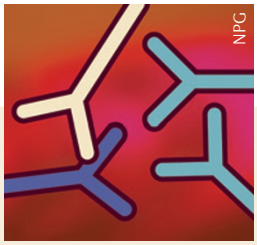
NEWS IN BRIEF



EMA backs approval of first biosimilar monoclonal antibodies

The European Medicines Agency (EMA) recommended the granting of marketing authorizations for two biosimilar versions of the blockbuster monoclonal antibody (mAb) infliximab (Remicade; Johnson & Johnson).

The lowdown: In recent years, regulatory frameworks in Europe, the United States and elsewhere have been established for the approval of biosimilars (or follow-on versions) of biologics. Biosimilars present much greater regulatory challenges than generic versions of small-molecule drugs owing to their structural complexity. Consequently, biosimilars approved in major markets so far have been peptides and relatively simple proteins, rather than highly complex products such as mAbs. The recommendation of the Committee for Medicinal Products for Human Use (CHMP) of the EMA to approve two biosimilar versions of a mAb therapy is therefore an important indicator of the feasibility of developing such products.

In order for a biosimilar to be approved in Europe, applicants need to show that its quality, safety and efficacy profile does not differ meaningfully from the pioneer biologic, and are required to implement a pharmacovigilance plan. Two biosimilar versions of infliximab, a mAb that is specific for tumour necrosis factor, were evaluated by the CHMP: Remsima (developed by Celltrion) and Inflectra (developed by Hospira). The recommendation for marketing authorization in Europe is for the same indications as Remicade, which include rheumatoid arthritis, Crohn's disease and psoriasis.

The immediate implications for future sales of Remicade (which were more than $US6 billion in 2012) of the EMA's recommendation are unclear, given the uncertainty over the extent of patent protection for Remicade in some European countries.

FDA approvals for first half of 2013

The US Food and Drug Administration (FDA) approved 13 new therapeutics in the first 6 months of the year.

The lowdown: Between January and June this year, the FDA approved 13 new molecular entities (TABLE 1). This tally is similar to the number approved in the first half of 2012, in which the total number of approvals soared to 39: a 15-year high for the FDA.

Notable approvals include ado-trastuzumab emtansine, an antibody–drug conjugate (ADC) indicated for HER2-positive metastatic breast cancer, which is the second recent approval in a new wave of cancer therapies based on ADC platforms (*Nature Rev. Drug Discov.* **12**, 329–332; 2013). Meanwhile, the antisense platform technology received a boost from the approval of mipomersen for the rare genetic disorder homozygous familial hypercholesterolaemia (*Nature Rev. Drug Discov.* **12**, 179; 2013).

Table 1 | **New molecular entities approved by the FDA: January to June 2013**

Agent	Lead company	Indication
Alogliptin	Takeda	Type 2 diabetes
Mipomersen sodium	Genzyme	Homozygous familial hypercholesterolaemia
Pomalidomide	Celgene	Multiple myeloma
Ado-trastuzumab emtansine*	Genentech	HER2-positive metastatic breast cancer
Ospemifene	Shionogi	Moderate to severe dyspareunia
Technetium Tc-99m tilmanocept	Navidea	Lymphatic mapping in patients with breast cancer or melanoma
Gadoterate meglumine	Guerbet	Contrast agent to visualize disruption of the blood–brain barrier
Dimethyl fumarate	Biogen Idec	Relapsing multiple sclerosis
Canagliflozin	Janssen	Type 2 diabetes
Fluticasone furoate plus vilanterol trifenatate	GlaxoSmithKline	Chronic obstructive pulmonary disease
Radium Ra-223 dichloride	Bayer	Castration-resistant prostate cancer
Dabrafenib mesylate	GlaxoSmithKline	*BRAF*^{V600E}-positive unresectable or metastatic melanoma
Trametinib dimethyl sulphoxide	GlaxoSmithKline	*BRAF*^{V600E}- or *BRAF*^{V600K}-positive unresectable or metastatic melanoma

*Approved as a biologics license application.

Canagliflozin became the first sodium-dependent glucose co-transporter 2 (SGLT2) inhibitor to be approved in the United States (*Nature Biotech.* **31**, 469–470; 2013), and trametinib became the first drug that targets MEKs (MAPK/ERK kinases) to be approved (*Nature Rev. Drug Discov.* **11**, 819–820; 2012).

End of the line for PPAR modulators?

Roche has terminated its development of aleglitazar, a dual peroxisome proliferator-activated receptor-α (PPARα) and PPARγ agonist for type 2 diabetes.

The lowdown: Roche pulled the plug on its programme for aleglitazar owing to the lack of efficacy and toxicity signals flagged by an independent data and safety monitoring board in a Phase III trial known as AleCardio.

This may be the final nail in the coffin for modulators of PPARs, as aleglitazar was the last remaining agent in late-stage trials. This follows major failures and programme terminations from numerous other companies, as well as the long-running controversy over the cardiovascular risks of the PPARγ agonist rosiglitazone (Avandia; GlaxoSmithKline).

Roche pushed ahead with aleglitazar in the hope that its receptor-binding profile might sidestep the cardiovascular risks seen with other dual PPARα and PPARγ agonists (*Nature Rev. Drug Discov.* **9**, 668–669; 2010). Eyes now turn to the small number of remaining candidates in Phase II trials, which include Genfit's GFT505, a dual PPARα and PPARδ agonist for non-alcoholic steatohepatitis, and InteKrin's INT-131, a partial PPARγ agonist for type 2 diabetes.