IN brief

Sanofi/Genzyme hostile

Its efforts to acquire Genzyme rebuffed in August, Sanofi-aventis has begun a hostile tender offer for the Cambridge, Massachusetts, biotech, for the $69 per share ($18.5 billion) it originally offered. Sanofi notified Genzyme of its intentions in a 4 October letter in which CEO Christopher Viehbacher reiterated that "Genzyme would become the global center for excellence for Sanofi-aventis in rare diseases" and would be managed as a stand-alone division, retaining the Genzyme brand. Genzyme's board recommended that shareholders reject the offer, labeling it "inadequate and opportunistic" and saying it "fails to recognize the company's plan to increase shareholder value." In May, Genzyme articulated a five-point plan, which includes rectifying manufacturing problems, which had led to censure by the US Food and Drug Administration (*Nat. Biotechnol.* **28**, 388, 2010), and disposing of non-core assets including its genetic testing services (sold to LabCorp of Durham, North Carolina, in September). Genzyme also said the offer fails to reflect the value of its pipeline, in particular, the development of its leukemia drug Campath (alemtuzumab) as a "potentially transformative" treatment for multiple sclerosis (MS). Genzyme reported follow-up data from its phase 2 study comparing the drug to high-dose interferon beta 1a, showing that, Campath treatment resulted in lower relapse rates and less increase in disability. *Mark Ratner*

Adverse-events fraud trial

A company's failure to disclose nonstatistically adverse clinical data does not constitute fraud argues BayBio, the San Francisco–based biotech company association, in an amicus brief submitted to the US Supreme Court. In *Matrixx Initiatives, Inc. et al. v. James Siracusano et al.*, which will be heard by the Court this term, Siracusano alleges that senior executives at Scottsdale, Arizona–based Matrixx misled investors about allegations that its cold remedy Zicam had caused a loss of smell in some patients and that the company's failure to disclose the complaints led to investment losses. Matrixx claimed that because the adverse-event reports were not statistically significant, the company had no duty to disclose. BayBio COO Jeremy Leffler notes, "Laws requiring disclosure of anecdotal evidence can result in erroneous conclusions about a treatment's safety and effectiveness," he says. "As the voice for Northern California's life science companies, we believe that the laws should require disclosure of significant data collected by organizations." Matrixx had received several complaints about Zicam from 1999 to 2003, with two doctors compiling data on ten affected patients. But Matrixx officials did not publicly mention the allegations and resulting lawsuits. The US District Court of Arizona granted Matrixx's motion to dismiss the lawsuit in March 2006. In October 2009, however, the US Court of Appeals for the 9th Circuit reversed that decision rejecting, among other things, the statistically insignificant argument. *Michael Francisco*

pen-grown fish. In the face of that ecological collapse, there are fitful efforts to restore Atlantic wild salmon along with anxiety that escaped aquaculture-raised or transgenic salmon could upset those efforts.

The AquaBounty transgenic salmon are to be bred and hatched at an enclosed facility on Prince Edward Island along the east coast of Canada, and then transported for growth to an inland facility in Panama. Together these facilities offer "better security and reduce the chances for escape," adding to biological safeguards, including triploid and, thus, sterile, female-only fish, that render them unable to interbreed with wild Atlantic salmon, Stotish says.

"We supply the technology, but don't want to be the producers," he continues. Nonetheless, the company envisions transgenic salmon being grown not only in Panama but in confined facilities throughout the United States, yielding local jobs and reducing dependence on imports. This role for transgenic salmon would dovetail neatly with broader growth in aquaculture, an industrial approach that, at 90 tons per year, accounts for about one-half of all fish and seafood consumed worldwide, Stotish says, citing figures from the UN Food and Agriculture Organization in Rome to show that aquaculture is steadily expanding.

Larisa Rudenko, who heads the FDA's Animal Biotechnology Interdisciplinary Group evaluating the company's product, points out: "We're not evaluating the future business plans of AquaBounty." Instead, the agency sought advice from the Veterinary Medicine Advisory Committee (VMAC) on whether the construct is safe for the fish, effective, safe for consumers, and unlikely to escape or cause problems for wild salmon.

"Any failure of a multiple confinement system means that, once AquAdvantage salmon escape, the release cannot be undone because these fish are mobile organisms with very low but not zero likelihood of having some fertile escapees," says biologist Anne Kapuscinski of Dartmouth College in Hanover, New Hampshire. "It is crucial to conduct a full environmental impact statement [EIS] that assesses the potential genetic and ecological impacts that AquAdvantage salmon could have on wild fish and other aspects of the environment. This is even more crucial because of the scientific uncertainty surrounding how these transgenic salmon will function in different environments, the importance of Atlantic salmon as a major global commodity and the existing commitment of US society to restore threatened and endangered salmon populations and conserve aquatic biodiversity."

Although no one seriously questions whether these transgenic salmon grow at twice the rate of their wild counterparts, as AquaBounty claims, doubts over safety issues abound. The word 'preliminary' came up repeatedly during discussions with VMAC, suggesting that, despite having at least a decade to build a case for approving transgenic salmon, FDA officials and AquaBounty scientists have developed only an incomplete picture on several critical issues.

"This assessment of a genetically engineered salmon…will set a precedent for future approvals of GE animals," says Michael Hansen, senior scientist of Consumers Union in Yonkers, New York. "Unfortunately, the evidence of FDA's evaluation of the AquAdvantage salmon suggests that FDA has set the bar very low.... This analysis does not conform to FDA standards for assessment of a new animal drug." He expresses specific safety concerns over potentially heightened allergenicity of the GE fish and poorly executed studies of hormone levels in the fish and their possible health effects on consumers.

Some VMAC members voiced criticisms. "Although I have no particular concerns about the [DNA] construct, it seems inconsistent not to look at the whole profile for safety concerns," says Gregory Jaffe, the consumer representative on VMAC, who is from the Center for Science in the Public Interest in Washington, DC. Committee member Michael Apley, a veterinarian at Kansas State University in Manhattan, agrees: "We are struggling for a definition of what's safe, and this is an incredibly important precedent." For instance, he and others note that there is little information about disease resistance among the transgenic fish. They also have concerns over a condition called jaw erosion that develops in some transgenic—but not unmodified—fish.

The fish are "probably safe" but there are "doubts," says VMAC chair David Senior of Louisiana State University in Baton Rouge. Senior urged the FDA to include full data sets and to consider conducting a comprehensive EIS. He and others also comment that, if FDA were to approve the AquaBounty fish, the agency should make sure that the company establishes strong site management at both the Panama and Prince Edward Island facilities not only to avoid accidents but also to protect against theft and vandalism.

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