Food and Drug Administration
Center for Biologics Evaluation and Research

SUMMARY MINUTES
176th VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE

September 22, 2022

Committee Members
Hana El Sahly, M.D., Chair
Adam Berger, Ph.D.+
CAPT. Amanda Cohn, M.D.
Andrea Shane, M.D., M.P.H., M.Sc.
Archana Chatterjee, M.D., Ph.D.
Arnold Monto, M.D.
David Kim, M.D. M.S. M.H.A.
Eric Rubin, M.D. Ph.D.
Henry Bernstein, D.O. MHCM, FAAP
Hayley Altman-Gans, M.D.+
Jay Portnoy, M.D.
Holly Janes, Ph.D.
Paul Offit, M.D.
Stanley Perlman, M.D., Ph.D.
Steven Pergam, M.D., M.P.H.

Industry Representatives
Paula Annunziato, M.D. ***

Consumer Representative
Jay Portnoy, M.D.*

Designated Federal Officers (DFO)
Sussan Paydar, Ph.D.
Prabhakara Atreya, Ph.D.
Christina Vert, M.S.

Committee Management Staff
Joanne Lipkind
Karen Thomas
LaShawn Marks

Temporary Voting Members
Dean Follmann, Ph.D.
L. Clifford McDonald, M.D.
Vincent Young, M.D., Ph.D.
William Petri, Jr., M.D., Ph.D.

Speakers and Guest Speakers
Alice Guh, M.D., MPH - CDC Speaker
Qun Wang, Ph.D. - FDA Speaker
Omolara Adewuni, M.D. - FDA Speaker
Zhong Gao, Ph.D. - FDA Speaker
John Scott, Ph.D. - FDA Responder
Lihan Yan, Ph.D. - FDA Responder
Lee Jones - Rebiotix Speaker
Sahil Khanna, MBBS, MS - Rebiotix Speaker
Linda Bencke, PharmD - Rebiotix Speaker
Jonas Pettersson, M.D., Ph.D. - Rebiotix Speaker
Colleen Kraft, M.D., MSC, FIDSA - Rebiotix Speaker
Scott Berry, Ph.D. - Rebiotix Responder
Karen Kuphal, Ph.D., MBA, PMP- Rebiotix Responder
Ken Blount, Ph.D. - Rebiotix Responder
Greg Fluet - Rebiotix Responder

FDA Participants
Peter W. Marks, M.D., Ph.D.
Doran Fink, M.D., Ph.D.
Jay Slater, M.D.

+Not Attending
*Consumer Representative
*>Acting Consumer Rep
***Industry Representative

These summary minutes for the September 22, 2022, meeting of the Vaccines and Related Biological Products Advisory Committee were approved on October 14, 2022.

I certify that I participated in the September 22, 2022, meeting of the Vaccines and Related Biological Products Advisory Committee and that these minutes accurately reflect what transpired.

-----S-----	-----S-----
_____	_____
Sussan Paydar, Ph.D. Designated Federal Officer	Hana El Sahly, M.D. Chair

On September 22, 2022, at 8:30 a.m. Eastern Standard Time (EST), the 176th meeting of the Vaccines and Related Biological Products Advisory Committee (VRBPAC) took place in open session to discuss the Biologics License Application # 125739 (BLA - 125739) from Rebiotix Inc. for a product, Rebyota (Fecal Microbiota, Live), with a requested indication to "reduce the recurrence of *Clostridioides difficile* infection (CDI) in adults following antibiotic treatment for recurrent *Clostridioides difficile* infection."

Dr. Hana El Sahly, the Chair, called the meeting to order. The DFO, Dr. Sussan Paydar made administrative remarks, conducted roll call, and invited the committee members to introduce themselves. She read the Conflict of Interest (COI) statement for the public record.

Dr. Peter Marks, Director for the Center for Biologics Evaluation and Research (CBER), FDA made a 5-minute FDA Welcome remarks. Dr. Qun Wang, the Review Committee Chair from CBER, FDA made a 20- minutes presentation titled Biologics License Application for Rebyota (Fecal Microbiota, Live) followed by a 5-minute Q & A. The guest speaker, Dr. Alice Guh from Centers for Disease Control and Prevention (CDC) made a 20-minute presentation titled "Current Epidemiology of Clostridiodes difficile (CDI) in adults in the United States" followed by a 10-minute Q & A.

On behalf of the Sponsor, Rebiotix Incorporated, 5 presentations were made for a total of 60 minutes, starting with an Introduction by Dr. Lee Jones, Founder and Past President and CEO of Rebiotix, followed by presentations on "Effective Management of C Difficile, An Unmet clinical Need" by Sahil Khanna, "RBX2660 Safety" by Dr. Lindy Bancke, "RBX2660 Safety" by Jonas Pettersson, and finally "Clinical Perspective by Colleen Kraft. The Committee was then provided 30 minutes for Q & A.

The committee was given a 10-minute break before reconvening at 11:45AM ET for two back-to-back FDA presentations for a total of 60 minutes titled "Rebyota (fecal Microbiota, Live): Review of Efficacy and Safety" by Dr. Omolara Adewuni, Medical Officer, and Dr. Zhong Gao, Mathematical Statistician, both employees of CBER, FDA. The Committee was then provided 30 minutes for Questions and Answers before being released for a 40-minute lunch break.

After lunch, an Open Public Hearing (OPH) session was held in which 19 pre-registered public speakers made oral comments only. The names of OPH speakers and their oral remarks may be obtained from the transcript posted on the website.

Following the OPH session, the committee was given a 10-minute break before starting the 120-minute "Committee Discussion and Voting".

After Committee Discussion, there was a voting was session held for 2 Voting questions and Vote Explanation. The following two voting questions were presented to the Committee of 17 voting members:

Voting Question #1:

Are the available data adequate to support the effectiveness of REBYOTA to reduce the recurrence of *Clostridioides difficile* infection (CDI) in adults 18 years of age and older following antibiotic treatment for recurrent CDI?

The voting results were as follows: 13 Yes, 4 No, 0 Abstain

Voting Question #2:

Are the available data adequate to support the safety of REBYOTA when administered to adults 18 years of age and older following antibiotic treatment for recurrent CDI?
The voting results were as follows: 12 Yes, 4 No, 1 Abstain

Committee members noted the modest treatment effect estimated in each of the two placebo-controlled trials that contributed to the demonstration of effectiveness but acknowledged that even a modest treatment effect could be clinically meaningful for patients with recurrent CDI that have not responded to other available treatment options. Some committee members expressed concern about the statistical robustness of the Phase 3 Bayesian posterior credible interval resulting from the limited number of patients enrolled in the trial. However, other committee members acknowledged the difficult circumstances involved with trial recruitment in the setting of the FDA IND enforcement discretion policy for FMT to treat CDI not responding to standard therapies, and these committee members opined that given the patient population and seriousness of the condition, the Phase 3 effectiveness results were sufficiently persuasive. Some committee members also expressed concern about imbalances in serious adverse events between treatment and placebo groups; however, committee members acknowledged that FDA did not appreciate any clear basis for a causal association in its review of these adverse events, and the imbalances were difficult to interpret due to the diminishing placebo group size resulting from cross-over of the sickest placebo recipients to open-label treatment. There was broad consensus across the committee that if REBYOTA were approved, post-marketing evaluation of both safety and effectiveness would be critical to further define the benefits and risks of the product.

Following the voting discussion, Dr. Marks thanked the Members of the Committee, Sponsor, presenters, Open Public Hearing speakers, FDA presenters, and Advisory Committee staff. The meeting was then adjourned by Dr. Paydar on September 22, 2022, at 4:53 PM ET.

Additional information and details may be obtained from the transcript and the recording of the webcast of the meeting that may be viewed at:

Vaccines and Related Biological Products Advisory Committee September 22, 2022 Meeting Announcement - 09/22/2022 | FDA