

## Flagship Takes a Stab at Microbiome Therapy With Seres Health

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We live every day with trillions of bacterial neighbors that do all sorts of mysterious things in our guts, good and bad. The broadening scientific understanding of the “[microbiome](#),” powered by the modern tools of genomic analysis, has been in the news for a while.

Today, Cambridge, MA-based [Flagship Ventures](#) is betting the knowledge has come far enough that it can be the basis for developing new drugs.

The latest company to emerge from Flagship VentureLabs, [Seres Health](#), is coming out of stealth mode (at least partially) after a little more than two years of toiling behind closed doors. The Cambridge-based startup has raised \$10.5 million in Series A venture financing from Flagship, Enso Ventures, and others. It has 15 employees, says co-founder and CEO [David Berry](#). Seres has the usual big-name [scientific advisory board](#) and has recruited [Roger Pomerantz](#), the former head of worldwide licensing and acquisitions at Merck, to be its chairman of the board.

Unlike most biotech startups seeking their first bit of public attention, Seres has advanced all the way to its first clinical trial, and dosed its first patient, with an internally developed treatment. The initial product candidate is for antibiotic-resistant infections with [C. difficile](#), a bug that causes nasty diarrhea that can sometimes be deadly.

Given that the “microbiome” is a catch-all term for trillions of bacterial species with different genomes, it’s a hard thing to understand in detail. The genes of all those bugs express themselves differently when you’re healthy or when you’re sick, adding to the complexity. It would be understandable for drug developers to throw up their hands and say it’s impossibly complex, impossible to figure out where a drug should appropriately intervene.

Most of today’s antibiotics aren’t too concerned with the subtle balancing act between “good and bad” bacteria, and act more like a “hand grenade” that wipes out all kinds of bacteria, Berry says. That indiscriminate killing potentially can give rise to all kinds of odd long-term health consequences.

The goal at Seres, Berry says, is to essentially tread more lightly with drugs that alter what he calls the “functional ecology” of a diseased person’s microbiome, and tip it back into a healthy state. At least in concept, Seres is shooting for the same result as what doctors see from [fecal transplants](#)—in which stool from a healthy person is transplanted into a diseased person.



David Berry, CEO of Seres Health

“The microbiome has been an area we’ve been intrigued by all the way back to 2006,” Berry says. “We’ve been looking at it, trying to figure out what the signal is relative to the noise. What we started to realize is that there’s a fundamental underlying biology of the microbiome that hadn’t previously been fully understood and appreciated.”

Here's the basic gist of what Seres does: The company takes stool samples from populations of people who are healthy, and diseased populations, and looks for what might be awry in the bacteria. Once it has an idea of the "functional ecology" at work in the microbiome of the diseased populations, it selects a specific group of what you could call "good" bacteria that it believes will co-opt the disease networks and tip the balance back toward that of health, Berry says. "We've had an ability to do that, which has produced a series of different candidates for us," he says.

The products themselves are a group of live bacterial organisms that Seres says it can package into a pill form like any other. He didn't say how many of these "good" bugs have to go into a single pill, or how Seres manufactures these products consistently. It's not a fermentation-based process, Berry says.

When I asked him how these products are manufactured consistently up to FDA standards—a really important thing—he declined to go into detail other than to say, "We've spent quite a bit of time figuring this out. We have quite a bit of IP around this. Making sure you get right organisms and you can formulate them properly is quite important."

Berry added that Seres has recruited John Aunins, an expert in vaccine manufacturing at Merck, to help it nail down the intricacies of consistently making a live biological product into a drug. Many vaccines are made of live, weakened viruses, so the idea of making a live product has some precedent.

There are a couple of other notable startups taking a crack at drugs that work on the microbiome—Cambridge, MA-based [Vedanta Biosciences](#) and South San Francisco-based [Second Genome](#). Both of those companies have secured some modest support from Johnson & Johnson, and both are still in preclinical development. Both also are different than Seres. Second Genome is developing traditional small-molecule chemical compounds as therapies, and while Vedanta is also using a live cocktail of microbes, it is aiming that product candidate against inflammatory bowel disease.

Peter DiLaura, the CEO of Second Genome, said fecal transplants have been effective, which has stirred excitement about the potential of what live bacterial therapeutics might do. One drawback, however, will be the manufacturing challenges, he says.

"It's certainly an interesting approach—there are questions about the sort of mechanism of action they're using," DiLaura says.

The lead drug candidate to come from Seres's approach to microbiome drug development is called SER-109. It's designed to treat patients who have *C. difficile* infections that are resistant to vancomycin, a powerful antibiotic given in hospitals. This bug, which often lurks in hospitals and strikes the elderly, is estimated to kill as many as 14,000 people a year in the U.S., Seres says, although data has traditionally been hard to gather on the true extent of the bug's reach. By going after *C. difficile*, Seres essentially aspires to compete with Lexington, MA-based Cubist Pharmaceuticals (NASDAQ: [CBST](#)), which recently acquired a potent antibiotic against "C. diff" from [Optimer Pharmaceuticals](#).

Although Seres says it has begun its first clinical trial, there is no public listing of the trial on [clinicaltrials.gov](#). Berry said he wasn't ready to discuss any details of the study, such as how many patients it seeks to enroll, whether it will be randomized and controlled, or which people are involved at which clinical sites.

All of the technology at Seres has been internally developed, meaning none of it comes from any license from an external source, Berry says. Besides the lead product candidate against *C. diff* infections, Seres aims to make microbiome-based treatments against infectious, metabolic, and inflammatory diseases.