Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
November 16, 2023

Location: All meeting participants were heard, viewed, captioned, and recorded for this advisory committee meeting via an online teleconferencing and/or video conferencing platform.

Topic: The Committee received updates on the accelerated approval program in oncology and two new drug applications (NDAs) approved under 21 CFR 314.500 (subpart H, accelerated approval regulations) that have not met their agreed-upon milestones for completion of confirmatory trial(s). Confirmatory trials are postmarketing studies to verify and describe the clinical benefit of a drug after it receives accelerated approval. These updates provided information on the status of all accelerated approvals granted in oncology, including products with delayed confirmatory trials, and the status of confirmatory trials for the specific NDAs to be discussed, including any ongoing and planned trials.

The two products discussed were: (1) FOLOTYN (pralatrexate), NDA 022468 submitted by Acrotech Biopharma Inc, indicated for the treatment of patients with relapsed or refractory peripheral T-cell lymphoma (PTCL), and (2) BELEODAQ (belinostat), NDA 206256 submitted by Acrotech Biopharma Inc, indicated for the treatment of patients with relapsed or refractory PTCL. Based on the updates provided, the Committee had a general discussion about delayed confirmatory trials as well as a focused discussion on next steps for the two products, FOLOTYN (pralatrexate) and BELEODAQ (belinostat), approved for PTCL. The overall goal was the continued optimization of the accelerated approval process with a focus on decreasing the amount of time to verify (or fail to verify) clinical benefit, while continuing to provide early availability of promising oncology products.

These summary minutes for the November 16, 2023 meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration were approved on January 15, 2024.

I certify that I attended the November 16, 2023 meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/	**/s/**
Moon Hee V. Choi, PharmD	Andy Chen, MD, PhD
Acting Designated Federal Officer, ODAC	Acting Chairperson, ODAC

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
November 16, 2023

The Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on November 16, 2023. The meeting presentations were heard, viewed, captioned, and recorded through an online teleconferencing and/or video conferencing platform. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and Acrotech Biopharma Inc. The meeting was called to order by Andy Chen, MD, PhD (Acting Chairperson). The conflict of interest statement was read into the record by Moon Hee V. Choi, PharmD (Acting Designated Federal Officer). There were approximately 499 people online. There were 8 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 received updates on the accelerated approval program in oncology and two new drug applications (NDAs) approved under 21 CFR 314.500 (subpart H, accelerated approval regulations) that have not met their agreed-upon milestones for completion of confirmatory trial(s). Confirmatory trials are postmarketing studies to verify and describe the clinical benefit of a drug after it receives accelerated approval. These updates provided information on the status of all accelerated approvals granted in oncology, including products with delayed confirmatory trials, and the status of confirmatory trials for the specific NDAs to be discussed, including any ongoing and planned trials.

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Attendance:

Oncologic Drugs Advisory Committee Members Present (Voting): Ranjana H. Advani, MD; Toni K. Choueiri, MD; Mark R. Conaway, PhD; William J. Gradishar, MD; Christopher H. Lieu, MD; David E. Mitchell (*Consumer Representative)*; Jorge J. Nieva, MD; Ashley Rosko, MD; Daniel Spratt, MD

Oncologic Drugs Advisory Committee Members Not Present (Voting): Pamela L. Kunz, MD; Ravi A. Madan, MD; Alberto S. Pappo, MD; Neil Vasan, MD, PhD

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

Temporary Members (Voting): Andy Chen, MD, PhD (*Acting Chairperson*); Gita Thanarajasingam, MD; Alexander A. Vinks, PhD, PharmD, FCP; Richard A. Zavadowski, (*Patient Representative*)

FDA Participants (Non-Voting): Richard Pazdur, MD; Marc Theoret, MD; Paul Kluetz, MD; Nicole Gormley, MD; Nicholas Richardson, DO, MPH; Yvette Kasamon, MD; Gautam Mehta, MD

Acting Designated Federal Officer (Non-Voting): Moon Hee V. Choi, PharmD

Open Public Hearing Speakers: Sophia Phillips, MS (National Center for Health Research); Steven Horwitz, MD (statement read by Natasha Galasso, MSW); Sonny Talamantes; Francine Foss, MD; Bradley Haverkos, MD; John C. Reneau, MD, PhD; Reuben Mathew, MD, MSPH; Janet Filemyr Krommes, MD (Arthritis, Rheumatic and Bone Disease Associates, Voorhees NJ and Doctors For America)

The agenda was as follows:

Call to Order and Introduction of Committee	**Andy Chen, MD, PhD** Acting Chairperson, ODAC
Conflict of Interest Statement	**Moon Hee V. Choi, PharmD** Acting Designated Federal Officer, ODAC
FDA Opening Remarks	
Timely Completion of Confirmatory Trials after Oncology Accelerated Approvals	**Gautam Mehta, MD** Acting Cross-Disciplinary Team Leader Division of Oncology Products 2 Office of Oncologic Diseases (OOD) Office of New Drugs (OND), CDER, FDA
Clarifying Questions	
FDA Introductory Comments	**Nicholas Richardson, DO, MPH** Deputy Director Division of Hematologic Malignancies 2 (DHM2) OOD, OND, CDER, FDA
APPLICANT PRESENTATIONS	**Acrotech Biopharma Inc**
Introduction	**Ashish Anvekar** President Acrotech Biopharma

APPLICANT PRESENTATIONS (CONT.)

Disease Background and Treatment Landscape	**Owen A. O'Connor, MD, PhD** American Cancer Society Research Professor Professor of Medicine, University of Virginia Comprehensive Cancer Center Director, Translational Orphan Blood Cancer Research Center Director, Program for T-Cell Lymphoma Research Professor, Microbiology, Immunology and Cancer Biology University of Virginia
Post Marketing Requirements (PMR) Studies: Phase 1 Results and Phase 3 Design	**Swaminathan Iyer, MD** Professor of Medicine Director, T Cell Lymphoma Program Department of Lymphoma / Myeloma University of Texas MD Anderson Cancer Center
PMR Study Timeline	**Ashish Anvekar**

FDA PRESENTATIONS

Pralatrexate (NDA 022468) and Belinostat (NDA 206256)	**Yvette Kasamon, MD** Clinical Team Leader DHM2, OOD, OND, CDER, FDA
Clarifying Questions	

BREAK

OPEN PUBLIC HEARING

Questions to the Committee/Committee Discussion

ADJOURNMENT

Questions to the Committee:

1. **DISCUSSION:** Discuss the delays in post-approval confirmatory trials for pralatrexate and belinostat, and whether the current plan to verify the clinical benefit of these products in patients with peripheral T-cell lymphoma is reasonable considering the Sponsor's proposed timelines.

   Committee Discussion: Overall, the Committee members expressed that the Applicant's current plan and timeline to verify clinical benefit was not reasonable. Members also raised issues with delayed initiation of the confirmatory trial, limited dose optimization, and whether conduct of the

trial in a previously untreated PTCL population was appropriate given the time it will take to complete the trial. The Committee advised the Agency and Applicant to strategize other possible mechanisms to expedite the timeline to verify clinical benefit since the current plan will result in an accelerated approval of approximately 20 years from the initial approval of pralatrexate. This included consideration of an additional confirmatory trial in the relapsed or refractory setting in patients with PTCL. Please see the transcript for details of the Committee's discussion.

2. **DISCUSSION:** Discuss strategies to promote timely completion of the confirmatory trial for pralatrexate and belinostat, and insights from this experience that may facilitate completion of confirmatory trials for future accelerated approvals.

   Committee Discussion: Committee members noted that there has been a major change in the regulatory landscape for accelerated approval and the Committee expressed full support for the changes that have been made that allow FDA to require confirmatory studies to be underway at the time of the accelerated approval. The Committee suggested strategies to promote timely completion of the confirmatory trials that included: 1) conducting a study in a focused population where there might be a greater potential for benefit 2) conducting multiple studies in different treatment settings (i.e., relapsed or refractory population and frontline therapy) 3) making eligibility criteria less restrictive, and 4) the Applicant's allowing access to drug(s) to other Sponsors such as cooperative groups, which may conduct additional trials that could support timely verification of clinical benefit. Please see the transcript for details of the Committee's discussion.

The meeting was adjourned at approximately 1:49 p.m.