

Beneficial bugs

Microbiome R&D uncovering new therapies for a range of diseases

By Peter Winter, Editor

The growing scientific and public interest about the role played by microorganisms in the maintenance of overall health and prevention and treatment of disease has not gone unnoticed by federal regulators. In a statement by FDA Commissioner Scott Gottlieb in August, he commented that “the U.S. Food and Drug Administration is playing a key role in sorting through the science and the science fiction of this evolving field.”

In addition, the agency convened a workshop along with the NIH last week that discussed the use of microbiome-based products and how manipulation of the microbiome could potentially be used to prevent or treat a variety of different diseases. (See *BioWorld*, Sept. 18, 2018.)

The initiatives by the FDA will be welcomed by the industry as scientific research about the microbiome is now being translated into products that are poised to begin clinical testing. That increasing development is leading to expansive market projections, with some analysts predicting a 10 percent to 20 percent compound annual growth over the next five years.

Funding flows

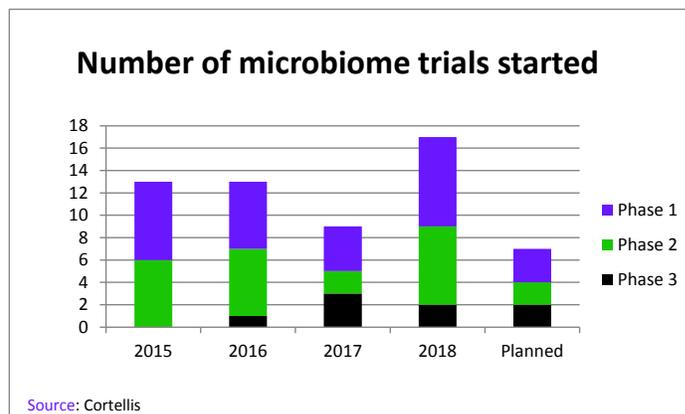
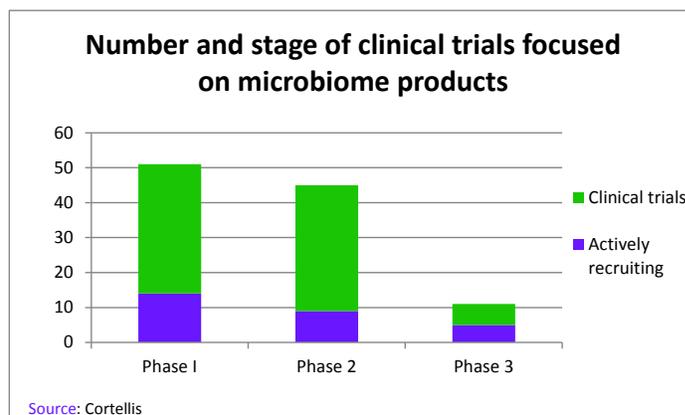
The dramatic emergence of the field is attracting significant investments. Evelo Biosciences Inc., for example, graduated to the public ranks following an IPO completed in May, which netted the firm \$75.8 million. (See *BioWorld*, May 10, 2018.)

The company is exploring ways to leverage the ability of bacteria to activate the immune system to fight cancer by targeting the gut-body network.

Preclinically, Evelo showed that certain monoclonal microbials can down-regulate or up-regulate immune responses throughout the body by acting on the gut-body network.

In its second-quarter financial report, the company updated its pipeline progress, reporting that the first subject was dosed in April in its 96-subject phase I trial of lead product candidate EDP-1066, a monoclonal microbial for the treatment of inflammatory diseases. The study is designed to evaluate the safety and tolerability of a range of daily doses of EDP-1066 in healthy volunteers and in patients with psoriasis and atopic dermatitis.

Evelo also gained FDA acceptance for its IND to begin a 70-patient open-label phase II trial of EDP-1503, a monoclonal microbial for the treatment of cancer, to be conducted at the University of Chicago. It is designed to evaluate the safety,



tolerability and efficacy of EDP-1503 in combination with a checkpoint inhibitor in patients with metastatic melanoma. The company has entered a research collaboration with scientists at Harvard University to study the gut-body network to further elucidate the mechanisms by which microbes acting on cells in the gut have the potential to treat disease elsewhere in the body. Under the multiyear agreement, Evelo has an exclusive option to license from Harvard intellectual property rights that may arise from the research collaboration.

Other companies receiving funding this year include:

- Kaleido Biosciences Inc., of Bedford, Mass., which generated \$101 million in an oversubscribed series C financing. It plans to use the proceeds to advance its pipeline. The company is developing chemistries to systematically drive functions of the microbiome organ using its microbiome metabolic

therapies (MMTs) to direct those functional outputs to treat disease and improve overall health. It is advancing a pipeline of MMTs in multiple therapeutic areas, including rare genetic disorders.

- Microbiome therapeutics company Finch Therapeutics Group Inc., which closed an oversubscribed \$36 million series B financing in March. It uses machine learning algorithms informed by high-throughput molecular data to reverse engineer successful clinical experience, building upon the science of fecal transplantation.
- Nextbiotix SA, which raised €7 million (US\$8.2 million) in a series A round to take a microbiome-based therapy for treating inflammatory bowel disease into clinical trials. The company's lead program will deploy a single strain of *Faecalibacterium prausnitzii*, a dominant member of the human gut microbiota, as a vector for molecules with immunomodulatory and pain-relieving properties. The bacterium constitutes about 5 percent of the fecal microbiota of healthy individuals but is depleted in the microbiome of IBD patients. (See *BioWorld*, July 6, 2018.)
- Ubiome Inc., which last raised \$83 million from a series C financing round. The company combines its precision sequencing of microbiomes with machine learning and artificial intelligence to assist in the development of wellness products, clinical tests and therapeutic targets. It claims to have the largest human microbiome database, with more than 250,000 samples at present. Its Smartgut product is a stool test that identifies microbes in the gut for patients with chronic gut conditions such as IBD, IBS, Crohn's disease and ulcerative colitis.

Early days

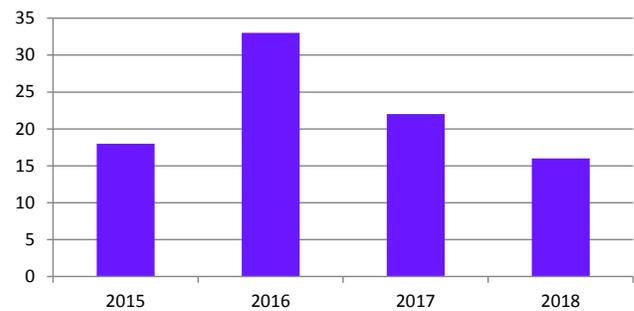
Potential microbiome therapies are still at preclinical and early stage clinical testing, but the number of products reaching clinical trials is increasing, according to data derived from Cortellis Clinical Trials Intelligence. (See Number and stage of clinical trials, and Number of microbiome trials started, page 1.)

The microbiome has been implicated in a wide range of conditions and can provide insights into predispositions to diseases ranging from IBD, metabolic disorders and cancer. The major focus of therapies under development are in gastroenterology, where understanding the gut microbiome in fact could eventually lead to new therapies. A number of companies are working in that area, including Salix Pharmaceuticals Inc., a wholly owned subsidiary of Bausch Health Companies Inc. In August, it entered a research agreement with Cedars-Sinai Medical Center to further investigate the microbiome in the treatment of GI disorders. Salix has the option to acquire any therapeutic invention discovered through the research.

Partnering

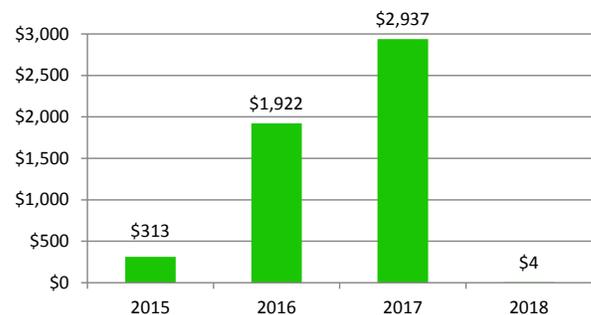
Not surprisingly, companies have been jockeying to gain a foothold in this exciting and emerging field and, as a consequence, the number of partnership deals that have been

Number of microbiome deals



Source: Cortellis

Value of microbiome deals (\$M)



Source: Cortellis

inked over the past four years has risen dramatically. (See Number and Value of microbiome deals, above.)

Microbiotica Ltd., for example, secured a \$534 million deal with Genentech Inc. to apply its microbiome technology in a broad-ranging collaboration in IBD. (See *BioWorld*, June 7, 2018.)

The company will analyze bacterial DNA in fecal samples taken before, during and after treatment, from patients participating in Genentech trials in IBD. That will generate microbiome signatures of drug response, for use in stratifying clinical trials, and for use as companion diagnostics.

Microbiotica's platform technology comprises the world's largest microbiome culture collection that has been built over a period of 10 years at the Wellcome Trust Sanger Institute.

In June, Lyon, France-based Maat Pharma, a clinical-stage microbiome therapy company, and SATT Lutech, entered a licensing agreement under which the company will receive global exclusive rights for the therapeutic application of allogeneic fecal microbiome transplants (FMT) to treat acute graft-vs.-host disease in patients following stem cell transplantation. The technology is based on research performed within the Clinical Hematology Department at Saint-Antoine Hospital and Sorbonne University, Paris, France.

The company said it is also developing FMT drugs to prolong survival in acute myeloid leukemia patients by reintroducing a functional microbiome after chemotherapy. ♦