IN brief

First HEV vaccine approved

China's Ministry of Science and Technology approved the first vaccine against the hepatitis E virus (HEV). The HEV 239 vaccine developed and manufactured by Xiamen Innovax Biotech in Xiamen, China, is distributed under the brand name Hecolin. China's regulator, the State Food and Drug Administration, based approval on clinical data from over 100,000 healthy participants from Jiangsu Province, aged 16–65 years. None of the participants developed HEV over a 12-month follow-up compared with 15 cases among the placebo group given a hepatitis B vaccine. (*Lancet* **376**, 895–902, 2010), resulting in a 95.5% efficacy over 19 months. HEV is endemic in Central and Southeast Asia, North and West Africa, and Mexico, with disease outbreaks resulting from contaminated food or water. The World Health Organization estimates there are about 14 million symptomatic cases worldwide resulting in 300,000 deaths and 5,200 stillbirths annually. Rakesh Aggarwal from the Sanjay Gandhi Postgraduate Institute of Medical Sciences in Lucknow, India, points to long-term efficacy and cost as potential concerns. Steven Gao, general manager at Innovax in Xiamen, says that efficacy four years after initial vaccination remains "very high," though no results are published. Innovax plans to launch Hecolin on the Chinese market later this year with worldwide distribution partnerships to follow. *Allison Proffitt*

India's GM clamor mounts

Industry leaders are calling for the fast-track clearance of biotech crops currently stuck in regulatory limbo. An industry coalition on February 27 issued the 'Bangalore Declaration', urging the Indian government to lift the two-year moratorium on *Bacillus thuringiensis* (*Bt*) brinjal or eggplant (*Nat. Biotechnol.* **28**, 296, 2010) and establish the Biotechnology Regulatory Authority of India (BRAI) as a single, national regulatory point for approving genetically modified (GM) crops. The industry is also campaigning for the abolition of a rule requiring GM crops to gain local government permission for field tests, which they say hinders R&D. "We have a *Bt* rice and a *Bt* cotton, but I am unable to test them because of this rule," says Kottaram K. Narayanan, managing director of Metahelix Life Sciences in Bangalore. According to the Department of Biotechnology (DBT) more than 50 GM crops—70% from the public sector—are at various stages of regulatory processing, but Raghavendra Rao, senior official of DBT, says, "all these crops in the pipeline are just standing at the gate of the Genetic Engineering Appraisal Committee (GEAC)" that is currently far from active. BRAI is expected to replace GEAC by 2013, but the legislation for establishing it has faced activists' opposition since 2010. The Coalition for a GM-Free India says it will never "open the doors for this unsafe technology." "I am frustrated with the way things are, but remain optimistic because our farmers desperately need GM crops," Narayanan said. *Killugudi Jayaraman*

Amgen swallows Micromet to BiTE into ALL market

On March 7, Amgen closed the $1.16-billion cash acquisition of Micromet first unveiled on January 26. The deal puts in Amgen's hands not only a cancer immunotherapy based on the bispecific monoclonal antibody (mAb) fragment blinatumomab (targeting B-cell antigen CD19 and T-cell receptor (TCR) component CD3) but also the underlying 'bispecific T-cell engager' (BiTE) technology that gave rise to it. Blinatumomab leads a group of therapies targeting adult patients with relapsed or refractory B-cell acute lymphoblastic leukemia (ALL) either based on mAb technology (**Table 1**) or engineered T cells (**Box 1** and **Table 2**). In early-stage trials, the Micromet mAb fragment has induced high rates of remission and has significantly prolonged survival in a patient group that ordinarily has very limited treatment options and very poor survival prospects.

Amgen originally encountered the BiTE technology in a partnering deal it entered with Micromet on solid tumors last year. Several other firms have ongoing BiTE-based drug development collaborations with Micromet, including Paris-based Sanofi; Boehringer Ingelheim of Ingelheim, Germany; Berlin-based Bayer Schering Pharma; and London-based AstraZeneca's MedImmune unit. "That in itself gives a pretty good indication of the excitement among our big pharma peers for this platform," says David Chang, vice president of global development for oncology at Thousand Oaks, California–based Amgen.

BiTE mAb fragments, unlike classic antibodies, possess two different minimal antigen-binding domains from two single-chain Fvs (scFvs) arranged in tandem on a polypeptide chain. The molecules are engineered to bind simultaneously a T-cell antigen and a tumor-associated antigen expressed by a cancer cell. This structural arrangement over-rides the normal inability of T cells to recognize antibodies directly (because of their lack of Fc gamma receptors) and thereby leads to a cytotoxic T-cell response directed against a tumor bearing the antigen presented on the BiTE molecule. Blinatumomab targets both CD19, a B-cell antigen, and CD3, a component of the TCR complex on the surface of T cells, which is essential for T-cell activation.

Biotech giant Amgen paid a hefty sum to get its hands on Micromet's bispecific T cell engager technology.

"It's pioneering technology based on a simple, elegant concept," enthuses Amgen's Chang. "You can view it as turbocharging immunotherapy."

Other tumor-associated antigens that Micromet has targeted with BiTE antibodies include carcinoembryonic antigen and prostate-specific membrane antigen. Blinatumomab is also undergoing trials in non-Hodgkin's lymphoma and could have use in other B-cell cancers, as CD19 is present throughout B-cell development, apart from the terminally differentiated plasma cell stage.

Blinatumomab, like its begetter, has a long history behind it. Rockville, Maryland–based Micromet was formed in 1993 in Munich, which remains its main R&D site (and which Amgen is retaining). It became a US-headquartered and NASDAQ-listed company in 2006 through a $127-million, stock-based takeover of CancerVax, of Carlsbad, California. Blinatumomab, originally known as MT103, entered clinical development in 2002. MedImmune, of Gaithersburg, Maryland, licensed North American rights a year later, but it exited the collaboration in March 2009, after its acquisition by London-based AstraZeneca. By the following November, the same company relinquished an option to buy its way back in. (MedImmune retains a current collaboration with Micromet focused on gastrointestinal tumors.)

But Micromet's progress in ALL is what has turned heads. In pediatric patients, ALL is largely curable by means of chemotherapy treatment (over two years or so), with five-year

Table 1 Selected antibody conjugates in development for ALL

Therapy	Developer	Mechanism	Antigenic target	Clinical status
Blinatumomab	Amgen	Bispecific T-cell engager antibody	CD19, CD3	Phase 2
Inotuzumab ozogamicin	Pfizer	mAb conjugated to a derivative of the DNA-binding antibiotic calicheamicin	CD22	Phase 2
Moxetumomab pasudotox	AstraZeneca	mAb conjugated to *Pseudomonas* exotoxin	CD22	Phase 1/2