

**Food and Drug Administration
Center for Drug Evaluation and Research**

**Summary Minutes of the Oncologic Drugs Advisory Committee
May 24, 2017**

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

Topic: During the morning session, the committee discussed the new drug application (NDA) 208051 for neratinib maleate, an application submitted by Puma Biotechnology, Inc. The proposed indication (use) for this product is as a single agent for the extended adjuvant treatment of adult patients with early-stage HER2-overexpressed/amplified breast cancer who have received prior adjuvant trastuzumab-based therapy. During the afternoon session, the committee discussed the new drug application (NDA) 208587 for L-glutamine powder (oral solution), submitted by Emmaus Medical, Inc. The proposed indication (use) for this product is for the treatment of sickle cell disease.

These summary minutes for the May 24, 2017, meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration were approved on June 28, 2017.

I certify that I attended the May 24, 2017, meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/S/

Lauren D. Tesh, PharmD, BCPS
Designated Federal Officer, ODAC

/S/

Brian I. Rini, MD, FACP
Acting Chairperson, ODAC

Summary Minutes
Oncologic Drugs Advisory Committee Meeting
May 24, 2017

The following is the final report of the Oncologic Drugs Advisory Committee (ODAC) meeting held on May 24, 2017. A verbatim transcript will be available in approximately six weeks, sent to the Office of Hematology and Oncology Products and posted on the FDA website at: <https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/OncologicDrugsAdvisoryCommittee/ucm547155.htm>

All external requests for the meeting transcript should be submitted to the CDER Freedom of Information Office.

The Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on May 24, 2017 at the FDA White Oak Campus, 10903 New Hampshire Avenue, Building 31 Conference Center, the Great Room (Rm. 1503), Silver Spring, Maryland. Prior to the meeting, members and temporary voting members were provided copies of the briefing materials from the FDA, Puma Biotechnology, Inc (morning session) and Emmaus Medical, Inc. (afternoon session). The meeting was called to order by Brian I. Rini, MD, FACP (Acting Chairperson); the conflict of interest statement was read into the record by Lauren D. Tesh, PharmD, BCPS (Designated Federal Officer). There were approximately 175 people in attendance. There were 12 Open Public Hearing speakers for the morning session and 7 speakers for the afternoon session.

Issue: During the morning session, the committee discussed the new drug application (NDA) 208051 for neratinib maleate, an application submitted by Puma Biotechnology, Inc. The proposed indication (use) for this product is as a single agent for the extended adjuvant treatment of adult patients with early-stage HER2-overexpressed/amplified breast cancer who have received prior adjuvant trastuzumab-based therapy. During the afternoon session, the committee discussed the new drug application (NDA) 208587 for L-glutamine powder (oral solution), submitted by Emmaus Medical, Inc. The proposed indication (use) for this product is for the treatment of sickle cell disease.

Attendance:

ODAC Members Present (Voting): Harold J. Burstein, MD, PhD; Bernard F. Cole, PhD; Heidi D. Klepin, MD, MS; Grzegorz S. Nowakowski, MD; Vassiliki A. Papadimitrakopoulou, MD; Courtney J. Preusse, MA (Consumer Representative); Gregory J. Riely, MD, PhD; Brian I. Rini, MD, FACP (Acting Chairperson); Thomas S. Uldrick, MD, MS

ODAC Members Present (Non-Voting): Phuong Khanh (P.K.) Morrow, MD, FACP (Industry Representative)

ODAC Members Not Present (Voting): Alberto S. Pappo, MD; Alice T. Shaw, MD, PhD; Bruce J. Roth, MD

Temporary Members (Voting): Ralph B. D’Agostino, Sr., PhD; Courtney Fitzhugh, MD (afternoon session only); Stanley Lipkowitz, MD, PhD (morning session only); Michael E. Menefee, MD (afternoon session only); Shirley H. Miller, MA (Patient Representative; afternoon session only); Lori M. Minasian, MD, FACP (morning session only); Stacy Nerenstone, MD (morning session only); Andrew D. Seidman, MD (morning session only); Patricia A. Spears, BS (Patient Representative; morning session only); Melanie E. Royce, MD, PhD (morning session only)

FDA Participants (Non-Voting): Richard Pazdur, MD; Julia Beaver, MD (morning session only); Laleh Amiri-Kordestani, MD (morning session only); Harpreet Singh, MD (morning session only); Amanda Walker, MD (morning session only); Joyce Cheng, PhD (morning session only); Ann Farrell, MD (afternoon session only); Kathy Robie-Suh, MD, PhD (afternoon session only); Rosanna Setse, MD, MPH, PhD; Che Smith, PhD (afternoon session only)

Designated Federal Officer (Non-Voting): Lauren D. Tesh, PharmD, BCPS

Open Public Hearing Speakers for the Morning Session: Stephanie Fox-Rawlings, PhD (National Center for Health Research); Kimberly Jewett (Kimberly Jewett Consulting, Inc.); Fern Gerard; Michelle D. Barry, Au.D.; Debbie Davis; Leslie Lurie; Andrew Gerard; Kandi Franklin; Allison Landherr; Linda D. Bosserman, MD, FASCO, FACP; Kara Kuhns; Jonathan Kuhns

Open Public Hearing Speakers for the Afternoon Session Afternoon Session: Stephanie Fox-Rawlings, PhD (National Center for Health Research); Rita Bellevue, MD; Juanita Gougis; Ashley Valentine, MRes; Ashley Valentine on behalf of her brother, Marqus Valentine; Mary E. Brown (Sickle Cell Disease Foundation of California); Miren Blackwood

The agenda proceeded as follows:

Morning Session:

Call to Order and Introduction of Committee

Brian I. Rini, MD, FACP
Acting Chairperson, ODAC

Conflict of Interest Statement

Lauren Tesh, PharmD, BCPS
Designated Federal Officer, ODAC

Opening Remarks

Laleh Amiri-Kordestani, MD
Medical Team Leader, Breast Cancer Group
Division of Oncology Products 1 (DOP1)
Office of Hematology and Oncology Products
(OHOP), Office of New Drugs (OND), CDER, FDA

APPLICANT PRESENTATIONS

Puma Biotechnology, Inc.

Introduction

Alan H. Auerbach, MS
Chief Executive Officer
Puma Biotechnology, Inc.

Unmet Clinical Need

Jose Baselga, MD, PhD
Physician-in-Chief
Memorial Sloan Kettering Cancer Center

Efficacy

Alvin Wong, PharmD
Vice President, Clinical Science and Clinical
Pharmacology
Puma Biotechnology, Inc.

Safety

Susan Moran, MD, MSCE
Vice President, Clinical Development
Puma Biotechnology, Inc.

Safety Perspective

Hope Rugo, MD
Professor of Breast Oncology
University of California, San Francisco Medical
Center

Clinical Perspective

Joyce O'Shaughnessy, MD
Medical Director
Texas Oncology-Baylor Charles A. Sammons
Cancer Center

FDA PRESENTATIONS

NDA 208051 – Neratinib

Harpreet Singh, MD
Medical Officer
DOPI, OHOP, OND, CDER, FDA

FDA Statistical Analysis

Joyce Cheng, PhD
Statistical Reviewer
Division of Biometrics V (DBV)
Office of Biostatistics (OB)
Office of Translational Sciences (OTS)
CDER, FDA

Safety Results

Amanda Walker, MD
Medical Officer
DOPI, OHOP, OND, CDER, FDA

Clarifying Questions to the Presenters

BREAK

Open Public Hearing

Questions to the Committee/Committee Discussion

ADJOURNMENT

Afternoon Session:

Call to Order and Introduction of Committee

Brian I. Rini, MD, FACP
Acting Chairperson, ODAC

Conflict of Interest Statement

Lauren Tesh, PharmD, BCPS
Designated Federal Officer, ODAC

Opening Remarks

Kathy Robie-Suh, MD, PhD
Medical Team Leader
Division of Hematology Products (DHP)
OHOP, OND, CDER, FDA

APPLICANT PRESENTATIONS

Emmaus Medical, Inc.

Introduction

Lan T. Tran, MPH
Emmaus Medical, Inc.

The Medical Need to Reduce Sickle Cell Crises

Victor R. Gordeuk, MD
Professor of Medicine
Division of Hematology and Oncology
Director, Comprehensive Sickle Cell Center
University of Illinois at Chicago

Efficacy and Safety

Yutaka Niihara, MD, MPH
Emmaus Medical, Inc.

Clinical Perspective/Benefit Risk

Wally R. Smith, MD
Florence Neal Cooper Smith
Professor of Sickle Cell Disease
Vice Chair for Research, Division of General
Internal Medicine
Virginia Commonwealth University

FDA PRESENTATIONS

NDA 208587: L-glutamine

Rosanna Setse, MD, MPH, PhD
Medical Officer
DHP, OHOP, OND, CDER, FDA

Statistical Review Considerations

Che Smith, PhD
Statistical Reviewer
DBV, OB, OTS, CDER, FDA

Safety

Rosanna Setse, MD, MPH, PhD

Clarifying Questions to the Presenters

BREAK

Open Public Hearing

Questions to the Committee/Committee Discussion

ADJOURNMENT

Questions to the Committee:

MORNING SESSION: neratinib maleate tablets

APPLICANT: Puma Biotechnology, Inc.

PROPOSED INDICATION: As a single agent for the extended adjuvant treatment of adult patients with early-stage HER2-overexpressed/amplified breast cancer who have received prior adjuvant trastuzumab-based therapy.

1. **VOTE:** Given the totality of evidence, is the risk-benefit profile of neratinib sufficient to support treatment in the proposed population?

YES: 14

NO: 4

ABSTAIN: 0

Committee Discussion: The committee voted in favor of the risk-benefit profile for the new drug application (NDA) 208051 of neratinib maleate for the proposed indication as a single agent for the extended adjuvant treatment of adult patients with early-stage HER2-overexpressed/amplified breast cancer who have received prior adjuvant trastuzumab-based therapy. Committee members commented that the proposed indication was too broad, with different subsets of patients more responsive to neratinib therapy than others. One committee member noted the need for specific biomarkers or indications that identify who should receive neratinib. Committee members also commented that the data presented by the sponsor and FDA were consistent and demonstrated efficacy. There was concern about the adverse event of diarrhea, but committee members noted that this adverse event was short-lived and manageable. Please see the transcript for details of the committee discussion.

AFTERNOON SESSION: L-glutamine powder

APPLICANT: Emmaus Medical, Inc.

PROPOSED INDICATION: For the treatment of sickle cell disease (SCD).

2. **VOTE:** Based on the available data presented and discussed, is the overall benefit-risk profile of L-glutamine for the treatment of sickle cell disease favorable?

YES: 10

NO: 3

ABSTAIN: 0

***Committee Discussion:** The committee voted in favor of the benefit-risk profile for the new drug application (NDA) 208587 for L-glutamine for the proposed indication of treatment of sickle cell disease. Committee members discussed the clinical need for treatment of this disease. Committee members expressed concern about the sponsor's effect and study results differential study drop-out rates between treatment groups in the pivotal study supporting the application. There was also discussion about differences in the statistical analytic methods used by the Applicant and FDA. However, the committee noted that the FDA's and Applicant's analyses favored the efficacy of the agent, with a modest but consistent benefit. The committee concluded that this benefit had a clinical impact, while presenting low risks for toxicity. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 4:20 p.m.