

ACT wins patent dispute

The Board of Patent Appeals and Interferences of the US Patent and Trademark Office (PTO; Arlington, VA) ruled in mid-March in favor of Advanced Cell Technology (ACT; Worcester, MA) in a dispute involving several patents to which the company holds exclusive license. The patents cover cloning procedures applicable to nonhuman mammals, including three key patents, the first awarded in 1999, to researchers at the University of Massachusetts (Amherst, MA) for their efforts to clone cows. ACT's methods have broad practical application in cloning animals and for introducing genetic modifications into animals for an array of agricultural, animal science, companion animal, and human medical applications. The company has agreements with other corporate partners to pursue those developments. The PTO ruling overcomes a challenge brought by Infigen (DeForest, WI) concerning an overlapping patent, issued in mid-2001, for similar procedures to clone pigs from somatic cells. Early this year, ACT announced its involvement in another similar but as yet unresolved dispute with the Roslin Institute (Edinburgh, UK) and its licensee, Geron Corporation (Menlo Park, CA), over using proliferating, somatic cells to produce cloned cows, sheep, or pigs. *JLF*

OGS falls to hostile takeover

One day after the UK's biotech entrepreneurs Chris Evans and Alan Goodman withdrew their bid for Oxford Glycosciences (OGS; Oxford, UK), Celltech (London, UK) announced it had purchased another 2.4 million shares, giving it 51.3% of OGS equity. The two entrepreneurs had hoped to outbid an earlier £101 (\$156) million cash offer from Celltech, but after completing due diligence, they decided OGS's liabilities were too great to justify intervention. Two other anonymous companies—believed to be leading venture capital firms—had been negotiating with OGS, but have also withdrawn. While initially dismissing Celltech's bid as "opportunistic," OGS's chief executive David Ebsworth admitted that a higher price would not be forthcoming. An all-share bid for OGS lodged by Cambridge Antibody Technology (Cambridge, UK) in February is essentially dead, analysts say (*Nat. Biotechnol.* 21, 343, 2003). Evans and

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New life in banteng gene pool



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He says the original animal died before siring any offspring, but some of his cells were saved in San Diego's "Frozen Zoo," a collection of tissue and genetic material from more than 400 species, about a third of which are endangered. The conservation-minded cloning was a joint effort between the zoological society, Trans Ova Genetics (Sioux Center, IA), and Advanced Cell Technologies (ACT; Worcester, MA). ACT participated in the only other endangered species cloning, that of a gaur calf that died two days after birth from an infection (*Nat. Biotechnol.* 18, 1129, 2000). A second banteng clone had to be put down, apparently suffering from large-offspring syndrome, but the first calf appears healthy, "bounding" around its pen. and will soon be sent to the San Diego Wild Animal Park among its banteng herd. *KP*

Goodman are now looking for alternative biotech consolidation opportunities, particularly by taking public companies private. Meanwhile, in March, Evans also announced that his venture capital fund Merlin Biosciences is to buy the stem cell research company ReNeuron (Guildford, UK) for £3.6 (\$5.6) million. Merlin floated ReNeuron in November 2000, unloading its shares on the stock market at 20 times the price for which Evans is now buying them back. *PM*

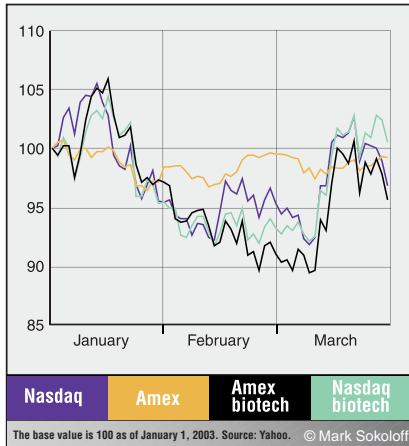
Novartis invests in Idenix

On March 26, Novartis (Basel, Switzerland) announced that it had purchased a majority share of Idenix Pharmaceuticals (Cambridge, MA), catapulting Novartis into the antiviral field and garnering potentially \$862 million for Idenix, a venture-funded company that had previously raised only \$70 million. The size of the transaction makes it one of the largest deals involving a private biotechnology company to date, and has analysts pondering whether it represents a new model for biotechnology/pharmaceutical company relationships. Mark Monane, principal equity analyst at Equity Research Group (New York), says, "The deals are much bigger now and reflect the growth and maturation of biotech." Under the terms of the agreement, Novartis will acquire 51% of Idenix stock for \$255 million, and will pay an additional \$357 million in milestone payments. With licensing fees and options for Idenix's hepatitis compounds, the value of the deal exceeds \$800 million. According to statements made by Novartis CEO Daniel Vasella, the company chose to partner with Idenix to gain quick entry into

the antiviral field, rather than developing its own line of compounds. While more deals of this size may be rare, this structure may be the wave of the future, where pharma takes a commanding interest, while leaving the biotech company's management intact. *LD*

EP bans stem cell research

The European Parliament (EP) shocked medical researchers by voting to ban all fetal stem cell research. In mid-April, it inserted last-minute amendments into the European Tissues & Cells Directive, requiring all member states to pass legislation prohibiting "research on human cloning for reproductive purposes [and research] to create human embryos for medical study." The amendments, which passed by a narrow margin (50 out of 626 votes), were tabled by Austrian Christian Democrat Marialiese Flemming and supported by Catholic conservative deputies from southern European countries where stem cell research is already banned. Royal Society President Lord May of Oxford (UK) criticized the amendments as a "cynical manipulation of the legislative process by a small group of zealots." (UK scientists are allowed to create human embryonic stem cells or to use surplus human embryos donated by couples undergoing *in vitro* fertilization treatment.) Describing the vote as "a potential setback...for millions of patients across the EU," the UK's BioIndustry Association said that individual European Union member states should be left to decide for themselves whether to impose the ban. The ban will only become mandatory if ministers of the fifteen member governments agree. *PM*



1Q financial roundup

In the midst of uncertainty generated by the war in Iraq, the biotechnology industry had a solid, albeit fairly quiet, first quarter of 2003 (1Q03). Public investors stayed in the shadows, landing no initial public offerings (IPOs) for the third straight quarter. However, the amount of funds raised from secondary public offerings increased dramatically from last quarter (see table), led by an impressive \$175 million round by Amylin Pharmaceuticals (San Diego, CA). The amount of PIPEs (private investment in public equity) increased from last quarter, led by Ribozyme Pharmaceuticals' (Boulder, CO) \$48 million financing in February. Consolidation continued at the fervor begun last quarter, most notably with Johnson & Johnson's (New Brunswick, NJ) \$2.4 billion purchase of Scios (Sunnyvale, CA; *Nat. Biotechnol.* 21, 219, 2003), and a question of who would finally land Oxford Glycosciences (Oxford, UK; see "OGS falls to hostile takeover"). The biotechnology industry also saw a number of product approvals significantly outnumber late-stage setbacks. Most notable were the US FDA approvals of Biogen's (Cambridge, MA)

US biotechnology industry fundraising (\$ million)

	1Q03	4Q02	1Q02
IPO	\$0	\$0	\$120
Secondary public	\$517	\$180	\$583
PIPEs ^a	\$204	\$77	\$373
Debt/other	\$369	\$567	\$3,789
Venture capital	\$549	\$528	\$711
Partnering ^b	\$1,203	\$2,354	\$1,025
Total	\$2,842	\$3,706	\$6,601

^aPIPE, private investment in public equity
^bPartnering figures based on total deal value disclosed for transactions worldwide
 Source: Burrill & Co.

Amevive, the first ever biologic to treat psoriasis, and Trimeris' (Durham, NC) Fuzeon, the first ever HIV fusion inhibitor. AB

BB acquires RiboTargets

The UK's 'fallen star' British Biotechnology (BB; Oxford, UK) has agreed to pay £26 (\$41) million in shares for privately owned RiboTargets (Cambridge, UK), in what might be the first of a series of acquisitions. The merged company, to be headed by RiboTargets CEO Simon Sturge, will focus on RiboTargets' structure-based drug discovery technology. Richard Parkes, chief biotech analyst at merchant bank ING Baring (London), noted the decision of RiboTargets' venture capitalist (VC) backers to sell out at such a low valuation "suggests the business was under-performing and they were keen to find a rapid exit." BB's chairman Peter Fellner says he and Sturge will be searching for further acquisitions. Meanwhile R&D staffing will be slashed, and BB's R&D backbone of 17 scientists is being transferred to the drug discovery company Evotec (Abingdon, UK). The cutbacks will save £3.1 (\$4.8) million in the first year post-merger and £6.4 (\$9.9) million annually thereafter. Combined with the company's cash reserves of

£43.5 (\$67.9) million, and £7.9 (\$12.3) million promised from RiboTargets' VC backers, Fellner and Sturge will have up to three years to turn the company around. But ING's Parkes said the deal has "little strategic focus and will do little to improve the attractiveness of BB's pipeline,...[being] little more than a prelude for further consolidation." PM

Agbiotech coming to Africa?

In an effort to bring agricultural biotechnology to farmers in sub-Saharan Africa, the African Agricultural Technology Foundation (AATF; Nairobi, Kenya) announced that major agbiotech companies—Monsanto (St. Louis, MO), DuPont (Wilmington, DE), Syngenta (Basel, Switzerland), and Dow AgroSciences (Indianapolis, IN)—will donate intellectual property rights to future projects. The intellectual property may include germ plasm, DNA libraries, and genetically modified plants. The AATF, which aims to be a bridge between private companies and small farmers, has held meetings between African public sector organizations and agriculture companies for the past two years, with support from The Rockefeller Foundation (New York), and the United States Agency for International Development (Washington, DC). "Becoming enmeshed in the arguments over GM foods that rage in the developed countries... is not what Africa needs now. Africa needs the ability to make its own decisions for its own situations," said Rockefeller Foundation President Gordon Conway in a speech last month. To be sure, the private companies signing on have their bottom lines in mind. "Africa is not a market at this point for the products we deliver to farmers in the developed world, [so] we don't see this as cutting into our market," says Chris Novak, biotechnology communications manager for Syngenta. "As Africa does develop, we can see them becoming our customers." KH

New product approvals

Product	Companies	Details
Phyzyme XP (phytase)	Diversa (San Diego, CA) Danisco Animal Nutrition (Marlborough, UK)	The US FDA granted marketing authorization on March 4 for Phyzyme XP, an animal feed enzyme. Phytase increases the absorption of organic phosphorus from feed and reduces output of phosphorus to the environment. Danisco holds exclusive worldwide marketing rights to Phyzyme XP, which will be manufactured by Diversa.
CosmoDerm and CosmoPlast (human-based collagen products)	Inamed (Santa Barbara, CA) Advanced Tissue Sciences (ATS; La Jolla, CA)	On March 12, the US FDA approved these two dermal fillers for the correction of facial wrinkles, acne scars, soft tissue contour deficiencies, and restoration of the lip border. Both products contain human collagen purified from human dermal tissue and developed by ATS. Inamed will market both CosmoDerm, which is used in the treatment of superficial lines, and CosmoPlast, which is used in the treatment of more pronounced wrinkles.
Fuzeon (enfuvirtide)	Trimeris (Durham, NC) Hoffman-La Roche (Nutley, NJ)	The US FDA granted accelerated approval for this treatment for HIV-1. Fuzeon is a fusion inhibitor that blocks HIV's ability to infect healthy immune (CD4) cells. Fuzeon represents the first new class of anti-HIV treatments in seven years. Nearly one million people in the United States have HIV/AIDS.

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Spring agbiotech roundup

Based on a nationwide survey, the US Department of Agriculture (USDA; Washington, DC) predicts that farmers will be planting slightly higher percentages of genetically modified (GM) corn and soybeans, and slightly lower percentages of GM cotton in 2003 compared to 2002. Farmers report that 38% of the corn they plant will be 'biotech' corn (herbicide-resistant, insect-resistant, or both) compared with 34% last year. Eighty percent of this year's soybean crop will be herbicide-resistant compared to 75% last year, whereas only 70% of cotton planted will be GM, instead of last year's 71%. Meanwhile, farmers and legislators in the US wheat belt continue the debate on Roundup Ready wheat varieties from Monsanto (St. Louis, MO). A vocal faction is insisting that provisions be made for separating GM and conventional wheat after harvest in order to serve customers who demand GM-free products. In a separate development, ProdiGene's (College Park, TX) penalty for planting pharmaceutical-producing plants in the corn belt may not be so tough as it appeared. Documents obtained by the Center for Science in the Public Interest (CSPI; Washington, DC) indicate that

Fast-track animal drug bill could apply to transgenics



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In late March, Senator Jeff Sessions (R-AL) introduced legislation, "The Minor Use and Minor Species Animal Health Act" (S. 741), intended to provide regulatory relief and speed the availability of drugs for animal use to veterinarians. However, the bill drew immediate fire from critics representing several dozen environmental and consumer groups, who say that the bill could undermine regulatory oversight of transgenic animals by the Food and Drug Administration (FDA; Rockville, MD). Since the mid-1980s when the federal Coordinated Framework for overseeing biotechnology products was devised, agency officials have planned to treat transgenic animals as 'drugs' for regulatory purposes. Examples of transgenic animals include salmon containing extra growth hormone genes, which feed more efficiently than unmodified salmon, pigs whose membrane proteins have been altered to make their organs better candidates for xenotransplantation, and cows and goats engineered to produce pharmaceutical and industrial products in their milk. In a letter addressed to members of Congress, these critics say, "the legislation as currently written will have the inadvertent effect of compromising and weakening current regulation of transgenic animals." However, they add, "We do not oppose the bill's goal of making available animal drugs for minor species and minor uses." *JLF*

those payments (\$3 million for the clean-up and a \$250,000 fine; *Nat. Biotechnol.* 21, 3, 2003) will not start until next year and then will be spread over two years on an interest-

free basis. "USDA created the illusion that ProdiGene's penalty was more severe than it actually is," says CSPI biotechnology project director Gregory Jaffe. *JLF*

Selected research collaborations

Company 1	Company 2	\$ (millions)	Details
Epigenomics (Berlin, Germany)	F. Hoffman-La Roche (Basel, Switzerland)	100	A three-year collaboration to develop a range of molecular diagnostic and pharmacogenomic cancer products. Epigenomics will be responsible for discovering markers for use in detection of cancers, their characterization, and prediction of treatment response to particular anti-cancer drugs. Roche will make an upfront payment of Euro4 (\$4.2) million, provide R&D funding, milestone payments, and royalties on product sales, the total value of which could be over \$100 million. Roche maintains global development and marketing rights for all resulting products.
Elan Pharmaceuticals (Dublin, Ireland)	Ingenium Pharmaceuticals (Munich, Germany)	60	A four-year alliance to develop therapeutics for pain management. Ingenium will use its functional genomic technologies to identify novel molecular targets, against which Elan will screen compounds in order to identify and develop therapeutics. The two firms will jointly fund the \$10 million initial research program. Ingenium could earn up to \$50 million in milestones for each product that reaches market. Ingenium retains the option to co-develop and co-commercialize any products developed.
metaGen (Berlin, Germany)	RNAx (Berlin, Germany)	*	An agreement to validate gene targets relevant for cancer. RNAx will provide its automated RNA interference (RNAi) technology to validate metaGen's targets. metaGen will own all derived results. Financial details were not disclosed.
Isis Pharmaceuticals (Carlsbad, CA)	Sequenom (San Diego, CA)	*	A collaboration to discover single nucleotide polymorphisms (SNPs) within Isis' antisense drug target regions. Sequenom will use its large collection of ethnically diverse samples to identify SNPs within the target regions in the general population. This research will eliminate antisense candidate regions that contain common genetic variation and will ensure that Isis' future antisense drugs are broadly applicable to the general population.
Immucor (Norcross, GA)	Inamed (Santa Barbara, CA)	*	An agreement for the production of human collagen mesh. Immucor will optimize the manufacturing process for the production of a human collagen raw material for Inamed. Inamed will continue to source its raw material needs from Advanced Tissue Sciences (La Jolla, CA). After completion of the development process, the firms intend to enter into a supply agreement.

*Financial details not disclosed

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