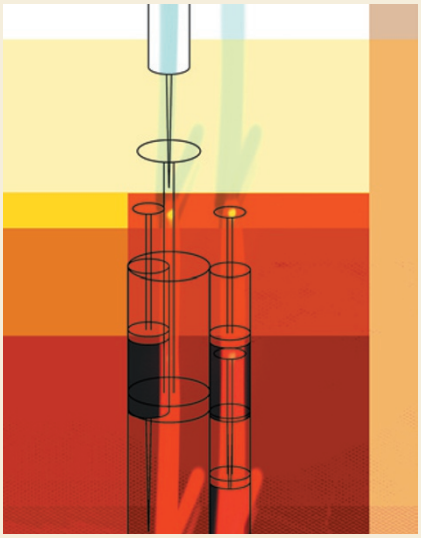
NEWS IN BRIEF

Cancer vaccines make progress



US- or EU-approved therapeutic cancer vaccines could be available in 2009.
The lowdown: Dendreon received positive news in March 2008 when the FDA agreed to a protocol amendment that would speed up the delivery of the final results of the Phase III trial — IMPACT, Immunotherapy for Prostate AdenoCarcinoma Treatment — of Provenge (sipuleucel-T). The additional information required by the FDA for approval of Provenge is now expected to be available in the second half of 2009. At the same time, Phase III data from the VITAL-1 trial of the advanced prostate cancer vaccine GVAX (Cell Genesys), a potential competitor to Dendreon, is expected. Cell Genesys signed a US$320 million development and commercialization deal in April 2008 for GVAX with Takeda, in which Takeda will gain global marketing rights.

Such cancer vaccine development deals with pharmaceutical companies have not been common. Of the ~13 therapeutic cancer vaccines in ongoing Phase III clinical trials only one other is co-funded by a pharmaceutical company: TroVax (Oxford BioMedica), a therapeutic vaccine against renal cell carcinoma. In March 2007, Sanofi–Aventis and Oxford BioMedica entered into an exclusive global licensing agreement to develop and commercialize TroVax in a deal worth up to $690 million. Results of the Phase III TroVax trial — TRIST (TroVax Renal Immunotherapy Survival Trial, designed to support product registration) — are expected in 2009. However, TroVax has a competitor that may achieve earlier EU-approval for use as a renal cell carcinoma vaccine: Oncophage (Antigenics). Antigenics received Russian approval of Oncophage in April 2008 for use in patients at intermediate risk of renal cell carcinoma recurrence, and plans to file for conditional European approval later in 2008.

Potentially beating all comers to the US or EU 'first therapeutic cancer vaccine' regulatory approval post, however, is Stanford University's 'vaccine (B-cell lymphoma)', developed in collaboration with Biovest International, for non-Hodgkin's lymphoma. The results of a Phase III trial are expected at the end of April 2008, and the collaborators hope to use these results in submissions for accelerated and conditional approvals in the US and Europe later this year.

FDA outlines drug-safety plan

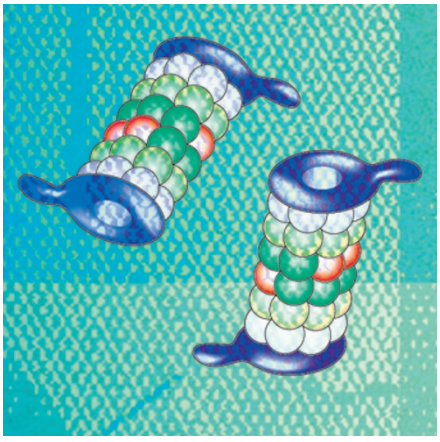
The US FDA has released the draft details of how it intends to spend the annual $29.29 million allocated for 5 years to improve drug safety.
The lowdown: When PDUFA IV was reauthorized through the FDA Amendments Act (FDAAA) in September 2007 it included additional funds to enhance drug safety. Now, the FDA has outlined how the additional PDUFA IV funds will be used to modernize the drug-safety system (http://www.fda.gov/cder/pdufa/PDUFA_IV_5yr_plan_draft.pdf). Initially, the FDA plans to strengthen management and operations by increasing staff experts in safety evaluation, risk management, epidemiology and medication errors, as well as additional regulatory project managers. With the additional staff the FDA plans to assess current and new methodologies to collect adverse event information, identify epidemiology best practices, expand database acquisition for targeted post-marketing surveillance, develop and validate risk management and communication tools, and improve post-market information technology systems.

Although not specifically included in the draft plan, the FDAAA also authorized the FDA to collect additional user fees to broaden the focus of drug safety — for example, to implement risk evaluation and mitigation strategies (REMS), post-market studies and safety labelling changes. At the end of March, the FDA published a list of 16 approved products for which manufacturers will be required to submit proposed REMS by 21 September 2008 (http://www.fda.gov/OHRMS/DOCKETS/98fr/FDA-2008-N-0174-N.pdf). The FDA plans to issue guidance on the preferred content of REMS as soon as possible.

Takeda spends $8.8 billion on Millennium

Takeda continues its 2008 spending spree by acquiring Millennium Pharmaceuticals.
The lowdown: In its biggest deal this year, Takeda has agreed to acquire Millennium for ~$8.8 billion. Millennium will become a wholly-owned subsidiary of Takeda, but will continue operations as a stand-alone business unit. In an unusual step, Takeda reportedly plans to offer Millennium employees retention bonuses to stay with the company for 12–24 more months after the takeover.

Millennium currently has ~15 investigational drugs in preclinical and clinical development for oncology and inflammatory disease indications. Through the acquisition Takeda also gains Millennium's US commercialization



rights of Velcade (bortezomib, a proteasome inhibitor) approved for the treatment of relapsed multiple myeloma, currently co-promoted with Ortho Biotech. Velcade achieved net sales of $83.5 million in the US for the first quarter of 2008, a 42% increase on net sales achieved for the first quarter of 2007. Janssen–Cilag (part of Johnson & Johnson) is responsible for commercialization in Europe and the rest of the world.

Boehringer Ingelheim wins EU anticoagulant approval race

The EU has approved Pradaxa for the prevention of venous thromboembolic events in adults following orthopaedic surgery.

The lowdown: Boehringer Ingelheim has beaten competitors Bayer and Bristol–Myers Squibb (BMS) to challenge the widely used anticoagulant warfarin with its oral direct thrombin inhibitor Pradaxa (dabigatran etexilate). There has long been a need for alternatives to warfarin owing to limitations such as a narrow therapeutic window, drug–drug and drug–food interactions, which increase the risk of serious adverse events. Now, Pradaxa has the opportunity to maximize market share in Europe before Bayer and BMS's factor Xa inhibitors, rivaroxaban and apixaban, respectively, achieve approval. Bayer's product rivaroxaban is expected to reach the market next as it submitted the drug for European approval in November 2007. BMS's factor Xa inhibitor apixaban remains in Phase III development following an agreement with Pfizer in 2007 to co-develop and commercialize the product.

Novartis' $11 billion eye deal

Novartis is to acquire a 25% stake in the leading eye-care company Alcon.

The lowdown: Novartis will acquire the minority stake in Alcon from majority stakeholder Nestlé for $11 billion. Further to this, Novartis will have exclusive rights to acquire Nestlé's remaining 52% stake for ~$28 billion between January 2010 and July 2011 to become the majority stakeholder. In the meantime, Novartis will have a representative on Alcon's Board of Directors to assess how the Novartis Ophthalmics division and its subsidiary company CIBA VISION will complement Alcon's eye-related businesses. In its press release, Novartis explained that Alcon would help limit risks within the Novartis portfolio based on its diversified payor structure with reduced risks of price regulation, leadership in a specialty health-care area, and greater access to businesses with discretionary consumer spending.

Alcon also has R&D opportunities that could be of interest to Novartis such as small-molecule 5-HT_2 (serotonin type 2) receptor agonists for the potential topical treatment of ocular hypertension and prostaglandin analogues for the potential treatment of glaucoma. Currently, Novartis has pharmaceutical products in clinical development for eye conditions including myopia, ocular hypertension and glaucoma. In addition, Novartis markets several products for conditions including ocular hypertension, choroidal neovascularization and age-related macular degeneration. In particular, Novartis acquired an exclusive license in 2003 to develop and market Lucentis (ranibizumab; Genentech) outside of North America for indications related to ocular diseases.

Global alliance for pharmacogenomics

The RIKEN Yokohama Institute Center for Genomic Medicine (CGM) and the NIH Pharmacogenetics Research Network (PGRN) have outlined their intention to establish a collaboration between US and Japanese scientists.

The lowdown: The alliance will bring together scientists from the CGM and the PGRN who conduct research in the fields of genetics, pharmacology, medicine and pharmacogenetics/pharmacogenomics to establish a series of collaborative studies to identify genetic factors that contribute to individual responses to medicines, including rare and dangerous side effects. Initial projects will include understanding genetic factors that influence the effectiveness of aromatase inhibitors for breast cancer treatment, discovery of new genetic factors linked to serious adverse events from pancreatic cancer drugs and working with the International Warfarin Consortium to tailor warfarin doses based on a patient's genetic profile. This collaboration comes at the same time as the FDA released its guidance on pharmacogenomic definitions and sample coding (http://www.fda.gov/OHRMS/DOCKETS/98fr/FDA-2008-D-0199-gdl.pdf), developed with an Expert Working Group (Efficacy) of the International Conference on Harmonisation, which includes the US, EU and Japan.