IN brief

Sarkozy's great biotech loan

Sarkozy reveals the spending plans.

President Nicolas Sarkozy has approved the national 'Grand Emprunt', French for 'big loan', a €35 ($73.7 billion) economic stimulus package to fund French industry and infrastructure. The borrowing scheme unveiled December 16 is heavily focused on education, research and innovation, with at least €5.5 billion ($7.9 billion) flowing into the life sciences, biotech, clean-tech and academic research. The Grand Emprunt is by far the biggest, though not the first, government-driven plan to benefit the biotech sector. In November, the Kurma Biofund was launched, as a joint partnership between the public financing body Caisse des Depots et Consignations (CDC) Entreprises, Paris, and venture capital group Natexis Private Equity, Paris. The €50 million ($71.5 million) fund, which will increase to €100 million ($143 million) next year, is open to newly-created biotech companies spinning off European academic centers. InnoBio, announced in October, is a €139 million ($199 million) fund aimed at boosting the development of small-to-medium enterprises working in drug discovery and related technology platforms such as imaging, diagnostics and bioproduction. This dedicated biotech fund was created by the government's Strategic Fund for Innovation (FSI), which will contribute €52 million ($74.4 million), with the rest provided by nine corporate pharma partners, including €25 million ($35.8 million) pledged by Paris-based Sanofi Aventis and London-based GlaxoSmithKline. That the national CDC deposit fund is part of these financial investment instruments shows the French government's resolve to push biotech onto its agenda. But André Choulika, France Biotech President, laments the small sums invested. "InnoBio represents the cost of ten days of R&D in big pharma," he says, "nevertheless it could act as a catalyst to attract additional private funding." Existing schemes coupled with the 'Grand Emprunt' could signal a turning point for the biotech industry. According to presidential advisors Arnold Munnich, head of pediatrics, Necker Hospital, Paris, and economist Bernard Belloc, University of Toulouse, the French government understands that long-term growth depends on bridging the gap between academia and industry and is putting its muscle behind public-private partnerships to ensure university tech transfer and research evaluation are upgraded and professionalized. Ramin Chaybani from Novoptim, a Paris-based business development consultancy for European biotechs, points out, "The diagnosis is correct. Now we need to wait and see whether these measures have a catalytic effect." *Golbahar Pahlavan*

Carmiel, Israel, a major boost by accelerating review of, and facilitating early access for patients to, competing products that are not yet formally approved. Shire's velaglucerase alfa for Gaucher's and Replagal for Fabry's disease, and Protalix's Uplyso (taliglucerase alfa) for Gaucher's are all moving much more quickly thanks to the Allston debacle. Reports suggest that relatively few patients were switched to these still-experimental drugs, but, at the very least, Genzyme's problems have helped to increase patient and physician awareness about these rival products. In December, Pfizer even jumped into the fray, inking a major deal with Protalix for the plant-generated Uplyso, including a $60 million upfront payment.

One of the key steps Genzyme has taken to upgrade its manufacturing processes is to assign Sandra E. Poole head of the Allston facility. Poole is a senior vice president and for the past few years oversaw the construction and European approval process for the company's new manufacturing facility in Geel, Belgium. Genzyme also developed a new test to detect vesivirus, which the company says was introduced by culture materials used in the manufacturing process.

The Allston plant was back in operation by last August, but November heralded reports of more contamination. This time, "foreign particles," steel and other materials, were uncovered in less than 1% of product vials packaged at the Allston plant. No patients appear to have been harmed by these foreign particles, and because some of the affected drugs were the only treatments available, the FDA did not demand a recall. Instead, the agency issued a warning cautioning physicians to carefully inspect any vials of drugs produced at the plant before using them. Shortly after, Genzyme also announced that the agency had completed its review of Allston and had "provided Genzyme with a Form-483 outlining remaining deficiencies, which were mainly related to the fill/finish capabilities at the facility."

It's not uncommon to see visible particles in some types of biotech products, mainly due to protein aggregation. But via e-mail, Patricia Hughes, from the Division of Manufacturing and Product Quality at the FDA's Center for Drug Evaluation and Research noted that, "According to the USP [United States Pharmacopeia], all parenterally administered articles [e.g., Genzyme's recombinant products] must be prepared in [a] manner designed to exclude particulate matter." Certain types of contaminants, such as fibers or metal shavings, can also indicate "poorly controlled operations or inadequate maintenance," she added. If a company is getting that kind of debris in the product, "Some part of your downstream filling system may not be set up right," says Bill Bees, senior vice president of operations at Cangene in Toronto, Ontario, which has a fill finish facility in Baltimore. For example, if a piece of equipment has been improperly assembled, metal shavings can arise when the ill-fitting pieces rub together.

Biomanufacturing experts acknowledge that contamination is a widespread concern in the industry, but many were disconcerted by the comments of Genzyme's senior vice president Geoff McDonough in the media. In an interview with the *Boston Globe* newspaper, McDonough stated that Genzyme's particle contamination rate was "within industry standards." The response of one manufacturing expert, speaking off the record, was "With that comment, they threw us all under the bus."

Genzyme CEO Termeer responded to the crisis by announcing changes to operating procedures and a new focus on quality in manufacturing. But the biggest changes yet may be foisted on the company by activist investors. On December 10, *The Wall Street Journal* reported Genzyme had named an independent director to its board after pressure from stockholder Relational Investors of San Diego. This new director is Robert Bertolini, who was chief financial officer at Kenilworth, New Jersey-based Schering-Plough when it pulled off a remarkable turnaround in 2008. According to the *Wall Street Journal*, Relational Investors head, Ralph Whitworth, who is renowned for activism, wants to see even more changes at Genzyme.

The good news finally seems to be trickling through. In December, the company announced the first new shipments of Cerezyme since the Allston plant was closed for cleaning. Shipping of Fabrazyme was also imminent as *Nature Biotechnology* went to press. Also in December the company announced an agreement with the FDA on a regulatory path for the long-delayed Lumizyme (a form of Myozyme for adults). The firm predicts its manufacturing capacity will increase fourfold from 2006 to 2012, both through new facilities and expansion of established plants. But it's going to take a massive effort for the company to undo all the damage. "They are taking the right steps by minimizing Allston's role while it's remediated," says Josh Schimmer, managing director and biotechnology analyst at Leerink Swann of Boston, "but they are having to scramble because they have done irreparable harm to the franchise." Schimmer approves of Bertolini's appointment and the fact that Genzyme is finally responding to shareholders' wishes. "The organization can be structured in such a way that these problems don't recur," he says.

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