diagnostic tool, if and when the recent findings are validated in a large prospective cohort study. "Once a patient has been diagnosed, we could look at their microbiome and tailor their treatment based on it," says Routy. Eventually, doctors could even modulate the microbiome to improve the treatment, but Routy says that is a few years away.

Biopharma companies are keeping close watch. Seres Therapeutics will collaborate with Wargo to develop a bacteria-containing pill to turn an unfavorable microbiome into a favorable one. David Cook, CSO of Seres, says the company had been working with spore-forming Clostridiales bacteria to treat *C. difficile* infections for some time. In 2016, Seres' lead compound, a stool-derived bacterial spore mixture for preventing *C. difficile* failed in mid-stage trials (*Nat. Biotechnol.* **34**, 1004–1005, 2016). The company then saw an opportunity to apply that knowledge to immunotherapy. "It was a happy accident that her [Wargo's] findings coincided with our area of deep expertise," he says.

Seres is now planning to start a phase 1 clinical trial with a rationally-designed mix of live bacteria, SER-401, specifically to improve PD-1 checkpoint inhibitors. The company will team up with Wargo and the Parker Institute for Cancer Immunotherapy in San Francisco, in patients with advanced metastatic melanoma. The company will not publicly disclose the composition of the bacterial cocktail yet, but Cook says it is "based on the signature seen in Dr. Wargo's data."

Seres has already seen some promising phase 1 results with a synthetically derived (microbiome inspired) live biotherapeutic product, SER-287, in patients with ulcerative colitis. "It established the ability to therapeutically modulate the immune system using microbiome drugs," says Cook. "With immune checkpoint inhibitors we're trying to do the same."

Another company, the Paris-based Enterome is taking a different approach. Instead of using live bacteria, its focus is on the chemicals and metabolites secreted by bacteria, which the company thinks will be more effective. "It is very difficult for the body to accept foreign bodies," says Pierre Belichard, the company's CEO. Enterome has two discovery programs focused on bacterial molecules to boost immunotherapy. One is a partnership with New York-based Bristol-Myers Squibb aimed at identifying bacteria-derived biomarkers for enhancing clinical responses for patients treated with the pharma's immunotherapy drugs (*Nat. Biotechnol.* **35**, 808, 2017). The biotech is also collaborating with Bristol-Myers Squibb to find bacteria-derived small molecules with a general adjuvant effect on checkpoint inhibitors. The other is an in-house program to spot bacterial gene sequences that mimic tumor epitopes that activate the immune system.

"Human [tumor] epitopes are unique. But if we compare them to ten million microbial sequences, in each and every case we find good mimics," says Christophe Bonny, Enterome's CSO. The idea is that a drug containing those epitopes can act like a vaccine, to activate the vast pool of T cells in the gut to target the tumor. The company has one candidate, EO2315, in preclinical development for glioblastoma, which it hopes to move into clinical trials later this year. But in principle any type of tumor should be susceptible to this approach, says Bonny.

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Evelo Biosciences, a Google-backed biotech based in Cambridge, Massachusetts, is working with Gajewski to develop and commercialize a drug based on his work. In July, Evelo raised $100 million to start testing in clinical trials single strains of naturally occurring microbes to act as cancer immunotherapies.

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Roche pays $1.7 billion to target tumors' genetic signatures

Roche will acquire oncology player Ignyta for $1.7 billion cash, in a deal that gives the Basel-based pharma entrectinib, a targeted agent designed to block cancer development driven by certain gene rearrangements, irrespective of where in the body the tumors are located. Alterations in the three *NTRK* genes as well as the *ROS1* and *ALK* receptor tyrosine kinase genes result in fusion proteins that transform healthy cells into cancer cells. Ignyta's investigational oral drug entrectinib is in the phase 2 STARTRK-2 basket trial where patients are assigned to different baskets according to tumor type and gene fusion signatures. In October, Ignyta, of San Diego, reported interim data showing that among patients with *ROS1* fusion-positive non-small cell lung cancer, entrectinib led to an overall response rate of 78% (25 out of 32 patients), as measured by investigator assessment, and 69% (22 out of 32 patients), as measured by blinded independent central review. Ignyta plans to seek entrectinib's approval to treat fusion-positive solid tumors, regardless of tissue of origin. Another company, Loxo Oncology, is also developing a tissue-agnostic tropomyosin receptor kinase (TRK) inhibitor to treat cancers where the *NTRK* genes (that encode the TRK family of proteins) have undergone fusion events. These fusions result in chimeric oncoproteins leading to ligand-independent activation and overexpression in tumors of all types (*Nat. Biotechnol.* **35**, 694–695, 2017). In November, Loxo partnered with Bayer of Leverkusen, Germany, to develop and commercialize larotrectinib (LOXO-101) and a second selective TRK inhibitor. Loxo has rights to larotrectinib, which inhibits TRKA, TRKB and TRKC from Array BioPharma.

"What [AbbVie has] done with Humira is just as unfair, just as morally wrong, but they did it over five years," said Ben Wakana, executive director of Patients for Affordable Drugs, reflecting on the 100% increase in the price of Humira since its launch in 2012, from $19,000 to more than $38,000. *The New York Times*, 6 January 2018.

"Men named Michael outnumber female CEOs presenting at #JPM18." Headline, *STAT*, 7 January 2018.

"Cyclodextrin has been stolen and now sold for $200 million dollars!! It's going to a billion++ dollars when approved. This was a drug funded and created by all of you who helped us." Chris Hempel, mother of twin girls with Niemann–Pick Type C disease, who developed cyclodextrin as a treatment for the disease based on work at UCSF, but now that Sucampo Pharmaceuticals has bought the rights to the drug, she fears the National Niemann–Pick Disease Foundation will be cut out from the process, including the financial benefits. *Forbes*, 8 January 2018.