Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
September 22-23, 2022

Location: Please note that due to the impact of the COVID-19 pandemic, all meeting participants joined this advisory committee meeting via an online teleconferencing platform.

Topic: During the first session of September 22, 2022, the committee discussed new drug application (NDA) 215643, for poziotinib tablets, submitted by Spectrum Pharmaceuticals, Inc. The proposed indication (use) for this product is for the treatment of patients with previously treated, locally advanced or metastatic non-small cell lung cancer (NSCLC) harboring HER2 exon 20 insertion mutations. Select patients with NSCLC for treatment with poziotinib based on the presence of HER2 exon 20 insertion mutations using an FDA-approved test.

During the second session of September 22, 2022, the committee heard an update on new drug application (NDA) 214383, for PEPAXTO (melphalan flufenamide) for injection, submitted by Oncopeptides A.B. This product was approved under 21 CFR 314.500 (subpart H, accelerated approval regulations) for use in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one CD38-directed monoclonal antibody. The confirmatory trial demonstrated a worse overall survival and failed to verify clinical benefit. Confirmatory studies are postmarketing studies to verify and describe the clinical benefit of a drug after it receives accelerated approval. Based on the updates provided, the committee had a general discussion focused on next steps for the product.

On September 23, 2022, the committee heard an update on new drug application (NDA) 211155, for COPIKTRA (duvelisib) capsule, submitted by Secura Bio, Inc. This product was approved under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for use in the treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least two prior therapies. The update includes the final overall survival data from the DUO trial (IPI–145–07) submitted in response to post-marketing requirement 3494–3 detailed in the September 24, 2018 approval letter, available at https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2018/211155Orig2s000ltr.pdf. Based on the updated overall survival information along with the safety data with duvelisib, the committee discussed a current assessment of benefit-risk.

These summary minutes for the September 22-23, 2022 meeting of the ODAC of the Food and Drug Administration were approved on December 11, 2022.

I certify that I attended the September 22-23, 2022 meeting of the ODAC of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/	**/s/**
She-Chia Chen, PharmD	Jorge A. Garcia, MD, FACP
Designated Federal Officer, ODAC	Chairperson, ODAC

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
September 22-23, 2022

The Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on September 22-23, 2022. The meeting presentations were heard, viewed, captioned, and recorded through an online teleconferencing platform. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA, Spectrum Pharmaceuticals, Inc., Oncopeptides A.B., and Secura Bio, Inc. The meeting was called to order by Jorge A. Garcia, MD, FACP (Chairperson). The conflict of interest statement was read into the record by She-Chia Chen, PharmD (Designated Federal Officer). There were approximately 1,025 people online on September 22nd and approximately 667 people online on September 23rd. On September 22nd, there were 8 Open Public Hearing (OPH) speaker presentations for the first session and 7 OPH speakers presentations for the second session. On September 23rd, there were 3 OPH speaker presentations.

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

Agenda: During the first session of September 22, 2022, the committee discussed new drug application (NDA) 215643, for poziotinib tablets, submitted by Spectrum Pharmaceuticals, Inc. The proposed indication (use) for this product is for the treatment of patients with previously treated, locally advanced or metastatic non-small cell lung cancer (NSCLC) harboring HER2 exon 20 insertion mutations. Select patients with NSCLC for treatment with poziotinib based on the presence of HER2 exon 20 insertion mutations using an FDA-approved test.

During the second session of September 22, 2022, the committee heard an update on new drug application (NDA) 214383, for PEPAXTO (melphalan flufenamide) for injection, submitted by Oncopeptides A.B. This product was approved under 21 CFR 314.500 (subpart H, accelerated approval regulations) for use in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one CD38-directed monoclonal antibody. The confirmatory trial demonstrated a worse overall survival and failed to verify clinical benefit. Confirmatory studies are postmarketing studies to verify and describe the clinical benefit of a drug after it receives accelerated approval. Based on the updates provided, the committee had a general discussion focused on next steps for the product.

On September 23, 2022, the committee heard an update on new drug application (NDA) 211155, for COPIKTRA (duvelisib) capsule, submitted by Secura Bio, Inc. This product was approved under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for use in the treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least two prior therapies. The update includes the final overall survival data from the DUO trial (IPI–145–07) submitted in response to post-marketing requirement 3494–3 detailed in the September 24, 2018 approval letter, available at https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2018/211155Orig2s000ltr.pdf. Based

on the updated overall survival information along with the safety data with duvelisib, the committee discussed a current assessment of benefit-risk.

Attendance:
ODAC Members Present (Voting): Ranjana H. Advani, MD (September 23 only); Jorge A. Garcia, MD, FACP (Chairperson); Pamela L. Kunz, MD (September 22 only); Christopher H. Lieu, MD; Ravi A. Madan, MD; David E. Mitchell (Consumer Representative); Jorge J. Nieva, MD (September 22 PM session and September 23 only); Ashley Rosko, MD (September 22 AM session only); Anthony D. Sung, MD (September 22 only)

ODAC Members Not Present (Voting): Jaffer A. Ajani, MD; Mark Conaway, PhD; Alberto S. Pappo, MD; Neil Vasan, MD, PhD

ODAC Member Not Present (Non-Voting): Jonathan D. Cheng, MD (Industry Representative)

Acting Industry Representative to the Committee (Non-Voting): Albert Kraus, PhD

Temporary Members (Voting): Andy I. Chen, MD, PhD (September 22 PM session and September 23 only); Stephanie Y. Crawford, PhD, MPH (September 22 PM session and September 23 only); John DeFlice, MD (Patient Representative for September 22 PM session only); Boris Freidlin, PhD, MS (September 22 PM session and September 23 only); Balazs Halmos, MD (September 22 AM session only); David Harrington, MA, PhD; Mary Kwok, MD (September 22 PM session only); Michele Nadeem-Baker, MS (Patient Representative for September 23 only); Grzegorz (Greg) S. Nowakowski, MD (September 22 PM session only); James (Jim) G. Pantelas (Patient Representative for September 22 AM session only); Mikkael A. Sekeres, MD, MS (September 22 PM session and September 23 only); Katherine Scilla, MD, FACP (September 22 AM session only); Anish Thomas, MD (September 22 AM session only); Scott A. Waldman, MD, PhD, FCP, FAHA, FNAI, FASPET (September 22 only)

FDA Participants (Non-Voting): Richard Pazdur, MD; Marc R. Theoret, MD (September 22 PM session and September 23 only); Julia Beaver, MD (September 22 AM session only); Harpreet Singh, MD (September 22 AM session only); Nicole Gormley, MD (September 22 PM session and September 23 only); Nicole Drezner, MD (September 22 AM session only); Bindu Kanapuru, MD (September 22 PM session only); Nicholas Richardson, DO, MPH (September 23 only); Justin Malinou, MD (September 22 AM session only); Jeanne Fourie Zirkelbach, PhD (September 22 AM session only); Alexandria Schwarsin, MD (September 22 PM session only); Deepti Telaraja, MD (September 23 only)

Designated Federal Officer (Non-Voting): She-Chia Chen, PharmD

Open Public Hearing Speakers:
- September 22 AM session: Susan Johnson; James M. Filipiak; Maria L. Urbano; Bill Brand; Michael Bocker; Kristen Leniz; Mary Modica; Joshua K. Sabari, MD
- September 22 PM session: Diana Zuckerman, PhD (National Center for Health Research); Jenny Ahlstrom; Jacob Laubach, MD, MPP; Scott Taylor Johnson; Ronald J. Ellars; Tara Patel, MD; Sibel Blau, MD

September 23: Diana Zuckerman, PhD (National Center for Health Research); Larry Saltzman, MD; Brian Koffman, MDCM (retired), MS, Ed (CLL Society, Inc.)

The agenda was as follows:

September 22, 2022 AM session

Call to Order	**Jorge A. Garcia, MD, FACP** Chairperson, ODAC
Introduction of Committee and Conflict of Interest Statement	**She-Chia Chen, PharmD** Designated Federal Officer, ODAC
FDA Introductory Comments	**Nicole Drezner, MD** Clinical Team Leader Division of Oncology 2 (DO2) Office of Oncologic Diseases (OOD) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATIONS	**Spectrum Pharmaceuticals, Inc.**
Poziotinib for NSCLC Harboring HER2 Exon 20 Insertion Mutations – Poziotinib Introduction	**Francois Lebel, MD, FRCPC** Executive Vice President R&D Chief Medical Officer Spectrum Pharmaceuticals, Inc.
Unmet Need and Mechanism of Action	**John Heymach, MD, PhD** Professor of Medicine and Chair Thoracic/Head and Neck Medical Oncology The University of Texas MD Anderson Cancer Center
Efficacy	**Gajanan Bhat, PhD** Senior Vice President, Clinical and Data Science Spectrum Pharmaceuticals, Inc.
Safety	**Francois Lebel, MD, FRCPC**
Clinical Perspective	**Mark Socinski, MD** Executive Medical Director AdventHealth Cancer Institute
FDA PRESENTATION	
Poziotinib for HER2 exon 20 insertion mutation-positive non-small cell lung cancer (NSCLC)	**Justin Malinou, MD** Clinical Reviewer DO2, OOD, OND, CDER, FDA

	Jeanne Fourie-Zirkelbach, PhD Team Lead, Clinical Pharmacology Division of Cancer Pharmacology 2 Office of Clinical Pharmacology Office of Translational Sciences, CDER, FDA
Clarifying Questions to Presenters	
BREAK	
OPEN PUBLIC HEARING	
Questions to the Committee/Committee Discussion	
LUNCH	

September 22, 2022 PM session

Call to Order	**Jorge A. Garcia, MD, FACP** Chairperson, ODAC
Introduction of Committee and Conflict of Interest Statement	**She-Chia Chen, PharmD** Designated Federal Officer, ODAC
FDA Introductory Comments	**Nicole Gormley, MD** Director Division of Hematologic Malignancies II (DHM II) Office of Oncologic Diseases (OOD) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATIONS	**Oncopeptides AB**
Introduction	**Jakob Lindberg** Chief Executive Officer Chief Scientific Officer Oncopeptides AB
Treatment Patterns and Unmet Need with Triple-Class Refractory Multiple Myeloma	**Paul Richardson, MD** R.J. Corman Professor of Medicine Harvard Medical School Dana-Farber Cancer Institute
OCEAN Study Clinical Results	**Klaas Bakker, MD, PhD** Executive VP and Chief Medical Officer Oncopeptides AB
Clinical Perspective	**Yvonne Efebera, MD, MPH** Professor, Medical Director of Blood and Marrow Transplant and Cellular Therapy Ohio Health

FDA PRESENTATION

Melphalan flufenamide (PEPAXTO) NDA 214383	**Alexandria Schwarsin, MD** Clinical Reviewer DHM II, OOD, OND, CDER, FDA

Clarifying Questions to Presenters

BREAK

OPEN PUBLIC HEARING

Questions to the Committee/Committee Discussion

ADJOURNMENT

September 23, 2022

Call to Order	**Jorge A. Garcia, MD, FACP** Chairperson, ODAC
Introduction of Committee and Conflict of Interest Statement	**She-Chia Chen, PharmD** Designated Federal Officer, ODAC
FDA Introductory Comments	**Nicholas Richardson, DO, MPH** Clinical Team Leader Division of Hematologic Malignancies II (DHM II) Office of Oncologic Diseases (OOD) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATIONS	**Secura Bio, Inc.**
Introduction	**David Sidransky, MD** Clinical Advisor, Secura Bio Professor of Oncology, John Hopkins University
Disease Background & Unmet Need in CLL/SLL	**Susan O'Brien, MD** Professor of Medicine Division of Hematology/Oncology University of California at Irvine
Efficacy & Safety	**Matthew Davids, MD, MMsc** Director, Clinical Research Division of Lymphoma Dana Farber Cancer Institute
Overall Survival and Benefit/Risk	**David Sidransky, MD**
Clinical Perspective	**Matthew Davids, MD, MMsc**

FDA PRESENTATION

Duvelisib – NDA 211155

Deepti Telaraja, MD
Clinical Reviewer
DHM II, OOD, OND, CDER, FDA

Clarifying Questions to Presenters

BREAK

OPEN PUBLIC HEARING

Questions to the Committee/Committee Discussion

ADJOURNMENT

Questions to the Committee:

September 22, 2022 AM session

1. **DISCUSSION:** Discuss the overall risk:benefit of poziotinib 16 mg once daily given its limited response rate with poor durability, high rate of toxicity, inadequate dosage optimization, and delayed confirmatory trial.

   Committee Discussion: *A majority of the Committee members shared multiple concerns when discussing the overall risk:benefit of poziotinib 16 mg once daily. These concerns include low overall response rate, poorly tolerated safety profile at the currently proposed dosage, and inadequate dose optimization. In addition, the delayed confirmatory trial and its related enrollment issues, such as diversity and whether it's reflective of the US patient population were discussed. Some Committee members questioned the implication of a different dosage in the confirmatory trial versus the dosage studied in the pivotal trial. Other Committee members acknowledged the importance of dosage optimization, but also the noted that it is very difficult to execute. Please see the transcript for details of the Committee's discussion.*

2. **VOTE:** Do the current benefits of poziotinib outweigh its risks for the treatment of patients with NSCLC with HER2 exon 20 insertion mutations?

   Vote Result: Yes: 4 No: 9 Abstain: 0

   Committee Discussion: *The majority of the Committee members voted "No", indicating that the current benefits of poziotinib do not outweigh its risks for the treatment of patients with NSCLC with HER2 exon 20 insertion mutations. These Committee members noted concerns in the lack of dosage optimization and uncertainty related to the completion of the confirmatory trial. The Committee members who voted "Yes", stated that poziotinib shows sufficient efficacy, that the toxicities are manageable, and the drug could provide another option for patients. Please see the transcript for details of the Committee's discussion.*

September 22, 2022 PM session

1. **DISCUSSION:** Discuss the benefit-risk profile of melphalan flufenamide for the currently indicated patient population considering the results of the confirmatory OCEAN trial.

   Committee Discussion*: A majority of the Committee members shared a common concern when discussing the benefit-risk profile of melphalan flufenamide for the currently indicated patient population. Specifically, there were concerns regarding the marginal PFS benefit and the potential detriment in overall survival. These Committee members agreed that the result of the confirmatory OCEAN trial did not confirm clinical benefit in the indicated patient population. Some Committee members noted that it would be challenging to explain the mild progression-free survival and negative result in overall survival to their patients if melphalan flufenamide was one of the treatment options. The Committee members further noted that the post-hoc analyses presented regarding the transplant subgroups should be used for hypothesis generation as opposed to labeling or as an indication for use. The Committee members acknowledged that there is a huge need in this heavily treated patient population, however, we should not use drugs that cause harm. Please see the transcript for details of the Committee's discussion.*

2. **VOTE:** Given the potential detriment in overall survival, failure to demonstrate a progression-free survival benefit, and lack of an appropriate dose, is the benefit-risk profile of melphalan flufenamide favorable for the currently indicated patient population?

   Vote Result: Yes: 2 No: 14 Abstain: 0

   Committee Discussion: *The majority of the Committee members voted "No", indicating that the benefit-risk profile of melphalan flufenamide is not favorable for the currently indicated patient population given the potential detriment in overall survival, failure to demonstrate a progression-free survival benefit, and lack of an appropriate dose. A majority of the Committee members who voted no reiterated that post-hoc analyses should be considered merely hypothesis-generating and need to be tested in a prospectively designed trial. The Committee members who voted "Yes", noted that melphalan flufenamide may be beneficial to some of the patient population, however, the member also acknowedged the posthoc nature of the analysis and that the results need to be confirmed in a prospective clinical trial. Please see the transcript for details of the Committee's discussion.*

September 23, 2022

1. **DISCUSSION:** Discuss the benefit-risk profile of duvelisib for the currently indicated population considering the updated results of the DUO trial.

   Committee Discussion: The *Committee members noted the challenges with the design of the DUO trial that included the allowance of crossover, the differences in how the treatments were administered, and the collection of safety data. Some Committee members commented*

that the overall survival data from the DUO trial was confounded by patient crossover between study groups. Thus, some Committee members questioned how to apply the overall survival data to a current assessment of benefit-risk. The Committee members also commented that for an indolent disease, progression-free survival is an important efficacy outcome for patients along with overall survival. Other Committee members expressed that it is important to adequately evaluate the risk of toxicity due to treatment in the indicated patient population as the underlying disease is associated with risks as well. Please see the transcript for details of the Committee's discussion.

2. **VOTE:** Given the potential detriment in overall survival, duvelisib-associated toxicity, concerns with the selected dose, and the safety issues with the PI3K inhibitor class, is the benefit-risk profile of duvelisib favorable in patients with relapsed or refractory CLL or SLL after at least two prior therapies?

   Vote Result: Yes: 4 No: 8 Abstain: 0

   Committee Discussion: *The majority of the Committee members voted "No", indicating that the benefit-risk profile of duvelisib is not favorable in patients with relapsed or refractory CLL or SLL after at least two prior therapies given the potential detriment in overall survival, duvelisib-associated toxicity, concerns with the selected dose, and the safety issues with the PI3K inhibitor class. These Committee members expressed concerns over the toxicity profile of duvelisib. The Committee members further noted that the design of DUO trial made it difficult to interpret the survival information. The Committee members who voted "Yes", noted that duvelisib shows efficacy in some CLL patients and expressed the unmet need in this population. Please see the transcript for details of the Committee's discussion.*

The meeting was adjourned at approximately 6:10 p.m. on September 22, 2022, and at approximately 1:30 p.m. on September 23, 2022.