

IN brief

Isis inks two antisense deals

Isis Pharmaceuticals of Carlsbad, California, ended 2012 with two noteworthy deals, one with Cambridge, Massachusetts-based Biogen Idec and another with London, UK-based AstraZeneca around five cancer targets. Under the Biogen Idec deal, Isis receives an upfront payment of \$30 million, and up to \$200 million in license fees, plus milestone payments per program, to develop and commercialize Isis' antisense drugs against three undisclosed neurologic targets. These new programs expand a previously established collaboration to develop antisense drugs for spinal muscular atrophy and myotonic dystrophy type 1. The AstraZeneca deal nets Isis \$31 million in the near term plus potential milestone payments. That deal includes an Isis compound targeting STAT3. In October, a US Food and Drug Administration (FDA) advisory panel meeting for the company's antisense drug, Kynamro (mipomersen), turned into a "proxy [discussion] on antisense technology," says Stephen D. Willey, an analyst at St. Louis-based Stifel Nicolaus. The recent deals indicate that "Clearly, potential partners know that Isis has been refining and improving that technology," he adds. Isis CEO Stanley Crook concurs. "Our second-generation antisense drugs have much higher affinity, increased potency and are more stable," he says. The company has 28 drugs in development. "Investors are particularly interested in the spinal muscular atrophy program now," says Willey. The FDA's decision on Kynamro was due January 29.

Malory Allison

Forty fight rust and rot

More than 40 institutes around the world are teaming up to use biotech tools to improve food security in sub-Saharan Africa and India. The Sustainable Crop Production Research for International Development (SCPRID) will provide a total £16 (\$25.5) million for 11 projects aimed at developing crops that will resist pests or survive in harsh environments. Each project will include at least one UK-based partner and another from a developing nation. Grants will be funded by the UK Biotechnology and Biological Sciences Research Council (BBSRC), the Department for International Development, the Bill and Melinda Gates Foundation and India's Department of Biotechnology and will be administered by the BBSRC. Geneticist Cristobal Uauy at the John Innes Centre in Norwich, UK, will lead a five-year sequencing project on wheat rust spread and evolution. His team, including collaborators in Kenya, Ethiopia and India, will screen germplasm from the open-access Watkins Landrace Wheat Collection. Uauy's collaborator, pathologist Ruth Wanyera of the Kenyan Agricultural Research Institute in Njoro, aims to develop new rust-resistant wheat varieties adapted to local conditions. Although SCPRID grant holders' intellectual property resides with their host institutions, which can conduct commercial development, they have agreed to offer BBSRC a royalty-free license to distribute technologies "at reasonable cost to people most in need in developing countries." Lucas Laursen

Commercial entities have been slow to come aboard the TB race until fairly recently, Spigelman says. "Some of the drug companies are putting resources behind [TB], such as Janssen with Sirturo and Otsuka with delamanid, but they are few and far between," Spigelman says. The first new chemical entity for TB to become the subject of a conventional licensing deal in decades was ethylenediamine (SQ109), developed by Sequella of Rockville, Maryland. In April 2011, ethylenediamine garnered an equity investment along with potential milestone payments and royalties from a syndicate of Russian venture capitalists, Maxwell Biotech Venture Fund, in exchange for the rights to develop the treatment in Russia. How much Maxwell invested upfront was not disclosed, but the deal could be worth up to \$50 million to Sequella.

Alan Klein, executive vice president of corporate development at Sequella, says Sirturo's success "should engender a bit more activity" by companies that have stayed on the sidelines, and spur others "who may have had an inactive or semi-active TB program to get back into it, either through their own research and development efforts" or a deal with another firm. At the moment, the space is driven mainly by research collaborations between firms—Sequella has them with Janssen, Pfizer and Sanofi "to name a few," Klein says—and by agreements with not-for-profit groups.

Thanks to Sirturo, New Brunswick, New Jersey-based J&J may earn a priority review voucher, an incentive created by FDA in 2007 to reward companies developing drugs to treat neglected tropical diseases. The approval also provides other companies

with the regulatory parameters for moving MDR-TB drugs towards approval (FDA also awarded the big pharma an accelerated approval for Sirturo). "We're taking the same tack that J&J is taking," Klein says. "We've completed our phase 2a, and we're moving into phase 2b." The next trial will be similar to J&J's trials, he says, serving as a phase 2b/3 study for registration globally. The exact mechanism for SQ109, Sequella's second-generation antibiotic is unclear, but research suggests that the compound (a 1,2-diamine related to ethambutol) could work by disrupting the microorganism's cell wall assembly.

Now that it's approved, it is unclear how soon Sirturo might reach patients in the countries where it's most needed. "Any new bedaquiline-containing regimen for MDR would have to be adopted by the government, and only then can we start using it," says Shelly Batra, co-founder and president of New Delhi-based Operation ASHA, which provides TB treatment, education and compliance monitoring in 2,053 slums and villages in six Indian states, as well as two provinces in Cambodia.

Meanwhile, Andries hopes Sirturo will change how experiments are done to find new MDR-TB candidates. "We lost a lot of time in the search for new antibiotics by taking the wrong strategy, which is target-based research," he says. "If you work as a researcher in a university, or at a place where you do not have access to a big library of original compounds, then that is obviously the only thing you can do. But if you have access to such a library, it would be a shame to test them for single targets only."

Randy Osborne Atlanta

IN their words



"I had allowed myself to slip into a world of relativism, where the ends justify any means. It's very hard to imagine how I became that kind of person." Joseph Skowron III, a former fund manager at FrontPoint Partners, on being sentenced to a five-year

prison term for insider trading. The firm collapsed after illegal transactions involving a Human Genome Sciences' hepatitis C drug. (*Bloomberg News*, 27 November 2012)

"The GE salmon has no socially redeeming value. It's bad for the consumer, bad for the salmon industry and bad for the environment. FDA's

decision is premature and misguided." Andrew Kimbrell, executive director of the Center for Food Safety, a Washington, DC-based advocacy group, following the FDA's >16-year assessment of AquaBounty's genetically engineered salmon. (*New York Times*, 21 December 2012)

"We're through many cost-cutting programs, restructurings and portfolio arrangements. When you put that together with record levels of cash available and improving, but still moderate R&D productivity, we think there will be more big pharma M&A activity in 2013." Henry Gosebruch, managing director of health-care mergers and acquisitions at JPMorgan Chase & Co. Biotech analysts predict \$10-billion-plus deals in 2013. (*Bloomberg News*, 7 January 2013)