Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Antimicrobial Drugs Advisory Committee Meeting July 26, 2018

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) 210607, tafenoquine tablet, 100 milligram (mg), sponsored by 60 Degrees Pharmaceuticals, LLC, for the proposed indication of prevention of malaria in adults for up to 6 months of continuous dosing.

These summary minutes for the July 26, 2018 meeting of the Antimicrobial Drugs Advisory Committee of the Food and Drug Administration were approved on November 6, 2018.

I certify that I attended the July 26, 2018 meeting of the Antimicrobial Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/S/
Kalyani Bhatt, BS, MS
Acting Designated Federal Officer
AMDAC

/S/
Lindsey R. Baden, MD
Chairperson, AMDAC

Final Summary Minutes of the
Antimicrobial Drugs Advisory Committee Meeting
July 26, 2018

The Antimicrobial Drugs Advisory Committee (AMDAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on July 26, 2018, 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 60 Degrees Pharmaceuticals, LLC. The meeting was called to order by Lindsey R. Baden, MD (Chairperson). The conflict of interest statement was read into the record by Kalyani Bhatt, BS, MS (Acting Designated Federal Officer). There were approximately 100 people in attendance. There were three (3) 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) 210607, tafenoquine tablet, 100 milligram (mg), sponsored by 60 Degrees Pharmaceuticals, LLC, for the proposed indication of prevention of malaria in adults for up to 6 months of continuous dosing.

Attendance:
Antimicrobial Drugs Advisory Committee Members Present (Voting): Lindsey R. Baden, MD (Chairperson); Dean A. Follmann, PhD; Michael D. Green, MD, MPH; Barbara M. Gripshover, MD (via phone); Vincent Lo Re, MD, MSCE; Ighovwerha Ofotokun, MD, MSc; Peter Weina, PhD, MD, FACP, FIDSA

Antimicrobial Drugs Advisory Committee Members Not Present (Voting): Nina Clark, MD; Amanda H. Corbett, PharmD, BCPS, FCCP; Demetre C. Daskalakis, MD, MPH; Jonathan R. Honegger, MD; Joanna M. Schaenman, MD, PhD

Antimicrobial Drugs Advisory Committee Member Not Present (Non-Voting): Nicholas A. Kartsonis, MD (Industry Representative)

Temporary Members (Voting): Warren B. Bilker, PhD; Josh A. Mailman, MBA (Patient Representative); Thomas A. Moore, MD, FACP, FIDSA; Michele J. Orza, ScD (Acting Consumer Representative); Kathrine R. Tan, MD MPH; Julie M. Zito, PhD

Acting Industry Representative to the Antimicrobial Drugs Advisory Committee (Non-Voting): Ercem S. Atillasoy, MD (Industry Representative)

FDA Participants (Non-Voting): Edward Cox, MD, MPH; Xianbin Li, PhD; Sumathi Nambiar, MD, MPH; Sheral Patel, MD; Yuliya Yasinskaya, MD

Acting Designated Federal Officer (Non-Voting): Kalyani Bhatt, BS, MS

Open Public Hearing Speakers: Remington Nevin MD, MPH, DrPH (The Quinism Foundation); Victor Zottig, PhD (US Army Medical Material Development Activity); Kevin Baird, PhD (Nuffield Department of Medicine University of Oxford; statement read by Lois Kaufman, PhD)

The agenda was as follows:

Call to Order and Introduction of Committee	**Lindsey R. Baden, MD** Chairperson, AMDAC
Conflict of Interest Statement	**Kalyani Bhatt, BS, MS** Acting Designated Federal Officer, AMDAC
FDA Opening Remarks	**Yuliya Yasinskaya, MD** Clinical Team Leader Division of Anti-Infective Products (DAIP) Office of Antimicrobial Products (OAP) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATIONS	**60 Degrees Pharmaceuticals, LLC**
Overview and Background Development of ARAKODA™	**Geoffrey Dow, PhD** Chief Executive Officer 60 Degrees Pharmaceuticals, LLC
Unmet Medical Need ARAKODA Military and Civilian Travelers	**Stephen Toovey, MD, PhD** Infectious and Tropical Disease Physician **Mark Reid, MBA** ADF Veteran
Efficacy	**Jonathan Berman, MD, PhD** Senior Vice President for Clinical Affairs Fast-Track Drugs & Biologics
Safety	**Bryan Smith, MD** Chief Medical Officer 60 Degrees Pharmaceuticals, LLC
Neuropsychiatric Safety	**Geoffrey Dow, PhD (cont.)**
Benefit/Risk Assessment	**Stephen Toovey, MD, PhD (cont.)**
Clarifying Questions	

FDA PRESENTATIONS

Presentation of Clinical Efficacy	**Xianbin Li, PhD** Statistical Reviewer Division of Biometrics IV Office of Biostatistics Office of Translational Sciences, CDER, FDA
Presentation of Nonclinical Pharmacology and Toxicology	**Owen McMaster, PhD** Pharmacology/Toxicology Reviewer DAIP, OAP, OND, CDER, FDA
Presentation of Clinical Safety	**Sheral Patel, MD** Medical Officer DAIP, OAP, OND, CDER, FDA

Clarifying Questions

LUNCH

OPEN PUBLIC HEARING

Questions to the Committee/Committee Discussion

ADJOURNMENT

Questions to the Committee:

1. **VOTE:** Has the applicant provided substantial evidence of the effectiveness of tafenoquine for the prevention of malaria in adults for up to 6 months of continuous dosing?
   a. If yes, please provide any recommendations concerning labeling.
   b. If no, what additional studies/analyses are needed?

   Vote Result: Yes: 11 No: 2 Abstain: 0

   Committee Discussion*: The majority of the committee agreed that the applicant provided substantial evidence of the effectiveness of tafenoquine for the prevention of malaria in adults up to 6 months of continuous dosing. The members who voted "YES", agreed that the 3 placebo studies (043, 045 and TQ-2016-02) provided consistent data of the efficacy of tafenoquine. Though these data are older they appear compelling and there is no reason to doubt them. Regarding labeling, the committee members commented that it should reflect that tafenoquine is for age group at equal to or greater than 16 year-old, and less than 65 year-old given the available data. Regarding additional studies, it was noted that of these 3 studies, 2 studies were done in the semi-immune population, and 1 study was done in the non-immune population. The committee recommended to have a challenge study done for non-immune population. Furthermore, the committee suggested a future prophylactic study being done in age groups at equal to or greater than 65 year-old and pediatric population. Additionally, the committee also recommended a safety study being done at the post-*

prophylactic period from 1 week up to 1 year. The committee urged to have a post-marketing surveillance monitoring and/ or study to capture any adverse event occurring especially in elderly travelers. The members who voted "NO", recommended to have an efficacy study being done with a larger sample size in all age groups and including observations of adverse events, especially ocular adverse events. Please see the transcript for details of the committee discussion.

2. **VOTE:** Has the applicant provided adequate evidence of the safety of tafenoquine for the prevention of malaria in adults for up to 6 months of continuous dosing?

   a. If yes, please provide any recommendations concerning labeling.
   b. If no, what additional studies/analyses are needed?

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

   Committee Discussion*: The majority of the committee agreed that the applicant provided adequate evidence of the safety of tafenoquine for the prevention of malaria in adults for up to 6 months of continuous dosing. Regarding labeling, the committee members recommended that the FDA ensures it reflects this regimen is for longer-term use with lacking data in elderly and pediatric population, and provides guidance on proper dosing for patients with body weight less than 50 kg. The committee also recommended the labeling should reflect cautions in patients with G6PD deficiency and history of psychologic dysfunctions. For additional studies, it was noted that the applicant provided more than 20 studies, which included more than 3,000 people; however, the committee recommended a safety study with a minimum sample size of 10,000 people should be done in general population in the future. The committee shared their concern of the neuropsychologic adverse events and recommended further studies in addition to a large post-marketing study to observe tafenoquine related adverse events mandated by the FDA. The committee members who voted "YES", suggested the applicant provided adequate safety data for the proposed indication; however, these committee members strongly recommended the FDA mandates post-marketing/surveillances studies. The committee members who voted "NO", suggested the safety data were small; for instance, the duration of follow-ups was short, and it lacked data in elderly or pediatric population. These members also recommended more post-marketing surveillances being done at 4 weeks up to 1 year. In addition, the members also suggested more safety data are needed for further analysis of serious adverse events such as ocular, hematologic and psychiatric events. Furthermore, some of these members expressed concern of small sample size and it was hard to differentiate whether tafenoquine behaves more like primaquine or mefloquine in regards to psychiatric and ocular adverse events. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 3:52 p.m.