

## VENTUREWIRE

### Startups Look to 'New Frontier' of Microbiomes to Fight Disease

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A crop of venture-backed companies aims to treat a wide range of diseases by tapping into the powers of bacterial populations flourishing inside the body.

More than 100 trillion microorganisms live in and on humans. While it is a skin-crawling thought, their presence is essential: Microbes synthesize vitamins, aid digestion and help the immune system function properly. Emerging research suggests that imbalances in this microbial population, or microbiome, cause or contribute to illnesses.

Through microbiome-based treatments, startups hope to treat infections, diabetes, autoimmune diseases, rare disorders and other conditions. If they succeed they could shake up several multibillion-dollar pharmaceutical markets.



Total amounts raised by several noteworthy microbiome startups.

"It has the potential to be a new frontier in medicine," **Leerink Partners** analyst Joseph Schwartz said.

In June, venture-backed **Seres Therapeutics Inc.** went public on the promise of a microbiome-based therapy for recurrent infections from *Clostridium difficile*, or *C. difficile*, a bacterium that causes diarrhea and inflammation of the colon. Seres, founded in 2012, raised more than \$130 million in venture funding from **Flagship Ventures** and others.

While early research is promising, the approach remains unproven. Companies manipulating microbial populations also must take precautions to avoid causing new health concerns or other unintended consequences.

"There is tremendous potential for the microbiome to improve health," said Jessica Metcalf, a microbiome researcher at the **University of Colorado Boulder** and the **University of California, San Diego**. Microbial therapy "has to be well-studied for every disease type to make sure we're not [getting] an outcome we don't expect."

Startups are building on an early approach to microbial therapy, fecal transplants, in which a healthy donor's stool is used to repopulate a patient's microbiome with beneficial bacteria. The therapy, which treats recurrent *C. difficile* infections, cures up to 90% of patients when given through colonoscopy, according to Sasha Lieberman, a nonprofit management fellow for OpenBiome, a nonprofit stool bank that supplies donated fecal material for transplants.

In recent years, new DNA-sequencing and software systems have enabled scientists to characterize microbial communities and learn how they function in humans. This has led to the creation of companies like Seres, which aims to replace fecal transplants with an oral capsule. The capsule contains spores, which are like seeds for about 50 bacterial species found in healthy people.

The medicine causes certain bacteria to multiply in the colon and consume nutrients that would otherwise feed *C. difficile*. After curing 29 of 30 patients in early clinical trials, the product has moved into a larger clinical studies. Seres also aims to treat the inflammatory-bowel disease ulcerative colitis through a separate drug that recently entered the clinic.

Venture-backed competitor **Second Genome Inc.** hopes to tame bowel inflammation by targeting a human receptor activated by molecules that microbes release. Because its product is a conventional, small-molecule drug, Second

Genome avoids regulatory and manufacturing hurdles that come with developing a microbial therapy, Chief Executive Peter DiLaura said. Second Genome, formed in 2009, has attracted \$16.2 million from **Advanced Technology Ventures**, **Morgenthaler Ventures** and others.

Seres and Second Genome aim to help people who don't benefit from first-line inflammatory-bowel treatments and prevent these patients from needing immune-suppressing medications. The potential of microbiome therapy in inflammatory-bowel disease has caught the attention of top companies in the field, including **Janssen Biotech Inc.** and **AbbVie Inc.**

Janssen has joined with Second Genome to study bacterial populations' role in ulcerative colitis, while **AbbVie** is collaborating with startup Synlogic to treat inflammatory-bowel disease through synthetic biotics, or bacteria engineered to perform therapeutic functions. Synlogic, which has secured \$70 million from investors such as Atlas Venture and **New Enterprise Associates**, is also developing synthetic biotics for the rare conditions urea cycle disorder and phenylketonuria.

Startups also seek to improve existing drugs. **MicroBiome Therapeutics LLC** combines the Type 2 diabetes medicine metformin with one of its "microbiome modulators" that is designed to reduce metformin's gastrointestinal side effects and improve its glucose-lowering abilities. MicroBiome, which has raised an undisclosed amount from investors such as BVM Capital, has other microbiome modulators in development that could be used for prediabetes, diabetes and other conditions.

Evelo Therapeutics, which recently launched with \$35 million from Flagship, plans to use certain bacteria to stimulate an immune-system attack on cancer, an approach that may be particularly effective when combined immunotherapies known as checkpoint inhibitors. By comparing bacteria associated with tumors with microbes from healthy people, Evelo also seeks to understand tumor microbiomes, which could lead to improvements in current cancer therapies and to new, microbiome-based treatments.

Microbiome companies have moved into a growing number of diseases as the connection between microbes and health has emerged. At one time the microbiome was thought to be limited to a certain set of niches, but now its impact is known to be much more widespread, according to Flagship General Partner David Berry.

"The microbiome is not just a local phenomenon, it's effectively everywhere," Dr. Berry said.

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