Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
October 28, 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: The committee discussed biologics license application 761176, for ^{131}I-omburtamab solution for injection, submitted by Y-mAbs Therapeutics, Inc. The proposed indication (use) for this product is for the treatment of central nervous system/leptomeningeal (CNS/LM) metastases in pediatric patients with neuroblastoma following standard multimodality treatment for CNS disease.

These summary minutes for the October 28, 2022 meeting of the ODAC of the Food and Drug Administration were approved on November 22, 2022.

I certify that I attended the October 28, 2022 meeting of the ODAC of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/
Philip Bautista, PharmD, MPH
Acting Designated Federal Officer, ODAC

/s/
Christopher H. Lieu, MD
Acting Chairperson, ODAC

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
October 28, 2022

The Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research, met on October 28, 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 and Y-mAbs Therapeutics, Inc. The meeting was called to order by Christopher Lieu, MD, (Acting Chairperson). The conflict of interest statement was read into the record by Philip Bautista, PharmD, MPH (Acting Designated Federal Officer). There were approximately 560 people online. There was a total of three 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 biologics license application 761176, for ^{131}I-omburtamab solution for injection, submitted by Y-mAbs Therapeutics, Inc. The proposed indication (use) for this product is for the treatment of central nervous system/leptomeningeal (CNS/LM) metastases in pediatric patients with neuroblastoma following standard multimodality treatment for CNS disease.

Attendance:

Oncologic Drugs Advisory Committee Members Present (Voting): Christopher H. Lieu, MD (Acting Chairperson); David E. Mitchell (Consumer Representative); Jorge J. Nieva, MD; Neil Vasan, MD, PhD

Oncologic Drugs Advisory Committee Members Not Present (Voting): Ranjana H. Advani, MD; Jaffer A. Ajani, MD; Mark R. Conaway, PhD; Jorge A. Garcia, MD, FACP; Pamela L. Kunz, MD; Ravi A. Madan, MD; Alberto S. Pappo, MD; Ashley Rosko, MD; Anthony D. Sung, MD

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

Temporary Members (Voting): Rochelle Bagatell, MD; Natia Esiashvili, MD; David Harrington, MA, PhD; Michael Hudgens, PhD; Michele Jonsson Funk, PhD, FISPE; E. Anders Kolb, MD; Tobey J. MacDonald, MD; Gianna (Gigi) McMillan, D.Bioethics (Patient Representative); Julie R. Park, MD; Donald (Will) Parsons, MD, PhD; Nita Seibel, MD; Brigette Widemann, MD

FDA Participants (Non-Voting): Richard Pazdur, MD; Paul Kleutz, MD; Gregory Reaman, MD; Harpreet Singh, MD; Martha Donoghue, MD; Donna Rivera, PharmD, MSc; Amy Barone, MD; Gautam Mehta, MD; Somak Chatterjee

Acting Designated Federal Officer (Non-Voting): Philip Bautista, PharmD, MPH

Open Public Hearing Speakers Present: Elise Solloway; Diana Zuckerman (National Center for Health Research); Mark Unger

The agenda was as follows:

Call to Order	**Christopher H. Lieu, MD** Acting Chairperson, ODAC
Introduction of Committee and Conflict of Interest Statement	**Philip Bautista, PharmD, MPH** Acting Designated Federal Officer, ODAC
FDA Introductory Comments	**Amy Barone, MD** Cross-Disciplinary Team Leader Division of Oncology 2 (DO2) Office of Oncologic Diseases (OOD) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATIONS	**Y-mAbs Therapeutics, Inc.**
Introduction	**Rikke Valentin Oxholm Lillesø** Vice President, Global Regulatory Affairs Y-mAbs Therapeutics, Inc. **Thomas Gad** Founder Y-mAbs Therapeutics, Inc.
Disease Background & Unmet Need	**Kim Kramer, MD** Attending, MSK KIDS Department of Pediatrics Director, Faculty Development and Wellness Memorial Sloan Kettering Cancer Center Professor of Pediatrics New York Presbyterian Hospital - Weill Cornell Medical Center

APPLICANT PRESENTATIONS
(cont.)

Efficacy	**Vignesh Rajah, MD** Chief Medical Officer Y-mAbs Therapeutics, Inc. **René dePont Christensen, MSc, PhD** Vice President of Biometrics Y-mAbs Therapeutics, Inc.
Safety	**Vignesh Rajah, MD**
Clinical Perspective	**Daniel A. Morgenstern, MB BChir, PhD** Staff Physician, Solid Tumor Program, Hematology/Oncology Associate Scientist, Translational Medicine SickKids Research Institute Associate Professor, Department of Pediatrics University of Toronto

FDA PRESENTATIONS

^{131}I-Omburtamab for neuroblastoma with central nervous system or leptomeningeal metastases	**Gautam U. Mehta, MD** Clinical Reviewer, Nervous System, Pediatrics and Rare Cancers DO2, OOD, OND, CDER, FDA
Clarifying Questions to Presenters	

LUNCH

OPEN PUBLIC HEARING

Questions to the Committee/Committee Discussion

ADJOURNMENT

Questions to the Committee:

1. **DISCUSSION**: Discuss whether data provided by the Applicant isolate the treatment effect of ^{131}I-omburtamab from the effects of multimodality therapy for CNS/LM relapse or if additional data are needed.

   Committee Discussion: *The committee members were generally in agreement that the data provided by the Applicant did not isolate the treatment effect of ^{131}I-omburtamab from the effects of multimodality therapy for CNS/LM relapse and stated that additional data were needed. Some members acknowledged the difficulty in isolating treatment effects when using an external control, especially in rare conditions such as neuroblastoma with central nervous system/leptomeningeal metastases, where small study sample sizes are expected. The committee members discussed the level of selection bias and the difficulty in adjusting for the confounding found in the study, which arose from the dissimilarities between the treatment group and the external control. The members highlighted the differences in multimodal therapies received and evolution of approaches to treatment over time. Some members highlighted that the treatment group received craniospinal irradiation, which is generally more effective in controlling disease than focal irradiation which individuals in the external control group received. The committee members stated that these differences made it challenging to make reliable comparisons between the treatment group and external control group and to isolate the treatment effect of ^{131}I-omburtamab. A few members recommended that the Applicant conduct a target trial emulation, which they noted utility when randomized trials are not feasible and reduce the risk of confounding and selection bias. Please see the transcript for details of the Committee's discussion.*

2. The Applicant has provided a comparison of ^{131}I-omburtamab following multimodality treatment in single-arm Study 03-133 to an external control derived from a German registry.

   VOTE: Has the Applicant provided sufficient evidence to conclude that ^{131}I-omburtamab improves overall survival?

   Vote Result: Yes: 0 No: 16 Abstain: 0

   Committee Discussion: *The committee members unanimously agreed that the Applicant did not provide sufficient evidence to conclude that ^{131}I-omburtamab improves overall survival. The committee cited the lack of a clinically meaningful and clear response rate and the level of confounding in the comparison between the treatment and external control groups. Please see the transcript for details of the Committee's discussion.*

The meeting was adjourned at approximately 2:30 p.m. ET.