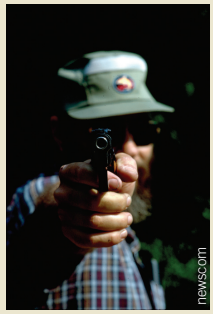
## Biofuels bandwagon

The US Department of Energy (DOE) will give $385 million to six companies to produce biofuels that are alternatives to corn-based ethanol. Experts say that for the biofuels industry to succeed, producers must decrease their dependency on corn and switch to cellulosic ethanol, which can be made out of prairie grasses and cheap leftovers in fields such as straw and corn stalks. "In order to grow beyond E10 [a blend of 10% ethanol and 90% gasoline] in any meaningful way, cellulosic needs to happen," says Brian Jennings at the American Coalition for Ethanol in Sioux Falls, South Dakota. But no one has yet been able to produce cellulosic ethanol on a large scale. Iogen, of Ottawa, Ontario, a recipient of a portion of the DOE funding, has built a demonstration plant that can produce cellulosic ethanol on a small scale by breaking down agricultural residues with an enzyme cocktail, and the company has plans to build a commercial-scale plant in Idaho. Another recipient, BlueFire Ethanol in Irvine, California, proposed a plant that makes ethanol out of green waste and wood waste from municipal landfills. It may take another four years or more before cellulosic ethanol can move from the lab to the refinery. In February, oil giant BP, in London, forked over a whopping $500 million to a group of researchers in California who are studying alternative biofuels technologies. *EW*

## Amgen under assault




The Securities and Exchange Commission is taking aim at Amgen over its delayed disclosure of a stopped clinical trial of its anemia drug Aranesp. Meanwhile, the company is also trying to allay investor concerns over negative data from a phase 3 study of the drug that prompted a recent label change.

In October 2006, a trial of Amgen's anemia drug Aranesp (darbepoetin alfa) was halted after an interim analysis showed it caused a statistically significant increase in disease recurrence in head and neck cancer patients. The trial, conducted in Denmark, was terminated two months later. Aranesp, approved for anemia associated with chronic renal failure as well as for chemotherapy-induced anemia in patients with nonmyeloid malignancies, brought Amgen, of Thousand Oaks, California, more than $4 billion last year. The company's handling of the trial's premature end has raised eyebrows. It privately reported the stopped trial to both the US Food and Drug Administration (FDA) and European regulatory authorities, yet made no mention in its quarterly conference call held January 25. When an industry newsletter reported the halt three weeks later, Amgen was forced to host an impromptu conference call to defend itself. "We do not disclose investigator-initiated study data—the investigators are in control" of that, asserted CEO Kevin Sharer, although he also admitted that "in retrospect, it would have been ideal" to disclose the news. The Securities and Exchange Commission has asked for additional information on the trial. Of more concern to investors and regulators may be a phase 3 study of Aranesp that looked at patients with active cancer not receiving chemotherapy or radiation but who had anemia. An interim analysis completed in the fourth quarter of 2006 showed no statistically significant difference in transfusion frequency between placebo and Aranesp but a statistically significant increased risk of death in the Aranesp-treated group. FDA has subsequently added boxed warnings to Aranesp, as well as to Amgen's Epogen and New Brunswick, New Jersey-based Johnson & Johnson's Procrit (both drugs are epoetin alfa) and adjusted their labels. It also has scheduled an Oncologic Drugs Advisory Committee meeting in May to discuss the erythropoiesis-stimulating drugs. *BH*

## Cabilly II revoked, again

S. San Francisco, California–based Genentech's grip on monoclonal antibody production techniques took a hard hit in February when the US Patent and Trademark Office (PTO) rejected the widely licensed Cabilly II patent, which Genentech holds. If upheld, the ruling would free dozens of licensees from royalty burdens and could cost the biotech giant hundreds of millions of dollars in lost license fees. The technique claimed in Cabilly II, which expires in 2018, is used in the manufacture of some of the most successful antibody drugs including Humira (adalimumab) from Abbott Labs of Abbott Park, Illinois, Remicade (infliximab) from Centocor of Malvern, Pennsylvania, Erbitux (cetuximab) from New York-based ImClone Systems and Synagis (palivizumab) from MedImmune of Gaithersburg, Maryland. Genentech says it earned $105 million from the patent in 2006. The PTO's lengthy ruling is its second rejection of Cabilly II: the first was made in September 2005, which Genentech appealed. The company will have one more opportunity to challenge the PTO determination; if rejected again, it could then take its claim to the courts. The process would take at least two years, experts say, and in the meantime, the patent remains valid. Genentech is already fighting for the validity of Cabilly II in a lawsuit brought by MedImmune (*Nat. Biotechnol.* **25**, 264–265; 2007) and the PTO's ruling could become a point of persuasion in that court case, legal experts say. Meanwhile, licensees may be eyeing the situation as an opportunity to stop paying royalties or renegotiate their agreements. "There are a lot of people who would like to shrug off the Cabilly patent obligation," says John Garvey, a partner at Foley & Lardner in Boston. *EW*

## Acambis retrenchment

The Cambridge, UK, vaccine company Acambis has replaced its chief executive, disposed of its financial director and will cut 40 workers from its 260-person staff in response to its failure to secure an expected US Project Bioshield (biodefense) contract worth up to $200 million for Modified Vaccinia Ankara smallpox vaccine. Acambis still generates revenues from a profitable US anti-terrorism smallpox vaccine contract, among other things, and has no immediate cash problems. But the firm has had to rethink its product strategy. Jonathan Senior of London-based investment adviser Evolution Securities says the restructuring could be intended "either to get Acambis in better shape for sale, or to turn it into a lean, mean acquisition machine." So far, Acambis has failed to build itself up through pipeline-building acquisitions. But Senior notes that the firm's chairman, Peter Fellner, is a known fan of biotech consolidation. To reduce cash burn, Acambis is expected to follow the industry trend of developing products only as far as phase 2. Sam Fazeli of the equity research firm Piper Jaffray in London noted this would allow it to cash in on its pipeline earlier. But he also cautioned that the firm's long-term value depends on its future acquisitions, given that "recent strategy changes leave us less than excited by the revenue potential of Acambis' vaccines." Acambis' new chief executive is Ian Garland, a former colleague of Fellner's at UK biotech firm Celltech Group, which was acquired by Brussels-based UCB in 2004. *PM*

*News in Brief written by Susan Aldridge, Jeffrey L. Fox, Mark Hollmer, Brady Huggett, Alla Katsnelson, Peter Mitchell & Emily Waltz*

## IGF-1 patent suit settled

A patent settlement between two bitter rivals over a treatment for short-stature children has yielded mixed results in the bid for a commercially viable drug to treat the condition. On March 6, Tercica, of Brisbane, California, announced it had settled a longstanding dispute over insulin-like growth factor 1 (IGF-1) with Insmed, in Richmond, Virginia. Tercica can continue to market Increlex (recombinant IGF-1), which it in-licensed from Genentech, in the US and EU. Insmed, for its part, agreed to take its rival drug Iplex (rIGF-1 plus the binding protein IGFBP-3) off the market to treat those same patients and to not seek EU marketing approval. But the struggling biotech can still seek marketing approval for Iplex for other non-short stature indications, such as severe insulin resistance and myotonic muscular dystrophy, by way of licensing development rights granted by Tercica and Genentech. The end result is bittersweet because "Insmed had the superior drug" in dosing terms to treat short-stature disorders, in a field where very few treatments actually work effectively, opines Matthew Osborne, analyst with Lazard Capital Markets in New York. Plus Insmed, which is in serious financial trouble, must still find funding to both launch Iplex and complete the larger clinical trials needed to gain wider approval. The streamlined legal picture may allow Tercica to finally gain sales traction for Increlex, which launched in the US in January 2006 (*Nat. Biotechnol.* **23**, 1192, 2005). With the competition gone, Osborne said, Tercica expects Increlex sales to top $7 million in 2007. Tercica will likely seek to reach children for whom typical human growth hormone therapy has failed and also broaden the market by encouraging doctors to treat IGF-1 deficiency rather than just growth hormone deficiency. But in any form, IGF-1 will never achieve anything near the lofty expectations once envisioned for the replacement protein, which at one time was thought of as a competitor to human growth hormone in many applications, and as a diabetes drug. *MH*

## French balk at biosimilars

The French Government adopted legislation in mid-February to prevent biosimilars from being treated as pure generics. The rule reflects awareness of and concern over the inherent variability of different versions of the same biologic—a nod in favor of the EU's definition of a biosimilar. Thus, there will be no automatic substitution for biologics in France as patents expire as there is for small-molecule drugs. The move has been welcomed by EuropaBio, the Brussels-based EU bioindustry association, as being in the interests of patient safety. Companies that face competition from biosimilars are also understandably cheered by the new law. Thomas Bols, director of government affairs at Amgen Europe, in Brussels, says Amgen has no argument with biosimilars entering the marketplace. "But we are concerned that these products are introduced in an appropriate way." He adds that the concept of automatic substitution of a generic for a branded drug should not be applied to biologics, which are more complex products than small molecules. Meanwhile, the US Senate is considering legislation that would give the Food and Drug Administration the power it currently lacks to approve biosimilars. The bill, introduced by New York Democratic senators Charles Schumer and Hillary Clinton, is supported by patient groups and healthcare plan providers who would like to see a sharp fall in the cost of biologic drugs. If, however, the FDA follows the European line on approvals, the costs of introducing products may deter manufacturers from entering the biosimilars market. *SA*

## New C-Path initiative

Scientists at several member companies recently began evaluating a set of five rapid assays for hepatotoxicity, and expect to identify the most promising in as soon as six months, according to William Mattes, Director of Toxicology at the Critical Path Institute (CPI) in Rockville, Maryland. The consortium of 16 biotech and pharmaceutical companies that belong to CPI are organized into four working groups, with the other three looking separately at biomarker assays for carcinogenicity, vascular toxicity and nephrotoxicity, he notes. For each of the working groups, the initial strategy is to identify practical assays to distribute among some of the member companies. In the case of hepatotoxicity tests, "we keep looking for new assays that may be buried in the literature, but we also have an active program to pursue five relatively simple tests that knocked around among member companies' labs," Mattes says. Although those tests are all in the public domain, "they're not widely used" but are considered "promising," he adds. The next step will be for the working group to develop a strategy for evaluating how the better assays perform when using clinical samples. "Although we don't yet have a clinical plan, we're intent on developing one," he says. CPI was created in part to coordinate collaborations with outside researchers and industry (*Nat. Biotechnol.* **24**, 885–887, 2006). *JLF*

**Selected research collaborations**

| Partner 1 | Partner 2 | $ (millions) | Details |
|---|---|---|---|
| Avalon Pharmaceuticals (Germantown, Maryland) | Merck & Co. (Whitehouse Station, New Jersey) | 200 | A deal to discover cancer therapeutics based on an undisclosed Merck target. Avalon will use its high-throughput analysis of gene expression signatures to identify potential compounds from Merck's library that might inhibit the target. Avalon may receive discovery, development, regulatory and commercial milestones and product royalties. Merck will head clinical development, regulatory approval and commercialization of any resulting candidates. |
| Organon (Oss, The Netherlands) | Pharmacopeia (Princeton, New Jersey) | 35 | A five-year partnership to discover therapeutics for neurological, immunological and other conditions. The partners will jointly generate compounds for development, and Pharmacopeia will receive an up-front payment and research funding. Organon will head development; Pharmacopeia will receive milestones and royalties and retains options to codevelop and cocommercialize resulting candidates. |
| Galapagos (Mechelen, Belgium) | University of Bristol (Bristol, UK) | 2.62 | A two-year collaboration to discover small molecule therapeutics for cancer targeting protein kinase B (PKB). Galapagos will apply its lead optimization technology to compounds discovered by the university: the compounds block PKB activation, thus promoting apoptosis. The university will pay Galapagos research fees. |
| Graffinity Pharmaceuticals (Heidelberg, Germany) | Amgen (Thousand Oaks, California) | * | A deal to discover small-molecule therapeutics with novel modes of action for various diseases. Graffinity will apply its drug discovery technology, which uses chemical arrays to test binding properties of small molecule fragments, to drug targets supplied by Amgen. Graffinity will receive technology access fees and success payments for hits generated. |

* Financial details not disclosed. *AK*