Gates champions CureVac

German biotech CureVac racked up $100 million in new funding to advance vaccines based on its mRNA platform. In November, Bill & Melinda Gates Foundation joined German billionaire Dietmar Hopp to back the University of Tubingen spin-off, which has now accrued $330 million. The venture syndicate included management firm Baillie Gifford, Chartwave Limited, Coppel Family, Elma Investments and Sigma Group. Tubingen-based CureVac uses natural, chemically unmodified mRNAs to develop a range of therapeutic and prophylactic vaccines against cancer and infectious diseases. Its most advanced candidate is in a phase 2b study in prostate cancer. The company is also exploring the platform to formulate molecular therapies that coax cells to produce their own protein therapeutics, an approach that has garnered close to a billion dollars for preclinical player Moderna Therapeutics. Earlier, in September, the German biotech opened operations in Cambridge, Massachusetts. In March, the Bill & Melinda Gates Foundation invested $52 million in CureVac, one of the foundation's largest investments.

Mexico dengue vaccine first

The first vaccine to prevent dengue, DengVaxia, now has the go-ahead to market in Mexico. On December 9 the Federal Commission for Protection against Sanitary Risks, approved the tetravalent dengue vaccine to prevent disease in all four dengue virus serotypes for individuals living in endemic areas. Lyon, France–based Sanofi Pasteur completed phase 3 clinical efficacy trials in Latin America in late summer 2014 (*Nat. Biotechnol.* **32**, 605–606, 2014). Dengue is caused by one of four related but distinct flavivirus serotypes spread by infected *Aedes aegypti* mosquitoes. No other approved vaccines or antivirals exist for dengue, the world's fastest-growing tropical disease. The World Health Organization estimates the virus causes 400 million infections each year. Observers raised doubts over the vaccine's prospects after a 20,000-patient trial in Central and South America resulted in 50%, 74% and 77% protection against serotypes 1, 3 and 4, respectively, but only 35% against serotype 2. The Mexican authorities' decision to grant marketing authorization is a historic milestone for Sanofi, that has been developing the vaccine for 20 years, CEO Olivier Brandicourt said.

> **"Geneticists are concerned transhumanists will use CRISPR on themselves."** Headline on Alex Perlman's story in *Motherboard,* reporting on the meeting convened in Washington, DC, on editing the human germline. (*Motherboard*, 3 December 2015)
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> In response to the above: **"As someone who uses CRISPR every day, I can only say: good luck, dudes."** (Deoxy Ribonucleic@c0nc0rdance 3h, 7 December 2015)

familiar with the history. "It's not like the FDA had been sitting on its hands," says Alison Van Eenennaam, an animal genomics extension specialist at the University of California, Davis, who served on a veterinary medicine advisory committee that reviewed the salmon. "The FDA did all sorts of consultations with industry and nongovernmental organizations for about ten years" in an attempt to figure out how to proceed in a way that satisfied stakeholders, she says. The FDA also during that time consulted with risk assessment experts and other regulatory authorities.

The chasm between the demands of the interested parties was expansive, and some contend that the FDA spent too much time trying to satisfy everyone. Among the litany of grievances, interested parties raised questions about the allergenicity of the salmon and the lack of long-term human feeding safety studies and the potential effects of elevated levels of insulin-like growth factor 1 found in the transgenic fish. Others contended that the rigor of the regulatory process was unnecessary, and still others called for the fish to be reviewed under a different regulatory route altogether.

FDA was "operating under the presumption that if you have an open dialog, you can get a consensus," says Stotish. "And there may be areas where that's possible. But when it comes to the review of scientific applications...it can't be by referendum. It can't be by consensus." Stotish notes that although the period without a clear regulatory pathway went on "far too long" the actions of individuals at the FDA were well-intentioned. "This was not a failure of the reviewers," he says. "And we're not bitter."

In the middle of the drama, the FDA in 2009 approved, to far less opposition, the first transgenic animal drug: ATryn—a recombinant

Box 1 AquaBounty's safety nets

Much of the fear surrounding engineered salmon is predicated on the idea that the fish could escape confinement and wreak havoc on wild populations. Those concerns have been raised by Congress members, activists and consumer groups.

After visiting AquaBounty's facilities and reviewing data submitted by the company, the FDA concluded that the likelihood of AquAdvantage salmon escaping confinement at any life stage is "extremely low" due to the "multiple, redundant" and physical and biological containment measures. The agency also concluded in its nearly 200-page environmental assessment that the chances of escaped fish surviving, reproducing and altering the environment are almost zero.

AquaBounty produces its salmon in two facilities: an egg production site on Prince Edward Island, Canada, and a grow-out facility in Panama. Both are land-based facilities with water flow systems that discharge into local rivers. At both facilities there are at least four barrier points in every possible water route that are inspected daily. The company's security measures against malicious mischief and natural disaster were "acceptable" at both sites, the agency said in the report.

Should fish escape the facility, the chances of them surviving are very low. The conditions of the local rivers adjacent to the production sites offer suboptimal habitats, the environmental report stated. At the Panama facility, downstream hydroelectric energy plants create lethally high water temperatures that would prevent migration past that point. Atlantic salmon do not inhabit the waters in the vicinity of the facility, which is perched at 5,000 feet above sea level. At the Canadian site, high salinity and, at certain times of the year, low water temperatures would not likely support early life stages of AquaBounty's fish. The waters may be suitable for some life stages during part of the year, although Atlantic salmon are not known to inhabit the waters near the site. In general, the chances of an escaped farmed fish being able to adapt to a wild prey diet is low, the report said.

If escaped fish manage somehow to survive, AquaBounty has incorporated another safety layer. The company produces all-female eggs using the reproductive methods gynogenesis and sex reversal, and renders them sterile with a pressure shock treatment common in aquaculture known as triploidy. This induces fish to have three sets of chromosomes, rather than two, and interferes with the formation of gametes—cells that become eggs or sperm. A triploid female should be effectively sterile, the FDA says, although there have been isolated reports of potential reproductive capabilities in such fish. AquaBounty must maintain a 95% triploidization success rate, and rates so far have been 99.8% on average.

The Canadian facility separately houses diploid salmon used for the production of AquAdvantage salmon. These fish are reproductively competent and contain the engineered growth hormone gene construct. It is these fish, the FDA reported, that would pose the "greatest potential risk to the environment" should an escape occur, although large numbers of escaped fish would be required for reproduction and establishment, the FDA said. *EW*