tazemetostat in patients with epithelioid sarcoma (ES). In addition, there was discussion and agreement that the response rate of 11-15% was considered clinically meaningful for this extremely rare subtype of sarcoma which committee members stated differed from other soft tissue sarcoma subtypes and conferred a very poor prognosis in the metastatic setting with unrelenting progression. The committee members placed this into context that they generally believed tazemetostat had a favorable tolerability profile and that benefits of standard therapies including doxorubicin or pazopanib were marginal for patients with ES. Please see the transcript for details of the committee discussion.*

2. **VOTE:** Does the demonstrated benefit of tazemetostat outweigh the risks of the drug in the proposed indication?

Vote Result: **Yes: 11** **No: 0** **Abstain: 0**

Committee Discussion: *The committee unanimously agreed that the demonstrated benefit of tazemetostat outweighs the risk of the drug in the proposed indication. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 11:55 a.m.