

IN brief

Provenge twists again

Just when Dendreon thought it had reached the promised land, with the approval of its prostate cancer vaccine Provenge (sipuleucel-T), the Seattle-based company is back in the hot seat. In July, the Center for Medicare and Medicaid Services (CMS), which oversees Medicare, announced an investigation into whether it should pay for the cancer vaccine, approved in April (*Nat. Biotechnol.* **28**, 531–532, 2010). It sounds fair that a treatment regime costing \$93,000 that offers 4 months' increase in median survival should be under such scrutiny, especially given that 75% of the potential patients, by Dendreon's reckoning, would be covered by Medicare. Yet, Dendreon consultant Jayson Slotnik of Foley Hoag in Washington, D.C. points out that this kind of analysis is rarely undertaken so soon after approval. "What new data will they be looking at?" he asks. CMS will not discuss an ongoing investigation, leaving to conjecture the reason for their decision to pursue this course. In a letter to CMS, Dendreon requests that the investigation be abandoned, or, at the least, brought to a speedy conclusion (the process takes a year) based on consistent results from four clinical trials, which recently appeared in the *New England Journal of Medicine*. Even that did not go smoothly, as an accompanying editorial questioned aspects of the trials. Meanwhile, on August 6, the FDA issued a warning to Dendreon about misleading promotions. *Laura DeFrancesco*

Lilly snaps up Alnara

Eli Lilly of Indianapolis, has acquired Alnara Pharmaceuticals, a two-year-old startup with a single drug—an enzyme supplement—currently under review by the US Food and Drug Administration. Alnara's lead product, Trizytek (liprotamase), is a nonporcine pancreatic enzyme therapy for patients with cystic fibrosis and other conditions in which the pancreas fails to produce enough enzymes needed to digest and absorb food. With the new deal, Lilly will gain a foothold in the enzyme replacement market, whereas the Cambridge, Massachusetts-based Alnara will benefit from the larger company's experience in the US, particularly in regulatory affairs, to help steer Trizytek into the clinic. "The deal sits with Lilly's new strategy of looking for niche markets where there are low levels of competition and less likelihood of pricing pressure," observes William Kridel, managing director of specialist investment banking group Ferghana Partners in New York. Kridel adds that Lilly may go on to do other such specialty deals. Trizytek contains protease, amylase and lipase enzymes made by microbial processes, and will be offered as an alternative to existing products made with pig enzymes. Alnara hopes to have the product on the market late this year. Trizytek once belonged to Altus Pharmaceuticals, which folded following the recent economic downturn. Altus transferred rights to liprotamase to the Cystic Fibrosis Foundation Therapeutics, which were then repurchased by Alnara. The terms of the deal were not disclosed. *Susan Aldridge*

for Morningstar, points out that "what Pfizer is doing with their new rare disease unit is similar to what we're seeing at GlaxoSmithKline and what we've already seen at Novartis. It is a little bit emblematic of what we're seeing across the industry, which is a shift toward rare diseases, away from the primary care model that had served the big pharmaceutical firms pretty well over the last couple of decades."

Until now, success stories in rare diseases have been the province of small biotech. BioMarin, of Novato, California, for example, has three drugs on the market, all approved for rare disease indications: Naglazyme (galsulfase) for the treatment of mucopolysaccharidosis VI (MPS VI), Aldurazyme (laronidase) for MPS I and Kuvan (sapropterin dihydrochloride) for phenylketonuria. Elsewhere, Brussels-based chemical company Solvay succeeded with Creon, its pancreatic lipase therapy for cystic fibrosis, which led to its acquisition by Abbott Laboratories of Abbott Park, Illinois. And since 1994, Genzyme has enjoyed a monopoly on Gaucher disease treatment with its drug Cerezyme.

Although one of the advantages for biotech companies that have traditionally targeted orphan disease indications has been the lack of competition from big pharma, the entry of multinational drug companies into the area might not be all bad news. According to Simeonidis, many biotech companies have steered away from rare diseases because investors have preferred to emphasize larger markets, which they perceived as providing greater product returns and being more attractive for a potential pharma buyout. Simeonidis believes that having big pharma in the sandbox could be immensely helpful for biotech companies seeking investor support for rare disease indications. And of course, playing with big pharma companies translates to increased opportunities for partnerships, licensing agreements and acquisitions.

Competition from pharma will affect mostly big biotech, analyst Conover believes. Genzyme is currently the prime example of a biotech company that, in the long term, may experience competitive pressure, as the new Pfizer rare disease unit will be focusing on Gaucher disease. Since 1994 Genzyme has offered the only effective therapy for Gaucher disease.

Simeonidis thinks Pfizer will find it hard to compete with Genzyme at least in the near term. "If you look three to five years down the line, you could see a company like Pfizer having an advantage over Genzyme in this arena because of the difference in the amount of resources available... but right now, I would not think a company like Biomarin or Genzyme would be threatened by the presence of Pfizer."

Biotechs enjoy a competitive edge when it comes to orphan drug marketing, as it is very different from that of mass market, blockbuster medicines. "Case management is very important, as is keeping track of individual patients and helping them navigate the reimbursement maze," says Joseph Schwartz, a bioanalyst for Leerink Swann in Boston. Many analysts question whether Pfizer and other large pharma are making the investment required to develop and market a successful minibuster orphan drug therapy, or simply shot-gunning different biotech business strategies to see if any of them stick. Biotech-like ideas have been known to fizzle in pharma hands, including GSK's EpiNova and New York-based Pfizer's Biotherapeutics and Bioinnovation Center in San Francisco, which was shuttered in 2009.

Industry observers also point out that pharma seems to undermine their own rare disease initiatives by putting them under the direction of junior scientists who do not have the authority to leverage company resources, or failing to invest enough money and manpower in the unit. One company that has been a trendsetter in rare diseases is Novartis. The pharma stands out from the pack in having not an isolated rare diseases unit within the company, but an innovative, company-wide rare diseases program that investigates small indications first, using it as a launch pad for common diseases after proven success. For example, Novartis's Ilaris (canakinumab), recently approved to treat familial cryopyrin-associated periodic syndrome (CAPS), has been granted orphan drug status. Ilaris is now also being developed as a possible therapy for type 2 diabetes and chronic obstructive pulmonary disease, which are potential blockbuster applications.

Patient recruitment remains a formidable challenge, however, and that may be one reason why companies tend to shy away from rare diseases. Timothy Wright, global head of translational sciences for Novartis, says, "I wouldn't say we've overcome that, but we've taken on the challenge, working with support groups, patient advocacy groups and with key investigators in the field who have large groups of patients with certain diseases and are connected to networks."

Pharma companies hoping to emulate Novartis's success in rare diseases will have to either develop these capabilities and resources within the company, or acquire them. Biotechs are brimming with assets related to rare diseases, along with intellectual property, so this trend toward orphan diseases in pharma could bring new opportunities rather than a competitive threat.

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