IN brief

Germany caps drug prices

Germany has enacted a law imposing price controls on newly licensed medicines. In the new system, the manufacturer's launch price will be valid for one year only. After that, the amount paid by health insurers will be capped at a nationally determined level, based on a preliminary assessment of the medicine's benefits. If it has no extra therapeutic benefit, reimbursement will be set at the same level as a medicine already on the market. The Medicines Market Restructuring Act, or AMNOG, will apply to most novel biotherapeutics, except orphan drugs where no comparable existing therapies exist, and whose annual sales remain below €50 ($64.5) million. According to Germany's Association of Research Pharmaceutical Manufacturers (VFA), in Berlin, AMNOG could cut €2 ($2.6) billion a year from the industry's revenues. "This is the biggest crisis ever faced by the industry," says VFA chief executive Cornelia Yzer. But Doris Pfeiffer, chief executive of the Association of Statutory Health Insurance Funds, in Berlin, says AMNOG would weaken the ability of individual health insurers to negotiate their own volume discounts, thus softening the blow to drug manufacturers. The UK also intends to introduce compulsory, value-based pricing of branded drugs starting in 2014. And this year Italy will enforce medicine price reductions totaling €1.3 ($1.7) billion. *Peter Mitchell*

Imperial's £140 million boost

Imperial Innovations is growing beyond its humble origins as Imperial College London's in-house tech-transfer department to an investment group encompassing the UK's four leading research universities. Imperial Innovations announced its intention to raise £140 ($223) million in equity through rights (whereby two new shares are issued for three existing shares) to expand investment in companies founded or based on technology from Oxford and Cambridge Universities, University College London and Imperial College. Susan Searle, its CEO, said they expect to invest about £60 million a year. Although Imperial Innovations invests in businesses in various scientific disciplines, Searle says that healthcare biotech can expect to receive about half the new funds. Mature biotech companies already in its stable may gain further, for instance, Circassia of Oxford, and London-based Polytherics, Myotec and Cell Medica. Searle says about 60% of the new funds are earmarked for investment opportunities presented by the new university collaborators. Mark Larche, founder of allergy vaccine company Circassia, now a consultant, says that although £140 million is a relatively small amount, when you multiply it by the venture capital investment that Imperial Innovations has skillfully brought in, it becomes quite substantial. He added, "Innovations meets a real unmet need, especially in the current economic climate when finding pre-seed funding is particularly difficult and VCs [venture capitalists] just aren't interested." *Jennifer Rohn*

Table 1 Selected stem cell therapies entering the clinic

Company	Cell type	Development progress	Indication
ReNeuron	ReN001 (adult neural stem cells derived from 12-week-old fetus tissue). Committed, not pluripotent. Genetically engineered to be conditionally immortal. Some technology licensed from StemCells	Phase 1. First patient has been treated	Ischemic stroke. Six months to two years after injury
StemCells	HuCNS-SC (adult stem cells derived from fetal tissue). Cultured but not altered. Same cells used for both Batten's and cord injury	Phase 1. First patient to be treated in early 2011 in Phase 1b	Chronic spinal cord injury
			Batten's disease
Neuralstem	NSI-566RSC, human spinal cord–derived neural stem cell lines	Phase 1	Amyotrophic lateral sclerosis
		IND filed	Chronic spinal cord injury
Geron	GRNOPC1 (oligodendrocyte progenitor cells, derived and differentiated from hESCs)	Phase 1	Spinal cord injury (acute—7 to 14 days after injury)

IND, investigational new drug; source: company websites

According to Chris Mason, chair of regenerative medicine bioprocessing in the Advanced Centre for Biochemical Engineering at University College London, the ReNeuron approach has faced several challenges. "It's been very tough for [ReNeuron]," he says. "They've got stem cells and gene therapy all in one, and the regulators in the US and in the UK have done tremendous due diligence on this process and have sought massive amounts of additional data from the company. It's been an excruciating process for so many years for the company, and no stone has been left unturned by the regulators, and I would therefore expect the phase 1 trial to sail through on safety." The stem cell gene modification required a go-ahead from the GTAC. The entire trial protocol needed an investigational new drug approval from the Medicines and Healthcare Products Regulatory Agency, the UK equivalent of the FDA.

The possibility of tumor or teratoma formation after cell transplantation has been an ongoing discussion. When ReNeuron approached the FDA in 2005 about a phase 1 trial, the possibility that the cell product might contain contaminating undifferentiated cells that would eventually proliferate and form a teratoma or 'de-differentiate' or transform to produce a benign or malignant tumor was high on the agency's list of concerns. At the time, there was relatively little experience to fall back on. Thus, when ReNeuron could not generate cells that would survive long enough *in vivo* to satisfy FDA's need to know if tumors might result, the company was stymied. That was probably the single biggest factor in the company taking its trial to Europe, according to ReNeuron's Sinden. This issue might be of even greater concern with ESCs because they can propagate indefinitely—without genetic engineering—and their pluripotency could also be a huge problem if cells intended to differentiate into neural tissue, for instance, become ectoderm-derived hair or tooth structures instead.

The new trial planned by StemCells in Europe aims to use neural stem cells to treat spinal cord injury. "Our choice of Switzerland was primarily driven by our relationship with the clinicians, and their expertise," says StemCells' McGlynn. "Some of the earlier clinical trials in spinal cord injury were conducted there, so it was a natural place for us" to start looking at clinical sites and talking to investigators and regulators.

Spinal cord injury is also in Geron's crosshairs. The company is preparing a phase 1 trial to treat people within 14 days of sustaining this sort of injury, with hESC-derived oligodendrocyte progenitors, before the scar tissue is formed. "If it's going to work, this is the type of study that will tell," says neurobiologist Stephen Minger who is global director of research and development of cell technologies at GE Healthcare in London. "I'm more skeptical about studies in patients who have chronic injury where you already have scarring in the cord," he says. "What you're asking the cells to do in that situation is to undo a very significant amount of damage, and I'm just not convinced that cells on their own are going to work." Minger admits that Geron's animal studies are elegant, but he cautions that rodents can regenerate and repair spinal cords on their own without intervention. "It's very hard to predict what will happen with any of these proposed therapies," he says. "But the field has to progress."

ReNeuron, StemCells and Neuralstem are going for chronic conditions, and efficacy will be a major test for them. "But if the therapy ultimately works," says Chris Mason, "the company with the most scalable platform able to