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Seres And Ferring Go Head-To-Head In Recurrent C. Difficile Market

Two New Microbiome Medicines Launched In 2023

by David Wild

After the historic approvals of Seres' and Ferring's microbiome-based treatments for recurrent *Clostridioides difficile* infection, the two companies are waiting to see who dominates the $1bn market. Physicians say patients will steer the choice of treatments.

For patients in the US with recurrent *Clostridioides difficile* infection (rCDI), the recent approval of two safe and effective treatments is a win. Now the question for *Seres Therapeutics, Inc.* and *Ferring Pharmaceuticals* is whether either will be able to dominate the market.

Rebyota (fecal microbiota, live – jslm) was approved by the US Food and Drug Administration in November 2022 and Vowst (fecal microbiota spores, live-brpk) received the regulator's nod just a few months later, in April 2023. Both are indicated for the prevention of rCDI in adults after antibiotic treatment for an initial recurrence. Arguably the greatest differentiator between the two is their mode of administration: Rebyota is instilled as a one-time enema, while Vowst is taken as four capsules daily for three days.

"You would think 100 out of 100 patients would pick capsules, but that's not the case," Jessica Allegretti, associate professor of medicine, Harvard Medical School, told *In Vivo*. "Some people don't like taking pills. Some people want you to do the work for them. And depending on the age of the patient, how sick they are and whether they have any swallowing issues, for example, rectal administration may be more attractive."

Roughly 500,000 people in the US develop CDI every year, approximately 30,000 die from the infection, and the illness exacts an annual economic toll ranging from $796m to $6.3bn. (Also see "*CDI Market Snapshot: Microbiome Therapies Begin Descent On Landscape*" - In Vivo, 19 Dec,

2022.) Antibiotics remain the only treatment for initial CDI and fecal microbiota transplantation (FMT) has proven highly effective for recurrent cases of CDI, but it carries risks of pathogen transmission, is only available under FDA enforcement discretion, and requires that a donor be screened, or that a clinician purchase stool from a stool bank.

“The key to both of these products being approved is that providers who wouldn't have gone through the rigmarole of doing FMT previously, wouldn't have screened donors, wouldn't have bought stool from a stool bank now have something that they can prescribe that is safe and effective,” Paul Feuerstadt, assistant clinical professor of medicine, Yale University School of Medicine, told *In Vivo*. “That, to me, opens up opportunities for patients and providers in a huge way.”

The estimated $1bn CDI market has drawn interest and investment from a number of companies targeting the microbial dysbiosis at the heart of the illness. Rebyota and Vowst are the only approved microbiome-based treatments for rCDI, but several others are in the pipeline. *Finch Therapeutics Group, Inc.*’s single pill microbiome treatment, CP101, was next in line for approval until the company recently and abruptly discontinued that program as it shuttered its business. (Also see "*Finch To Wind Down, Seek Value For Pipeline Assets And IP*" - Scrip, 24 Jan, 2023.) That gives Seres and Ferring several years before the arrival of the next potential entrant, *Vedanta Biosciences, Inc.*'s VE303.

Both treatments have strong efficacy and safety, but there are some differences in their supporting bodies of evidence. For example, according to subpopulation analyses presented at Digestive Disease Week 2023, Rebyota is safe and effective in inflammatory bowel disease (IBD) and immunocompromised patients, two populations at increased risk of rCDI and of more severe outcomes. Those findings are “a big deal,” said Feuerstadt, noting that he is not aware of similar data for Vowst.

Conversely, the Phase III Vowst study included difficult-to-treat patients with at least two recurrences of CDI, while the Rebyota pivotal Phase III trial enrolled those with one or more recurrences, an arguably less refractory population.

Despite the differences in supporting evidence and mode of administration, “I think the best product is the one that patients gain access to,” said Feuerstadt, who has been involved in research on both Vowst and Rebyota.

Like Allegretti, he said patients will guide the choice of treatment, after a thorough explanation of the risks and benefits and the supporting data, and a consideration of the modes of administration.

“I don't practice in a paternalistic way. We decide together what they're most comfortable with,”

Feuerstadt emphasized.

While Allegretti indicated oral administration would not always be the first choice for patients, a June 5 note by analysts at TD Cowen placed a strong emphasis on the value of Vowst's pill form, saying there was a clear patient preference for this approach. They also noted concerns about a lack of dose response seen in the Rebyota clinical program.

With patients ultimately expected to decide between Rebyota and Vowst, Seres and Ferring executives are thinking how they can influence end-users' decisions. *In Vivo* contacted both companies to hear more about their respective strategies.

Eric Shaff

President And CEO
Seres

What is your commercialization strategy with Vowst? What are your anticipated launch milestones?

Vowst was approved on April 26 and became available to patients on June 5. Seres entered into an agreement with Nestlé Health Science in July 2021 to jointly commercialize Vowst in the US and Canada. Under the terms of the agreement, Nestlé Health Science will leverage its existing infrastructure, including a gastrointestinal sales force and payer access team, to commercialize Vowst and will profit share 50/50. The Nestlé sales teams have been educating healthcare practitioners and seeking insurance coverage for Vowst over the past two months to ensure broad patient access to this important new therapy.

In connection with the 2021 License Agr

What is your pricing strategy?

Seres is driven by our mission of improv
Vowst is the first and only FDA-approve
We, along with our collaborators at Nest
We considered the following factors on
Both Seres Therapeutics and Nestlé He

Lionel Fajolle

Vice President Of Specialty Care
Ferring Pharmaceuticals US

Now Vowst is on the market, what is your commercialization strategy going forward for Rebyota?

Our main mission has always been and continues to be centered on the patient. In the many months leading up to the approval and launch of Rebyota, we were relentless in our preparation and focus on the patient. At Ferring, we strongly believe that ensuring broad patient access as well as an optimal patient experience with only one dose are keys to addressing the significant burden placed on patients and the healthcare system from rCDI.

A first mover advantage is first and foremost a demonstration of leadership in action. Being first to market concretely translated into being first to help patients, and that sense of pride is