IN brief

US funds vaccine centers for biodefense

The US Department of Health and Human Services (HHS) has allocated \$400 million for three Centers for Innovation in Advanced Development and Manufacturing for vaccine production, but some are concerned that excessive focus on influenza may leave the nation less prepared against other threats. A 2010 report prepared by HHS proposed establishing such centers to accelerate development of medical countermeasures against chemical, biological, radiological and nuclear threats, develop new vaccine production technologies, and enable rapid manufacture of existing vaccines. On June 19, the HHS Biomedical Advanced Research and Development Authority announced allocations of \$163 million for a center in Maryland, \$60 million for a center in North Carolina and \$176 million for a center in Texas. Each center partners with companies—Novartis's vaccine facility in Holly Springs, North Carolina, GlaxoSmithKline's Vaccines of Marietta, Pennsylvania, and Emergent BioSolutions Manufacturing in Baltimore, with researchers at Texas A&M (College Station), Michigan State University (Flint), Duke (Durham) and North Carolina State (Raleigh)—to accelerate response to future pandemics.

Maj. Gen. (ret.) Philip Russell, former director of the Walter Reed Army Institute of Research, an expert consulted by HHS, expressed disappointment in the implementation. "They combined influenza preparedness with biodefense against very strong recommendations from me and a lot of other people," he says. "They're totally unrelated problems, and totally unrelated issues." When this plan was devised, more funds were available for preventing flu outbreak than for bioterrorism, making this emphasis an expedient strategy. However, he believes that supporting efforts to mass produce and distribute flu vaccine will do little to facilitate R&D against novel threats. "We envisioned a single organization totally dedicated to advanced development and manufacturing of biodefense vaccines," says Russell. "But it seems like technical capabilities were secondary to lobbying power and decision making."

Michael Eisenstein

IN their words

"It could be the biggest upside surprise in the history of the pharmaceutical and biotech industry."

Following the flop of Pfizer/J&J's bapineuzumab's in August, ISI Group analyst Mark Schoenebaum ponders

the likely aftermath were Eli Lilly's Alzheimer's anti- β -amyloid antibody, solanezumab, approved. (*Bloomberg*, 8 August 2012)

Table 1 Selected companies with gene therapies in clinical development

Company	Product	Indication	Clinical status
uniQure	Alipogene (Glybera)	Lipoprotein lipase deficiency	Pending approval
	AMT-060	Hemophilia B	Phase 1/2
Advantagene (Auburndale, Massachusetts)	ProstAtak (AAV expressing herpes simplex virus thymidine kinase combined with valacyclovir)	Prostate cancer	Phase 3
		Glioma	Phase 2
		Pancreatic cancer	Phase 1/2
GlaxoSmithKline (London)	2696273 (GIADA) retroviral vector encoding adenosine deaminase (ADA) for <i>ex vivo</i> hematopoietic stem cell therapy	ADA deficiency in severe combined immunodeficiency (SCID)	Phase 3
Vical (San Diego)	Allovectin (4,853-bp DNA plasmid encoding human MHC class I HLA-B7 and chimpanzee β -2-microglobulin plus cytofectin DMRIE/DOPE)	Melanoma	Phase 3
Applied Genetic Technologies (Alachua, Florida)	AGTC-0106 (AAV vector carrying alpha-1 antitrypsin gene)	Alpha-1 antitrypsin deficiency	Phase 2
Bluebird Bio	Lenti-D (lentiviral vector encoding human ATP binding cassette subfamily D for <i>ex vivo</i> therapy of hematopoietic stem cells)	Adrenoleukodystrophy	Phase 2
	Lentiglobin (lentiviral vector encoding human beta-globin gene or a hybrid A-gamma/beta-globin for <i>ex vivo</i> hematopoietic stem cell gene therapy)	Beta thalassemia	Phase 2
Celladon (San Diego)	Mydcar (AAV1 encoding sarcoplasmic reticulum ATPase 2a)	Cardiomyopathy	Phase 2
Ceregene	Cere-120 (AAV2 encoding neuritin)	Parkinson's disease	Phase 2
	Cere-110 (AAV2 encoding nerve growth factor)	Alzheimer's disease	Phase 2
Genzyme (Cambridge, Massachusetts)	AAV-hAADC-2 (AAV2 encoding the human aromatic L-amino acid decarboxylase gene)	Parkinson's disease	Phase 2
Oxford BioMedica	ProSavin (equine infectious anemia virus encoding aromatic L-amino acid decarboxylase, tyrosine hydroxylase and GTP cyclohydrolase I)	Parkinson's disease	Phase 2 (complete)
Shenzhen SiBiono GeneTech (Shenzhen, China)	Gendicine (replication-defective adenovirus vector encoding human P53)	Lung cancer	Phase 2

The US National Institutes of Health Clinicaltrials.gov website lists 2,965 gene therapy trials, of which 1,103 are listed as recruiting. The vast majority of these are being run by academic investigators. AAV, adeno-associated virus; MHC, major histocompatibility complex; DMRIE, 1,2-dimyristyloxypropyl-3-dimethyl-hydroxyethylammonium bromide; DOPE, dioleoyl phosphatidyl ethanolamine.

of the gene drug in November 2011, uniQure stopped all investment in the product and abandoned the clinical and manufacturing infrastructure. The company is now rebuilding, and Aldag says he hopes the first patient to receive a commercial gene therapy will be treated in the first half of next year.

On a broader level, there remains more spade work to do in terms of agreeing upon reimbursement, convincing physicians and others to push through the wider adoption of gene therapy, admits Ena Prosser, partner at Fountain Healthcare Partners of Dublin, a venture capital firm that has invested in gene therapy companies. Even so, she notes one advantage some gene therapies will have—compared with mAbs and in terms of uptake, "the

[gene therapy] doses are so tiny, and this means you won't need the same multimillion dollar scale of investment in manufacturing facilities."

Alipogene is most obviously a role model for other gene therapies for monogenic inherited disorders, but it also paves the way for products in broader, multifactorial, noninherited diseases, such as ProSavin, developed by Oxford, UK-based Oxford BioMedica, which delivers genes for the three enzymes that are needed to generate dopamine, the neurotransmitter that is depleted in Parkinson's disease. "We are basking in reflected sunshine because there are now more ticks in the box for gene therapy," says Stuart Naylor, the company's CSO.

Although alipogene is targeted at an