

FDA approves PARP inhibitor for ovarian cancer

Months ahead of schedule, the US Food and Drug Administration approved Tesaro's small-molecule Zejula (niraparib) as a maintenance treatment for women with recurrent ovarian, fallopian tube or primary peritoneal cancer irrespective of their BRCA mutation or other biomarker status. The Waltham, Massachusetts-based biotech received a green light on March 27, far in advance of the Prescription Drug User Fee Act June 30 decision date, to treat women with ovarian cancer with partial or complete responses to previous platinum-based chemotherapy. Zejula is the third drug approved that inhibits the poly-ADP-ribose polymerase (PARP) enzyme, a DNA repair system that helps tumor cells repair damaged DNA strands; first was London-based AstraZeneca's Lynparza (olaparib) (*Nat. Biotechnol.* **33**, 116, 2015) and second, Boulder, Colorado-based Clovis' Rubraca (rucaparib). But Tesaro's drug could command a larger market share because, unlike its rivals, Zejula benefits not only women who test positive for the germline BRCA mutation. In the phase 3 trial, the small-molecule drug delayed cancer progression by 12.9 months compared with 3.8 months in the control arm. At the time of going to press, Tesaro had not disclosed Zejula's price but the company predicts \$1.9 billion a year in sales by 2022. The firm is also planning to conduct new trials with Zejula for metastatic ovarian, breast and lung cancers, including combination studies with Kenilworth, New Jersey-based Merck's anti-PD-1 antibodies Keytruda (pembrolizumab) and Basel-based Roche's anti-VEGF Avastin (bevacizumab). In March 2016, Tesaro entered a collaboration with Janssen Biotech, a Johnson & Johnson company, over commercialization rights to the drug in prostate cancer. New York-based Pfizer may be next in the approvals queue with tolaparib, a PARP inhibitor it acquired with the purchase of San Francisco-based Medivation for \$14 billion in 2016.

“The potential for quackery & snake oil salesmanship this will result in is mind boggling.” Anirban Maitra, scientific director of the Ahmed Center for Pancreatic Cancer at MD Anderson Cancer Center in Houston, tweets on FDA's decision to allow 23andMe to sell direct to consumer genetic testing results for ten conditions. (*Forbes*, 6 April 2017)

“This whole idea of genomic risk for common diseases is a real deal. I think 23andMe and other companies provide information and education; I think that's a good public service.” Eric Topol, director of the Scripps Translational Research Institute in La Jolla, California, comments on the FDA's decision to allow 23andMe to sell direct to consumer genetic testing results for ten conditions. (*Forbes*, 6 April 2017)

you can clean up the data and put it in a structured format that's ready for those algorithms.”

Indeed, large seed companies such as Monsanto, DuPont and Syngenta have for years been developing such machine learning tools—algorithms that can learn from data and make predictions. The *in silico* models predict biological outcomes, enabling breeders to focus on the genetic combinations with the highest probability of success in the field. To train the algorithms, the companies collect huge volumes of phenotypic and genomic data. And of course, the companies keep these tools close to the vest.

Now, Benson Hill Biosystems, a St. Louis, North Carolina-based crop improvement and cloud biology company, aims to make big data analyses available to small players. The company offers a computational platform called CropOS that can crunch genetic and phenotypic data to guide breeders' decisions on trait development and breeding regimes. It first developed the algorithms to help tweak photosynthesis. The company opened up the platform two years ago to other players in exchange for a fee or future royalties. The system runs on Amazon Web Services, a cloud computing platform that has been a huge enabler for small companies.

“Big seed guys have teams of people doing computational stuff, but for every company that has that in-house, there's a hundred breeders that don't,” says Matthew Crisp, a founder of Benson Hill. “That's the primary audience that needs to be empowered so that they can move the dial on this space.”

The more data people contribute to CropOS, the better the algorithms will get. “It's a great business model. They're convincing people to throw in their data so that everybody can benefit from everybody else's data,” says Peterson at The Yield Lab. “They're using the power of community.”

Access to a computational platform should drive down the cost and time of bringing a new plant trait to market, says Maughan, who is also a founder of predictive breeding company Hi Fidelity Genetics in Durham, North Carolina. Today's startups, equipped with such platforms, along with access to cloud computing and new gene editing tools such as CRISPR that make genetic modification quick and cheap, could, for the first time in years, compete in a marketplace dominated by corporate giants. “We're bullish on this,” says Maughan. “I don't think bringing a plant to market has to cost \$100 million.”

But many VC investors are still cautious. Few have more than one plant trait company in their portfolios. “There are alternative and

maybe better ways to crack that nut,” says Peterson. For example, instead of engineering a plant to fix nitrogen, equip it with a microbe that can do it for the plant, he says. “There are novel ways of doing what genetically modified crops do, but potentially better, cheaper and faster.”

Exiting a plant trait company presents a quandary for early-stage investors. For those who have turned to the public markets, “it's been a disaster story,” says Austin. Share prices for small biotech crop companies have “all just dropped off a cliff.” Exits typically come through acquisition by a major seed company—an increasingly narrow channel.

But that pool is poised to change. “We're starting to see interest from rather unique places,” says Scott Horner at Middleland Capital in Washington, DC. “That's the thing I've been most surprised about—the amount of inbound interest from the non-usual suspects.” Horner declined to name specific groups interested in his portfolio companies, but public examples abound. ChemChina, a state-owned chemical company in Beijing, purchased Syngenta for \$43 billion, and in April cleared antitrust hurdles.

Land O'Lakes, a food company in Arden Hills, Minnesota, last year bought Ceres, a biotech plant trait company in Thousand Oaks, California, that develops crops for animal feed. Land O'Lakes also bought satellite imaging company Geosys (Toulouse, France), and merged with crop nutrients firm United Suppliers (Ames, Iowa), which is developing data-based tools for farmers.

Other signs that investors are overcoming their reticence came in March, when Benson Hill Biosystems closed a \$25-million series B financing round, and crop microbe developer Inocucor Technologies of Montreal, drew in \$38.8 million. In the same month, crop epigenetics startup EpiCrop Technologies of Lincoln, Nebraska, raised \$3.2 million, and pennycress breeder Arvegenix of St. Louis, raised \$2.4 million.

And Sanjeev Krishnan, managing director at S2G Ventures in Chicago, says interest from outsiders will grow. “I think there will be new entrants that we don't even know about yet.”

Emily Waltz Nashville, Tennessee

“Asking the NSF to certify that what they do is in the national interest is like asking the Defense Department to certify that what they do is in the national interest.” Jonathan Moreno, a professor of medical ethics and health policy at the University of Pennsylvania, who served on President Barack Obama's transition team in 2008. (*STAT* 10 April 2017)