NEWS IN BRIEF

EMA recommended 39 new drug approvals last year

The European Medicines Agency (EMA) recommended the approval of 39 new therapeutics in 2015, in line with 40 product recommendations in 2014 and up from 34 recommendations in 2013.

The EMA's approval cohort includes small molecules, antibodies, blood products and vaccines. The FDA's Center for Drug Evaluation and Research (CDER), which by contrast only oversees the approval of small molecules and certain types of biologics, approved 45 products in 2015.

The vast majority of the EMA's recommendations went to products that were approved by the FDA in either 2014 or 2015. As such, approval trends — such as the high proportion of oncology and orphan product approvals — are the same. For a detailed analysis of the FDA's 2015 approvals, see *Nat. Rev. Drug Discov.* **15**, 73–76; 2016.

The EMA did, however, recommend approval for three products that have not yet been approved by the FDA. The EMA recommended UCB's brivaracetam, a synaptic vesicle glycoprotein 2A (SV2A) ligand, for the treatment of epilepsy. The FDA was set to make a decision on the approval of brivaracetam in the United States as *Nature Reviews Drug Discovery* went to press. The EMA recommended Grupo Ferrer's tiprolisant, an inverse histamine H3 receptor agonist, for the treatment of narcolepsy. And the EMA recommended Birken's Oleogel-S10, a betulin-rich birch bark extract, for wound healing.

Asher Mullard

Pfizer expands hunt for immuno-oncology biomarkers

Although the therapeutic potential for cancer immunotherapies is huge, many attempts to find biomarkers that can identify the patients who are most likely to respond have so far fallen flat. Programmed cell death 1 ligand 1 (PDL1) expression levels in tumours, for example, do not sufficiently predict which patients will respond to anti-PD1 and anti-PDL1 antibodies. Pfizer has as a result now partnered with Adaptive Biotechnologies to expand its search, exploring whether the immune system holds immunotherapy biomarker clues.

Adaptive uses a high-throughput immunosequencing approach to study a patient's T- and B-cell repertoire. In 2014, working with Merck & Co. and others, the biotech found that by characterizing and quantifying the types of T cells in and near tumours it could build a predictive model of drug response to Merck's now-approved PD1-binding pembrolizumab (*Nature* **515**, 568–571; 2014).

"Adaptive's ability to precisely measure a patient's immune response to cancer before and after treatment provides a universal tool that will help bolster our understanding of immuno-oncology approaches," said Chad Robins, President of Adaptive Biotechnologies. The companies did not disclose the financial terms of the deal.

Pfizer's immuno-oncology pipeline includes the Phase III PDL1-targeting avelumab. The company is also working on a 4-1BB-targeting antibody and an OX40-targeting antibody.

Some data suggest that overall mutational burden might predict who will respond to immuno-oncology treatments, with anti-PD1 antibodies reportedly working best in patients with the highest mutational burden in their tumours (*Science* **348**, 124–128; 2015).

Asher Mullard

Fragile X drug development flounders

Novartis has published the results of two Phase II trials of its metabotropic glutamate receptor 5 (mGluR5) inhibitor mavoglurant in Fragile X syndrome (FXS), 2 years after discontinuing development of the drug. Two Phase II trials — one in 175 adults and one in 139 adolescents — both failed to find any efficacy signal on their primary end point, the company now reports (*Sci. Transl Med.* **8**, 321fs1; 2016).

The trial results are a disappointment, although not yet a fatal blow, for the mGluR theory of Fragile X. This theory holds that the absence of Fragile X mental retardation protein (FMRP) can cause overactivation of mGluR signalling, leading to FXS. Because FXS is the most common single-gene disorder cause of autism, mGluR might have an important role in the origins of other autism spectrum disorders.

Speaking with *Nature Reviews Drug Discovery* last year, Novartis and other Fragile X experts said that the field was struggling to figure out how to best test Fragile X drugs. It remains unclear which patients are most likely to benefit, and which clinical end points are most likely to capture a response (*Nat. Rev. Drug Discov.* **14**, 151–153; 2015).

With the full results out, Novartis re-affirmed these concerns. "Challenges to translation of results in model organisms to humans for FXS thus include uncertainties around optimal patient selection, age of treatment onset, dosages and durations of treatment, differences in pharmacokinetics and pharmacodynamics, dose-limiting side effects, and biomarkers of CNS improvement," the Novartis scientists write. "If the understanding of targeted treatment effects in FXS is to progress, and if the mGluR theory of FXS is to be fully tested, it will be necessary to design new trial paradigms to investigate effects of mGluR agents in young children and to incorporate measures of learning into the protocol."

"The results of negative trials, while disappointing, can be crucial in refining our hypotheses and encouraging dialogue that will accelerate the process of bringing effective treatments to our patients," write another set of authors in an accompanying article (*Sci. Transl Med.* **8**, 321fs1; 2016).

Asher Mullard