MARKET WATCH

FDA new drug approvals in Q3 2019

The biggest approval of the third quarter was not a new drug, but an oral version of Novo Nordisk's semaglutide, branded Rybelsus, which has a consensus sales forecast of $3.3 billion in 2024. Rybelsus is entering a crowded field with over six other glucagon-like peptide 1 receptor agonists already approved, including Novo's once-weekly injectable version of semaglutide, Ozempic. The success of Rybelsus will be determined by its price and whether it also gains a label for reduction of cardiovascular risk, for which trial results are due in January 2020.

The other big-ticket approval of the quarter was AbbVie's Rinvoq (upadacitinib), a selective Janus kinase 1 (JAK1) inhibitor for rheumatoid arthritis. AbbVie had been hoping to avoid the safety issues that have dogged older JAK inhibitors such as Pfizer's Xeljanz (tofacitinib), which were thought to be due to targeting both JAK1 and JAK2, but still received a black-box warning for thrombosis on its label. This could limit its sales, although these are nevertheless forecast to exceed $3 billion by 2024 (TABLE 1).

The other JAK inhibitor approved in the quarter, Celgene's Inrebic (fedratinib) for myelofibrosis, also received a black-box warning, potentially threatening its previously lofty sales forecasts. Hepatic and gastrointestinal toxicities have also been reported for Inrebic, which could be considered when making comparisons with Incyte's Jakafi (ruxolitinib), the current market leader for myelofibrosis.

Of the raft of oncology products greenlighted by the FDA, Roche's Rozlytrek (entrectinib) for cancers with *NTRK* fusions is perhaps the most interesting, as another tumour-agnostic approval and because of Roche's decisions on pricing. In an attempt to take on rival Vitrakvi (larotrectinib; Loxo/Bayer), Rozlytrek's list price is $17,000 a month, compared with $33,000 per month for Vitrakvi. Roche is also focusing on Rozlytrek's additional approval in *ROS1*-positive non-small-cell lung cancer as a differentiator. In addition, the agency granted approval to Karyopharm Therapeutics' Xpovio (selinexor), a nuclear export inhibitor, in combination with steroids for the treatment of relapsed or refractory multiple myeloma and Daiichi Sankyo's Turalio (pexidartinib hydrochloride) for tenosynovial giant cell tumours. Finally, Bayer's Nubeqa (darolutamide), a non-steroidal androgen receptor inhibitor, gained approval for non-metastatic castration-resistant prostate cancer.

The need to find new antibacterial drugs saw both Xenleta (lefamulin; Nabriva Therapeutics) and Merck and Co's Recarbrio (a combination of imipenem, cilastatin and the new β-lactamase inhibitor relebactam) granted fast-track designation and approved under the FDA's Qualified Infectious Disease Product designation. Xenleta is a first-in-class semisynthetic pleuromutilin antibiotic for community-acquired bacterial pneumonia (CABP). An estimated 1 million people in the US are hospitalised with CABP, and Xenleta's low toxicity could make it a more appealing option than established antibiotics. However, given that these are cheaper, Xenleta could face slow uptake, and the current consensus sales forecast for 2024 is $259 million.

Another first-in-class approval was Harmony Biosciences' Wakix (pitolisant), a selective histamine H_3 receptor inverse agonist, for the treatment of excessive daytime sleepiness in adults with narcolepsy. Finally, also in the central nervous system area, Kyowa Kirin's Nourianz (istradefylline), a selective adenosine A_{2A} receptor antagonist, was approved as an add-on treatment to levodopa for patients with Parkinson disease.

Table 1 | **Selected FDA new drug approvals in Q3 2019**

Date	Drug (brand name; company)	Properties	Indication	2024 global sales forecast
3 Jul	Selinexor (Xpovio; Karyopharm Therapeutics)	XPO1 inhibitor	Multiple myeloma	599 million
16 Jul	Cilastatin; imipenem; relebactam (Recarbrio; Merck & Co.)	Bacterial PBP inhibitor; β-lactamase inhibitor	Urinary tract and intra-abdominal bacterial infections	NA
25 Jul	Ferric maltol (Accrufer; Shield Therapeutics)	Haemoglobin regulator	Iron deficiency	176 million
30 Jul	Darolutamide (Nubeqa; Bayer/Orion)	Androgen receptor antagonist	Non-metastatic CRPC	637 million
2 Aug	Pexidartinib (Turalio; Daiichi Sankyo)	CSF1R/KIT/FLT3 inhibitor	Tenosynovial giant cell tumour	164 million
14 Aug	Pitolisant hydrochloride (Wakix; Harmony Biosciences)	Histamine H_3 receptor inverse agonist	Narcolepsy	NA
14 Aug	Pretomanid (NA; Novartis/TB Alliance)	Unclassified	Tuberculosis	NA
15 Aug	Entrectinib (Rozlytrek; Roche)	ALK/ROS1/TRK inhibitor	*NTRK*-positive solid tumours; metastatic NSCLC	342 million
16 Aug	Fedratinib (Inrebic; Celgene)	JAK2 inhibitor	Myelofibrosis	378 million
16 Aug	Upadacitinib (Rinvoq; AbbVie)	JAK1 inhibitor	Rheumatoid arthritis	3,054 million
19 Aug	Lefamulin (Xenleta; Nabriva Therapeutics)	PTC inhibitor	Community-acquired bacterial pneumonia	259 million
27 Aug	Istradefylline (Nouriast; Kyowa Kirin)	Adenosine A_{2A} receptor antagonist	Parkinson disease	142 million
12 Sep	Tenapanor (Ibsrela; Ardelyx)	NHE3 inhibitor	IBS with constipation	694 million

ALK, anaplastic lymphoma kinase; CRPC, castration-resistant prostate cancer; CSF1R, macrophage colony stimulating factor receptor 1; FLT3, FMS-like tyrosine kinase 3; IBS, irritable bowel syndrome; JAK, Janus kinase; NHE3, sodium–hydrogen exchanger 3; NA; not available; NSCLC, non-small-cell lung cancer; PBP, penicillin-binding protein; PTC, peptidyl transferase centre; TRK, tropomyosin receptor kinase; XPO, exportin. EvaluatePharma October 2019, Evaluate Ltd.

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Competing interests
The author declares no competing interests.