

## IN brief

## Heplisav's topline

The investigational hepatitis B vaccine Heplisav could provide difficult-to-immunize patients with more robust protection than that offered by currently marketed vaccines. Heplisav—jointly developed by Berkeley, California-based Dynavax and partner Merck of Whitehouse Station, New Jersey—was evaluated against London-based GlaxoSmithKline's Engerix-B in a phase 3 trial in patients with end-stage renal disease. The study shows that Heplisav offers 95.1% seroprotection, compared with 81.1% with Engerix-B. The new vaccine combines Dynavax's immunostimulatory sequence (ISS 1018), a short DNA sequence that targets Toll-like receptor 9, with hepatitis B surface antigen. Because Heplisav stimulates the innate immune system, it triggers a robust and rapid antibody response even in patients that respond poorly to existing vaccines using two—rather than three—doses. But the US Food and Drug Administration (FDA) put Heplisav on hold after a single case of Wegener's granulomatosis occurred in this phase 3 trial (*Nat. Biotechnol.* **26**, 484, 2008). The recently released data will form part of the companies' response to the FDA's request for more data. Robin Davison of Edison Investment Research is skeptical of the vaccine's future: "The hepatitis B vaccine market is already well served. Although nonresponders are always a problem, a niche market is a smaller one," he says.

—Susan Aldridge

## Cloning shop

Two Austin, Texas-based companies have joined forces to create a 'one stop' cloning and licensing service for livestock breeders. The merger of Start Licensing and Viagen will enable customers to secure licenses for reproducing breeding stock to preserve traits of prized animals—such as disease resistance and superior-quality meat—and contract in-house cloning services from one provider. Start Licensing, set up in 2005 by Geron of California and Phoenix, Arizona-based Exeter Life Sciences, manages and licenses a portfolio of 80 patents for nuclear transfer cloning technologies, including those developed at the Roslin Institute in Edinburgh, while ViaGen, a subsidiary of Exeter, offers cloning services for breeders who lack in-house expertise. The move comes just months after the US Food and Drug Administration (FDA) concluded that food from cloned animal sources is safe to eat (*Nat. Biotechnol.* **26**, 249–250, 2008). Steve Stice of Aruna Biomedical, Georgia, previously of ViaGen, thinks the technology will struggle to find more than a niche market. "There is a demand, but how big is debatable. Until the major food producers are willing to say they will use these animals in their production systems, the market will be fairly limited," he says. Smithfield Foods, a major pork producer, owns a stake in the new enterprise but is not planning to produce meat products from cloned animals.

—Hayley Birch

**Table 1** Additional selected gene therapies in advanced clinical development

Company (location)	Gene therapy	Stage of development
Amsterdam Molecular Therapeutics (Amsterdam)	Glybera (alipogene tiparovec); AAV-1 vector encoding lipoprotein lipase	Orphan status; pre-registration trial of 13 subjects with lipoprotein lipase deficiency
Introgen (Austin, Texas)	INGN-241; an E1-deleted, replication-incompetent adenoviral vector encoding melanoma-differentiation-associated gene-7 ( <i>mda-7</i> ); interleukin-24	Phase 3 in metastatic melanoma
GenVec Gaithersburg, Maryland)	TNFerade; an E1-, E3- and E4-deleted adenoviral vector encoding human TNF- $\alpha$ under the control of the radiation-inducible early growth response promoter	Phase 3 in pancreatic cancer
MolMed (Milan)	Retrovirus encoding herpes simplex virus thymidine kinase transduced <i>ex vivo</i> into hematopoietic stem cells	Phase 3 in graft-versus-host disease
Vical (San Diego)	Alloectin-7 (velimogene aliplasimid); DNA plasmid encoding the human leukocyte antigen-B7 (HLA-B7) and $\beta$ 2-microglobulin complex in context of cationic lipid mixture (DMRIE/DOPE)	Orphan status; phase 3 in chemotherapy-naive patients with metastatic melanoma
Oxford Biomedica (Oxford, UK)	Prosavin; combined lentivirus and equine infectious anemia virus vectors encoding aromatic amino acid decarboxylase, tyrosine hydroxylase and GTP-cyclohydrolase-1	Phase 2 in Parkinson's disease <sup>a</sup>
Targeted Genetics (Seattle)	tgAAC-94; AAV-2 encoding IgG1 Fc and the TNF- $\alpha$ receptor	Phase 2 in rheumatoid arthritis

Source: the Investigational Drugs Database.

<sup>a</sup>Phase 2 detailed interim results of the study are expected to be reported at the 16th Annual Congress of the European Society of Gene and Cell Therapy in Bruges, Belgium, November 13–16, 2008.

for Cerepro in glioma in Europe. In 2006, the European Medicines Agency's (EMA) European Committee for Medicinal Products for Human Use returned the company's previous marketing application, which had been based on a small phase 2 trial. But, as EMA's deputy head of sector for safety and efficacy Marisa Papaluca Amati is quick to point out, "It was a withdrawal, not a rejection."

In the meantime, another frontrunner in adenoviral gene therapy, Introgen's Advexin, has hit a snag at the FDA.

Paradoxically, while the EMA accepted Introgen's marketing application for Advexin (a recombinant, E1-deleted serotype 5 adenoviral vector encoding the p53 tumor suppres-

or), about a month later the FDA said that the company's biologics license application (BLA) was incomplete.

Safety probably is not the issue in the FDA's refusal to accept Advexin's BLA, Dunn says. It could be the prospective biomarker analysis they used in the trial. "I'm wondering if the FDA didn't just go back on their word," after claiming that such data would be acceptable, Dunn ponders. This is significant because Introgen specifically designed their phase 3 trial to prospectively segment patients according to p53 abnormalities and p53 protein levels in pretreatment tumor samples (the company declined to reveal the identity of the mutations).

Preliminary results from this open-label, multicenter, randomized study, which

## SELECTED research collaborations

Partner 1	Partner 2	\$ (millions)
Ablynx (Ghent, Belgium)	Merck Serono (Darmstadt, Germany)	453
SBI Biotech (Tokyo)	MedImmune (Gaithersburg, Maryland)	*
PDL (Redwood City, California)	Bristol-Myers Squibb (New York)	710
Archemix (Cambridge, Massachusetts)	Ribomic (Tokyo)	200
Cytos (Zurich)	Pfizer (New York)	131.8

\* Financial details not disclosed.