U.S. FOOD & DRUG ADMINISTRATION

Vaccines and Related Biological Products
Advisory Committee Meeting
September 22, 2022

Biologics License Application for Fecal Microbiota, Live (REBYOTA)

Applicant: Rebiotix, Inc.

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Outline

- *Clostridioides difficile* Infection
- Description of REBYOTA
- Overview of the REBYOTA Biologics License Application (BLA)
  - Clinical Package
- Overview of Today's Agenda
- Voting Questions for the Committee

Clostridioides difficile Infection (CDI)

- *Clostridioides difficile* (*C. diff*) is a spore-forming, Gram-positive anaerobic bacterium
- Common cause of antibiotic-associated diarrhea and colitis
  - Half million infections in the US each year
  - 12,800 deaths in 2017
- About 1 in 6 patients who get *C. diff* infections will recur in the subsequent 2-8 weeks

https://www.cdc.gov/cdiff/what-is.html
https://www.cdc.gov/drugresistance/pdf/threats-report/clostridioides-difficile-508.pdf

Recurrent *C. diff* Infection

- **Risk factors for recurrence**
  - Older than 65 years
  - Prolonged antibiotic use
  - Weakened immune system
- **Treatment options for recurrent *C. diff* infection**
  - Antibiotics: Vancomycin, Fidaxomicin
  - Antibody-based therapy: Bezlotoxumab
  - Fecal microbiota for transplantation (FMT) therapy: unapproved, but available under IND enforcement discretion

REBYOTA: Description

- **REBYOTA (RBX2660)**: Supplied as a pre-packaged single-dose 150 mL fecal microbiota suspension containing $1x10^8$ to $5x10^{10}$ colony forming units (CFUs)/mL

- **Route of administration**: Rectal, 24-72 hours after the last dose of antibiotics for *C. diff* infection

- **Proposed indication**: Reduce the recurrence of *Clostridioides difficile* infection (CDI) in adults following antibiotic treatment for recurrent CDI

REBYOTA: BLA Clinical Package

- Rebiotix submitted a BLA for REBYOTA on November 30, 2021
- The clinical package includes data from 6 studies conducted in US and Canada
  - **Phase 2**: 2013-001, 2014-01 and 2015-01
  - **Phase 3**: 2017-01 and 2019-01
  - **Retrospective study**: 2019-02
- 978 subjects exposed to ≥1 dose of REBYOTA across the 6 studies

REBYOTA Clinical Studies

2014-01	2017-01	2013-001	2015-01	2019-01	2019-02
Phase 2 Randomized, double-blind, placebo controlled	Phase 3 Randomized, double-blind, placebo controlled	Phase 2 Open-label, uncontrolled	Phase 2 Open-label, historical controlled	Phase 3 Open-label, uncontrolled	 Retrospective, uncontrolled

Effectiveness:

- Primarily based on Bayesian analysis of data from studies 2014-01 and 2017-01

Safety:

- Pooled data from five studies: 2013-001, 2014-01, 2015-01, 2017-01 and 2019-01

Overview of Today's Agenda

9:00 am: **FDA Introduction - Biologics License Application for REBYOTA (30 min including Q & A)**

Peter Marks, MD, PhD, Center Director
Qun Wang, PhD, Review Committee Chair

9:30 am: **Current Epidemiology of *Clostridioides difficile* Infection in Adults in the United States (30 min including Q & A)**

Alice Y. Guh, MD, Centers for Disease Control and Prevention

10:00 am: **Sponsor Presentation (90 min including Q & A)**

Introduction: Lee Jones, Founder and Past President and CEO of Rebiotix Inc.
Effective Management of *C. difficile*, An Unmet Medical Need: Sahil Khanna, MBBS, MS, Mayo Clinic
RBX2660 Efficacy: Lindy Bancke, PharmD, Rebiotix Inc., a Ferring Pharmaceuticals
RBX2660 Safety: Jonas Pettersson, MD, PhD, Ferring Pharmaceuticals
Clinical Perspective: Colleen Kraft, MD, MSC, FIDSA, Emory University

Overview of Today's Agenda (Continued)

11:30 am:	**Break (10 min)**
11:40 am:	**FDA Presentations (90 min including Q & A)**
	FDA Review of Effectiveness and Safety - Fecal Microbiota, Live (Rebyota)
	Omolara Adewuni, M.D. Clinical Reviewer Zhong Gao, Ph.D. Statistical Reviewer
1:10 pm:	**Lunch (40 min)**
1:50 pm:	**Open Public Hearing (60 min)**
2:50 pm:	**Break (10 min)**
3:00 pm:	**Committee Discussion and Voting (120 min)**
5:00 pm:	**Meeting Adjourned**

Voting Questions for the Committee

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?

   Please vote Yes or No

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?

   Please vote Yes or No

Thank you!