

India's GM field trials

Field trials of genetically modified (GM) crops in India that were halted September 22, 2006, by a court order—following a petition filed in the public interest—have resumed under more stringent conditions. The Supreme Court on May 8 ruled that GM field trials can continue if they are at least 200 meters away from fields growing the same, but non-GM, crop. Those in charge of GM field trials must ensure there is no contamination and must use validated test protocol to detect contamination at a level of 0.01%. Also, toxicity and allergenicity data for released crops are required, and a named field scientist will be responsible for each trial. Within three days following the ruling, the government's Genetic Engineering Approval Committee cleared the backlog of approvals for field trials of transgenic cauliflower, brinjal, rice, castor, groundnut, tomato and potato, besides approving 49 new *Bacillus thuringiensis* cotton hybrids for commercial cultivation. But the anti-GM lobby points out that the new permission is for ongoing and earlier approved trials only and not for new GM crops. Aruna Rodrigues, who filed the petition in the Supreme Court, says that “it will be virtually impossible for [GM crop growers] to carry out field trials given our small landholdings, with isolation distances of 200 meters.” She also points out that the court stipulation of the test protocol for contamination being announced before field trials means that genetic sequences will be disclosed. She says that “international labs will therefore be deployed by civil society for back-up tests to ascertain whether farmers' fields and food have been contaminated.”

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Amgen goes shopping

Amgen, of Thousand Oaks, California, announced June 4 that it was buying Ilypsa, of Santa Clara, California, for \$420 million. It followed that news two days later with an announcement of the \$300 million purchase of Cambridge, Massachusetts-based Alantos Pharmaceuticals. Both deals are expected to be finalized in the third quarter. Ilypsa's ILY101, which has completed phase 2 trials for hyperphosphatemia in chronic kidney disease, and other Ilypsa drugs not as far along in development, fit well with Amgen's nephrology line, says analyst Christopher Raymond, with Robert W. Baird & Co. in Milwaukee,

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Cytos' big deal

A licensing deal worth up to CHF600 (\$482) million in upfront and milestone payments between Cytos Biotechnology and Basel, Switzerland-based Novartis for a phase 2 therapeutic vaccine for treating nicotine addiction has added to a market gathering steam since the launch in August 2006 of Chantix (varenicline), made by New York-based Pfizer. The vaccine at the center of the deal, Cyt002-NicQb, is from Schlieren, Switzerland-based Cytos' 'Immunodrugs' platform, which uses a virus-like particle to present to the immune system an epitope of interest in highly repetitive arrays. Cyt002-NicQb induces an antibody response to nicotine, which then prevents passage of the drug across the blood-brain barrier to the brain's reward centers. The deal, disclosed April 27, includes an upfront payment of CHF35 (\$28.2) million plus royalties on eventual product sales. Nabi Biopharmaceuticals, of Boca Raton, Florida, is developing a vaccine also, but its NicVax recently missed a primary endpoint in a phase 2b study, although a response was seen in a subgroup and the company is planning to advance to phase 3. London-based Celtic Pharma also has a product, TA-NIC, and is planning a phase 2b study that will recruit up to 600 smokers in the US. Philippe Lanone, analyst at Paris-based Ixis Securities, says the Nabi results “weren't bad,” but he favors the Cytos product because its Immunodrugs platform has achieved proof-of-concept in several other indications. Lanone estimates peak sales of \$800 million for CYT002-NicQb. Meanwhile, Chantix brought in \$162 million in the first quarter this year.

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There are several drugs being developed to fight nicotine addiction, although Pfizer is defining the market with its approved product, Chantix.

adding that Amgen “needed to diversify.” Alantos' diabetes drug, ALS2-0426, an oral dipeptidyl peptidase 4 (DPP-IV) inhibitor, will become Amgen's third and most advanced candidate for type II diabetes. Although ALS2-0426 faces competition from DPP-IV inhibitors already on the market, Raymond says Alantos' pipeline as a whole, including a matrix metalloproteinase-13 (MMP-13) inhibitor for osteoarthritis, might pay off for Amgen. The acquisitions come amid concerns over Amgen's erythropoietin-stimulating agents (ESAs) Epogen (epoetin alfa) and Aranesp (darbepoetin alfa), an ESA with a longer half-life than Epogen. Amgen's stock price has fallen in recent months following news in March that the US Food and Drug Administration (FDA) is requiring labeling changes for ESAs, and in May an FDA panel recommended additional restrictions for Aranesp when used against chemotherapy-induced anemia (*Nat. Biotechnol.* 25, 607–608, 2007). VR

Provenge delayed

On May 8, the US Food and Drug Administration turned down Seattle, Washington-based Dendreon's application for approval of its Provenge (sipuleucel-T) autologous vaccine for treating prostate cancer. The announcement blindsided many investors, who had bid up the company's shares nearly fivefold

following an FDA Advisory Committee's earlier recommendation (by a 13–4 vote) to approve Provenge in late March, briefly pushing Dendreon's valuation to more than \$2 billion. FDA was not convinced that Provenge had demonstrated reasonable evidence of efficacy (*Nat. Biotechnol.* 25, 493, 2007). It will instead wait for data from an ongoing phase 3 trial called IMPACT, which looks at overall survival of men with metastatic, androgen-independent prostate cancer. The FDA action was “very disappointing” and “quite a surprise,” CEO Mitchell Gold told investors, especially given the panel's vote. The company said that IMPACT could serve as a registration trial for Provenge, basing that opinion on its communications with the FDA. An interim analysis from the trial is expected in 2008 and a final analysis of IMPACT in 2010. On May 31 Dendreon announced that FDA had confirmed that positive interim or final survival data from IMPACT “would address their request for the submission of additional clinical data in support of our efficacy claim.” Ten days earlier, the biotech firm cut 40 jobs connected with the now-delayed launch of Provenge, or 18% of the workforce. Provenge was reviewed by the FDA Center for Biologic Evaluation & Research—not the Center for Drug Evaluation & Research, which some consider to be a stricter committee in terms of efficacy.

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Money-back guarantees?

The UK National Health Service (NHS) and drug manufacturer Janssen-Cilag, of Surrey UK, are considering a novel scheme of risk sharing. The NHS has denied patients access to a number of high-ticket (mainly biotech) drugs because of their “incremental cost effectiveness ratio”—in other words, they don’t think the results are worth the money. In response, Johnson & Johnson, through Janssen-Cilag, has proposed to refund the cost of one of its drugs when patients don’t respond. This is a win-win situation, according to Andrew Jones of Ernst & Young in London. “Patients get access to a new medicine, the NHS ensures efficiency of expenditure, and the manufacturer secures an opportunity to get a return on its investment,” he says. The drug in question—Velcade (bortezomib), co-developed by Cambridge, Massachusetts-based Millennium and Johnson & Johnson—is approved for use in multiple myeloma patients experiencing a relapse. The agreement would allow patients that show a complete or partial response after four cycles (as determined by a certain threshold of myeloma protein detected in the blood) to stay on the drug, whereas those patients who don’t would be taken off it, and the cost of the drug refunded (about £24,500 [~\$48,000] per patient). Estimates vary as to what percentage of patients that would be—between 60% and 70% (company estimates) and 38% or less (NHS estimates). Other drugs that the NHS has refused payment on are Genentech/Roche’s Avastin (bevacizumab), ImClone Systems’ Erbitux (cetuximab), and OSI’s Tarceva (erlotinib). LD

New product approval

Product	Details
Torisel (temsirolimus), Wyeth Pharmaceuticals, Madison, New Jersey	On May 30, the US Food and Drug Administration approved Torisel for advanced renal cell carcinoma. Torisel, an inhibitor of mTOR, a protein kinase that regulates cell proliferation, increased patient life expectancy by 3.5 months in a clinical trial. Renal cell carcinoma is diagnosed in about 51,000 patients annually. The company expects it will be available in July.

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Obviousness patent ruling

A recent Supreme Court ruling on an automotive brake pedal sensor caught the attention of the biotech industry. The decision in *KSR International Co. v. Teleflex Inc.* was handed down April 30 and is considered an upset to a 40-year-old precedent related to the validity of patents for combinations of previous inventions. At issue is the doctrine of obviousness and patent enforcement. In *KSR v. Teleflex*, Federal Circuit appeals court in Washington, DC, had found that the brake pedal patent was not obvious according to precedent, called the “teaching, suggestion or motivation” (TSM) test, thereby handing victory to patentee Teleflex. The Supreme Court reversed that decision, finding that the TSM test was too rigid to be applied across all patent cases. Although the court did not throw out the TSM test, there is apprehension in the biotech industry, particularly among small companies that rely on intellectual property assets for their livelihoods. Paul Hastings, president and CEO of Oncomed in Redwood City, California, watched the case closely. “From my point of view, this whole obviousness case has more to do about pedals in the car and peanut butter sandwiches than it has to do with biotech. The part that’s scary for me is tying this to patent law throughout the universe, when every industry is different.” CS

BIO global conference

The Biotechnology Industry Organization (BIO)’s 2007 International Convention was held in May in Boston and drew more than 22,000 people, mostly from the world’s wealthiest countries. Missing were representatives of small biotechs from the rest of the world, whose attendance was hindered by costs and cultural barriers. Only 8% of attendees came from regions other than North America, Western Europe, Japan and Australia. The convention has always been held in the US or Canada, and the cost of an overseas flight, hotel, transportation, food and the registration fee can easily reach \$5,000 per person. “Five-thousand dollars is not affordable for small companies in poor countries,” says Roberto Valladares, CEO of Bioscan in Santiago, Chile, who four years ago helped form a funding group to send Chilean biotech representatives to the convention. Beyond the cost, the cultural and language barriers can be daunting. “BIO is a phenomenally intimidating meeting,” says Jim Foley, of Smart Biosciences in Philadelphia. “Knowing who you want to see and getting a meeting is a huge wall for companies from places like Africa.” BIO next year will hold its first annual global health conference, focused on neglected diseases prevalent in developing countries, although the event will be held in Washington, DC. EW

Selected research collaborations

Partner 1	Partner 2	\$ (million)	Details
Isis Pharmaceuticals Inc. (Carlsbad, California)	Bristol-Myers Squibb Co. (New York)	24	A three-year deal to discover antisense therapeutics for cardiovascular disease. BMY will have access to Isis’ research program on proprotein convertase subtilisin/kexin 9 (PCSK9), a cholesterol regulator. BMY and ISIS will develop second-generation antisense compounds. BMY will fund the work with an upfront licensing and research fee. Isis will receive milestone and royalty payments. BMY will be responsible for clinical development and commercialization.
Archemix Corp. (Cambridge, Massachusetts)	Takeda Pharmaceutical Co. (Osaka, Japan)	6	A multi-year partnership to develop aptamer-based therapeutics. Archemix will generate product candidates for three disease targets provided by Takeda. Archemix will receive research funding as well as milestone and royalty payments. Takeda will hold exclusive worldwide rights to any resultant research or product.
Affitech AS (Oslo)	Roche (SWX:ROG, Basel)	*	A collaboration to produce a human monoclonal antibody against an oncology target. Affitech will use its phagemid cloning vector library, high throughput capabilities and antibody technology. ROG will fund the research and conduct further development.
AnalytiCon Discovery GmbH (Potsdam, Germany)	Merck KGaA (FSE:MRK, Darmstadt, Germany)	*	A two-year collaboration to discover natural products-based small molecule therapeutics. AnalytiCon will apply its profiling technology to identify and characterize natural products compounds from plant and microbial extracts. The companies will jointly develop lead compounds through preclinical stage.

* Financial details not disclosed.

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