IN brief

Human embryos cloned

Stemagen in La Jolla, California has cloned human embryos by somatic-cell nuclear transfer, publishing the work in the January 2008 issue of *Stem Cells*. The cloned embryos were grown to the blastocyst stage, although the company failed to generate the sought-after self-propagating stem cell lines needed to develop therapies. Stem cell biologist Stephen Minger from King's College London notes that the work "does help the field a little," as the company managed to clone human blastocysts with an unusually high efficiency. (Their five successful blastocysts came from 29 donated oocytes, a feat that Stemagen's lead scientist, Andrew French, attributes to the quality of the donated oocytes.) Stemagen plans to build a bank of patient-matched or disease-matched cell lines from which it expects to earn royalties through collaborations with other companies experienced in differentiation and transplantation. In the UK, two institutions have been given the go-ahead to create mixed human-animal embryos for research. On 17 January, the Human Fertilisation and Embryology Authority granted one-year licenses to researchers at King's College London and Newcastle University to transfer the nuclei from adult human cells into an empty cow or rabbit egg. "The reason for using nonhuman eggs is the profound shortage of human eggs," says Minger, whose team plans to use tissue samples from people with known genetic faults—Alzheimer's disease, Parkinson's disease, spinal-muscular atrophy and five other degenerative neurological disorders—to create disease-specific cell lines to try to understand the disease process. *LM*

BiDil flops

The firm behind the first race-based drug, BiDil, could be up for sale. NitroMed, of Lexington, Massachusetts, said in mid-January that it was cutting employees from 90 to 20, discontinuing marketing activities for BiDil and asking New York–based Cowen and Co. to "advise it on strategic alternatives"—code meaning the company is considering offers. BiDil (isosorbide dinitrate and hydralazine hydrochloride) is approved to treat congestive heart failure in self-identified black patients. The product is a fixed-dose combination of two generics, and the exact mechanism by which they work together is unknown. The company and investment community once had high hopes for the product—NitroMed's stock was trading in the $20s around the time the drug was approved in 2005—but sales have totaled just $27.6 million since then through the first nine months of 2007. BiDil drew plenty of attention when first cleared—much of it negative—as many postulated that the approval was based more on NitroMed exploiting a new patent covering blacks (the original patent expired in 2007) than on sound clinical data (*Nat. Biotechnol.* **23**, 903, 2005). But the product mostly was hurt in the marketplace by its generic ingredients being readily available at a fraction of the cost, says Liana Moussatos, analyst with Pacific Growth Equities in San Francisco, who says the media backlash against the race-based approval "made no difference" to sales. *BH*

Table 1 The deal

Stages	Payments
Up-front cash to Isis	$175 million
Equity stake in Isis	$150 million for 5 million common shares of Isis at $30 per share. (Isis shares closed at $14.58 on 7 January, before deal was announced.)
Potential milestone payments to Isis	$825 million for drug development and regulatory objectives, $750 million for sales targets.
Development funding	Isis's maximum contribution during development is limited to $75 million. After two years all costs and responsibility shift to Genzyme.
Revenue split	Profit sharing begins at 70–30% in favor of Genzyme, but moves to 50–50% as drug revenues ramp to $2 billion.
Further considerations	Genzyme has exclusive options on rare disease and central nervous system products in Isis' pipeline.
Mipomersen patent expiration	2023.

(HeFH) over 13 weeks, LDL fell by an additional 46% beyond levels produced by existing lipid-lowering therapies. Finally, in a 13-week, eight-person phase 2 study reported in November, people with routine high cholesterol saw a 48% reduction in LDL beyond conventional therapies. Side effects seem negligible: in more than 250 people receiving mipomersen in phase 1 and phase 2 trials at various doses and in combination with other lipid-lowering therapies, the drug has so far been tolerated nicely with no evidence of hepatic dysfunction or toxicity.

The companies are preparing for the first new drug application for HoFH at the end of this year or early in 2009. Patients with HoFH, a monogenic autosomal dominant disease, may present with total cholesterol exceeding 500 mg/dl (optimal level is <200 mg/dl) and with LDL in the 400–600 mg/dl range (optimal level is <100 mg/dl). Because of these soaring lipid concentrations, especially in LDL, HoFH patients acquire early-onset atherosclerosis of the coronary arteries, with resulting myocardial infarction in their twenties, and are often unable to survive into the third decade of life. This indication has a *bona fide* unmet need that cries out for a fix and helps make the case for the FDA—compelling reasons for Genzyme's interest.

But the rarity of the condition means no steep growth curve in the beginning; Genzyme senior vice president James Geraghty says that any positive effect to his company's bottom line would come beyond "the first year or two after launch." By then mipomersen could have the FDA's blessing for its second indication of HeFH, in which only a single allele of the gene is present and the phenotype is less severe. It's still somewhat uncommon, occurring at a rate of one in 500 people (about 600,000 in the US), but 85% of affected men suffer a heart attack before age 60, and women with the disease have their own heart attacks about 10 years later.

SELECTED research collaborations

Partner 1	Partner 2	$ (million)
Amgen (Thousand Oaks, California)	Takeda Pharmaceutical (Osaka, Japan)	1,177
AlgoNomics (Ghent, Belgium)	Genmab (Copenhagen, Denmark)	*
Dyax Corp (Cambridge, Massachusetts)	Sanofi-Aventis (Paris and New York)	525

*Financial details not disclosed.