IN brief

New Alzheimer's endpoints?

The phase 2a success in Alzheimer's disease from Prana, of Melbourne, Australia, helped push its stock up 36% the day the news was made public, but the data could have a broader impact on the Alzheimer's disease field. Prana's drug, PBT2, a second-generation 8-OH quinoline, blocks the interaction between amyloid proteins and naturally occurring metal ions in the brain known to trigger beta-amyloid deposition. The data showed mild gains in tests of executive function and a marked reduction in a biomarker devised by the company to measure certain amyloid beta proteins (Abeta 42). But the gold standard measurement of efficacy for all approved Alzheimer's disease drugs is the ADAS-cog endpoint, which showed no benefit in the phase 2a trial. Clive Ballard, director of research at the Alzheimer's Society and professor of age-related diseases at King's College, London, says that the ADAS-cog test is "not very sensitive to treatment responses and changes occurring in early Alzheimer's disease." Elan of Dublin, Ireland, and Wyeth, of Madison, New Jersey, are also exploring alternative endpoints with bapineuzumab, a humanized monoclonal antibody that targets the beta-amyloid protein to dissolve the plaques associated with Alzheimer's disease. Bapineuzumab is the first antibody in phase 3 for Alzheimer's disease. The US Food and Drug Administration (FDA) in December gave the green light for the phase 3 trials based on results measured with the Neuropsychological Test Battery (NTB), a gauge of mental status that Elan devised, though both will be used.
—Susan Aldridge

GM grass trials blocked

A US court has blocked the resumption of open-air field trials involving genetically modified (GM) versions of creeping bentgrass and Kentucky Bluegrass. On March 17 the US Court of Appeals for the District of Columbia Circuit dismissed an appeal from Scotts Grass, of Marysville, Ohio, over testing the Roundup Ready grasses. The company appealed a 2007 ruling by a lower federal court, which found that officials of the US Department of Agriculture (USDA) had erred in approving plans for testing grass without first assessing environmental impacts. The GM grasses in field trials spread beyond the test fields to surrounding areas, including a protected 'National Grassland' area. Despite these findings, Scotts not only appealed the lower court ruling but also challenged the standing of one of the plaintiffs in that case, namely the Washington-based International Center for Technology Assessment (ICTA). "The court's ruling vindicates our challenge to USDA's inadequate review of these biotech grasses," says Joseph Mendelson, who is legal director of the Center for Food Safety in Washington, DC, a sister organization to ICTA, which initiated several lawsuits against the company and USDA (*Nat. Biotechnol.* **25**, 269, 2007).
—Jeffrey L Fox

In fact the Mumbai-based Organization of Pharmaceutical Producers of India (OPPI) that represents multinational (and some large Indian) companies views the compulsory license threat as a tempest in a teapot. "CLs in no way can be considered as an emerging trend for both pharmaceutical and biotech products," says OPPI director general, Tapan Ray.

Although it does consider national emergency reasonable grounds for a compulsory license, OPPI is opposed to granting them to extend commercial benefit to companies that manufacture copies of brand drugs. In the Natco case, Nepal has not given the generic version a nod, as it has not officially issued a notification to allow the generic drug version to be imported from India—a requirement under the Indian Patents Act for seeking compulsory licenses. "This has never happened in any country in the world and OPPI strongly believes that the situation will not be any different in India," says Ray.

This remains to be seen. "Although there hasn't been a biologics CL case as yet in India, it is certainly going to become prominent," says Shamnad Basheer, an associate at Oxford IP Research Center, UK. One driver for this is the Indian government's new 'biotechnology strategy', which is expected to facilitate the growth of biopharmaceutical companies that copy brand biologic drugs in a big way. Last May, Dr. Reddy's Laboratory in Hyderabad launched its second biosimilar drug Reditux, a copy of Roche's blockbuster Rituxan (rituximab), a monoclonal antibody used in the treatment of non-Hodgkin's lymphoma. Reddy's, which already sells Grafeel, a copy of Amgen's Neupogen (granulocyte-macrophage colony stimulating factor, which is used to boost white blood-cell production), announced in February it has eight more biologic copycats in its pipeline. "Assuming some of these are patented, Reddy's could try and avail itself of the Cipla ruling—whereby if the price is too high and it is not manufactured in India, this would be subjected to a CL," says Basheer.

Basheer warns, however, that growth of the sector will be unsustainable unless the Indian government moves to create a regulatory pathway for biogenerics; at the moment, there is a distinct lack of stringent regulations to address equivalence issues.

OPPI voices similar concerns. Because biologic drugs are difficult to replicate, the OPPI has suggested the authorities consider biosimilar drugs as new products and request all the necessary supportive data for their registration. The issue of biogenerics approval needs to be "urgently addressed," says Ray, a move expected to delay if not preempt compulsory licenses on biogenerics.

But Basheer argues that because drug prices are the key driver for compulsory licenses, the best way for big pharma and biotech to address this issue is by rethinking their model of pricing worldwide. He believes the increasing R&D collaboration between Indian generics and multinational companies may also reduce the incentives to apply for such licenses.

Another Catch-22 is that even if they do not like compulsory licenses, Western drug firms can't afford to stop marketing their products in India, says Mrinalini Kochupillai, a patents expert at Boston Law School. This is because "nonavailability in the local market is also one of the grounds for grant of CL," he says

One biologics sector, vaccines, has so far avoided compulsory licenses. There are several reasons they are not on the list of potential compulsory licenses, says Yennappu Madhavi, an expert on vaccine policy. Patents for the old vaccines in the immunization programs in most countries have expired, and, in fact, large pharma is not keen on producing them, she says.

But if a bird flu vaccine is produced, it ought to be available through compulsory licenses, says Cipla's chairman Yusuf Hamied. "In diseases like AIDS, tuberculosis, malaria or bird flu you cannot afford a monopoly." Hamied

SELECTED research collaborations

Partner 1	Partner 2	$ (millions)
Silence Therapeutics (London)	AstraZeneca (London)	*
CG Therapeutics (Seattle)	University of Washington at Seattle	*
Raven Biotechnologies (S. San Francisco, California)	Monogram Biosciences (S. San Francisco, California)	*

* Financial details not disclosed.