BIOBUSINESS BRIEFS

REGULATORY WATCH

# FDA new drug approvals in Q2 2018

The second quarter of 2018 saw an uptick in drug approvals as 15 new drugs received a green light from the FDA (TABLE 1), compared with 6 in the first quarter.

Among the most notable of the new crop was GW Pharmaceuticals' cannabidiol (Epidiolex), the first cannabis-derived drug to gain FDA approval. Epidiolex was cleared to treat two very rare types of severe childhood epilepsy, Lennox–Gastaut syndrome and Dravet syndrome, and is forecast to reach blockbuster sales of US$2.35 billion by 2024. However, it is hard to know how much of a threat over-the-counter cannabinoid-based oils present to products such as Epidiolex, and forecasts could be revised.

Another first was Amgen's erenumab (Aimovig), a monoclonal antibody (mAb) that targets the calcitonin gene-related peptide (CGRP) receptor. Erenumab is the first biologic to be marketed for migraine, but faces the prospect of three CGRP-specific mAbs that are in late-stage development rapidly following it to market. Despite what looks like fairly evenly matched efficacy among these drugs, erenumab has earned the biggest forecast in the class thanks to its first-mover advantage, with global sales of $1.7 billion in 2024.

Array BioPharma managed to score not one, but two approvals in June for its combination melanoma treatment, which incorporates the MEK inhibitor binimetinib and the BRAF inhibitor encorafenib. The combination is specifically for tumours with *BRAF*$^{V600E/K}$ mutations, which are thought to occur in almost half of all metastatic melanoma patients. Despite it being third to market behind both Novartis's and Roche's BRAF–MEK inhibitor combinations, its efficacy could account for combined sales estimates surpassing $1.6 billion in 2024. However, the rise of immunotherapy products could limit the size of the market for all three combination therapies.

The need for products to tackle the ongoing opioid crisis in the United States supported fast-track status and priority review for STADA Arzneimittel's lofexidine (Lucemyra), which became the first non-opioid treatment for the management of opioid withdrawal symptoms in May.

Three approved products had breakthrough designations. Ultragenyx Pharmaceutical's burosumab (Crysvita) was approved in April for patients with the rare genetic disease X-linked hypophosphataemia. Burosumab works by binding excess fibroblast growth factor 23, resulting in a reduction in serum phosphorus levels. Notwithstanding its orphan status, Crysvita is expected to have sales of $1 billion by 2024. Achaogen's plazomicin sulfate (Zemdri) gained approval for complicated urinary tract infections but was handed a complete response letter for a second indication of bloodstream infections.

Table 1 | **FDA new drug approvals in Q2 2018**

| Date | Drug (brand name; company) | Mechanism | Indication | 2024 global sales forecast |
|---|---|---|---|---|
| 17 April[a] | Burosumab (Crysvita; Ultragenyx Pharmaceutical/ Kyowa Hakko Kirin) | FGF23 mAb | X-linked hypophosphataemia | $1,091 million |
| 17 April | Fostamatinib (Tavalisse; Rigel Pharmaceuticals) | SYK inhibitor | Idiopathic thrombocytopenic purpura | $418 million |
| 19 April | Palonosetron and fosnetupitant (Akynzeo IV; Helsinn Group) | 5-$HT_3$ receptor antagonist and $NK_1$ receptor antagonist | Chemotherapy-induced emesis | NA |
| 3 May[a] | Recombinant coagulation factor Xa; inactivated (AndexXa; Portola Pharmaceuticals) | Factor Xa inhibitor antidote | Reversal of anticoagulation | $987 million |
| 16 May | Sodium zirconium cyclosilicate (Lokelma; AstraZeneca) | Potassium ion sorbent | Hyperkalaemia | $929 million |
| 16 May[b] | Lofexidine (Lucemyra; STADA Arzneimittel) | $\alpha_2$-adrenoceptor agonist | Opioid addiction | NA |
| 17 May | Erenumab (Aimovig; Novartis/Amgen) | CGRP receptor mAb | Migraine | $1,708 million |
| 21 May | Avatrombopag (Doptelet; Dova Pharmaceuticals) | Thrombopoietin receptor agonist | Thrombocytopenia | $399 million |
| 24 May | Pegvaliase (Palynziq; BioMarin Pharmaceutical) | PAL replacement therapy | Phenylketonuria | $486 million |
| 31 May | Baricitinib (Olumiant; Incyte/Eli Lilly) | JAK1/2 inhibitor | Rheumatoid arthritis | $1,415 million |
| 14 June | Moxidectin (NA; Medicines Development for Global Health) | γ-aminobutyric acid and glutamate channel modulator | River blindness | NA |
| 25 June[b] | Cannabidiol (Epidiolex; GW Pharmaceuticals) | Cannabinoid receptor agonist | Dravet syndrome; Lennox–Gastaut syndrome | $2,349 million |
| 25 June[a,b] | Plazomicin (Zemdri; Achaogen) | Bacterial 70S ribosome inhibitor | Urinary tract infections | $312 million |
| 27 June | Binimetinib[c] and encorafenib[c] (Braftovi and Mektovi; Array BioPharma) | MEK inhibitor and BRAF inhibitor | Melanoma | $743 million and $882 million |

[a]Breakthrough therapy designation. [b]Fast track. [c]Both components of the combination are new molecular entities. 5-HT, 5-hydroxytryptamine; CGRP; calcitonin gene-related peptide; FGF, fibroblast growth factor; JAK, Janus-associated kinase; mAb, monoclonal antibody; MEK, mitogen-activated protein kinase kinase; NA, not available; NK, neurokinin; PAL, phenylalanine ammonia lyase; SYK, spleen tyrosine kinase.

Portola Pharmaceuticals' andexanet alfa (AndexXa), a factor Xa inhibitor reversal agent, was approved in May.

Meeting the need to find treatments for river blindness resulted in one of the more interesting approvals of the quarter. A collaboration between the WHO's Special Programme for Research and Training in Tropical Diseases (TDR) and the Australian not-for-profit company Medicines Development for Global Health led to the June approval of moxidectin, which is already used in veterinary medicine. The product was awarded a priority review voucher because river blindness is a neglected disease.

Two products that could face sluggish post-launch sales are Eli Lilly's baricitinib (Olumiant) and BioMarin's pegvaliase (Palynziq). Lilly's JAK1/2 inhibitor for rheumatoid arthritis limped across the finish line in May, following a 3-month delay to its filing date and a complete response letter due to safety concerns. Now approved, but at the lower and less efficacious 2 mg dose, its label carries a black box warning. The drug, which at one point had 2022 sales forecasts of $1.83 billion, now faces a battle for sales with established biologics as well as upcoming JAK inhibitors such as AbbVie's upadacitinib. As for Palynziq, the BioMarin drug was intended to replace its older phenylketonuria product sapropterin dihydrochloride (Kuvan), but owing to the risk of anaphylaxis with Palynziq, its label has a black box warning and it will only be available through a REMS programme, and so the drug might struggle to meet the sales forecast of $486 million in 2024.

> Erenumab is the first biologic to be marketed for migraine

The quarter also saw approvals of two products in the thrombocytopenia space. Rigel Pharmaceuticals' thrombocytopenic purpura product, fostamatinib (Tavalisse), gained approval in April, and Dova Pharmaceuticals' avatrombopag (Doptelet), a treatment for thrombocytopenia, reached the market in May.

Other approvals in the quarter included Helsinn Group's fosnetupitant (Akynzeo IV), in combination with palanosetron for chemotherapy-induced nausea and finally, sodium zirconium cyclosilicate (Lokelma), part of AstraZeneca's $2.7 billion purchase of ZS Pharma, which was approved for hyperkalaemia.

*Lisa Urquhart is at EP Vantage, London, UK.*
*e-mail: lisau@epvantage.com*

doi:10.1038/nrd.2018.126
Published online 30 Jul 2018

**Competing interests**
The author declares no competing interests.