A view into the central nervous system disorders market

The market for drugs to treat central nervous system disorders is set for growth, supported by the continued strength of therapies for multiple sclerosis.

Biopharma Dealmakers

Global sales of prescription and over-the-counter (OTC) central nervous system (CNS) disease-related products totaled $86 billion in 2019. Sales were predicted to grow in 2020, but the field has been one of those hardest hit by the COVID-19 pandemic. The total 2020 forecast fell by $1.4 billion between March and June of 2020, as social distancing and lockdown measures made clinics more difficult to access. But, despite the uncertainties caused by the pandemic, analysts predict that the CNS product market will expand to $101 billion in 2022 and to $131 billion in 2025 (Fig. 1). With the help of pharmaceutical market analysts Evaluate Pharma, we analyze the products and companies underlying this expansion and highlight recent major deals in the space.

Top products

Therapies for multiple sclerosis (MS) accounted for 7 of the top 15 CNS products and 26% of CNS product sales in 2019—the highest market share, largely driven by products such as Biogen's Tecfidera (dimethyl fumarate) and Roche's Ocrevus (ocrelizumab). Tecfidera, an oral small-molecule drug, was the best-selling CNS product in 2019, with sales of $4.4 billion (Fig. 2). But Roche's injectable monoclonal antibody (mAb) Ocrevus, the product in the current top 15 that has the largest forecasted growth in sales up to 2025—$3.9 billion—could steal Tecfidera's crown as early as 2022. How soon this happens could depend, in part, on a patent battle that Biogen is engaged in with Mylan, which could see Tecfidera's patent life cut short from 2028 to 2021. The loss of patent protection for Novartis's oral small-molecule drug Gilenya (fingolimod) is also expected to lead to a large drop in sales of $2.6 billion by 2025.

Anti-psychotic products were third in the CNS market ranking 2019, after the subcategory of 'other CNS drugs', with a 13% market share (Fig. 1). They are predicted to retain this position in 2022 and 2025, with Johnson and Johnson's intravenous schizophrenia drug Invega Sustenna (paliperidone palmitate) a long-standing sales driver in this field, having been approved back in 2009. Among the emerging products in this area, Acadia

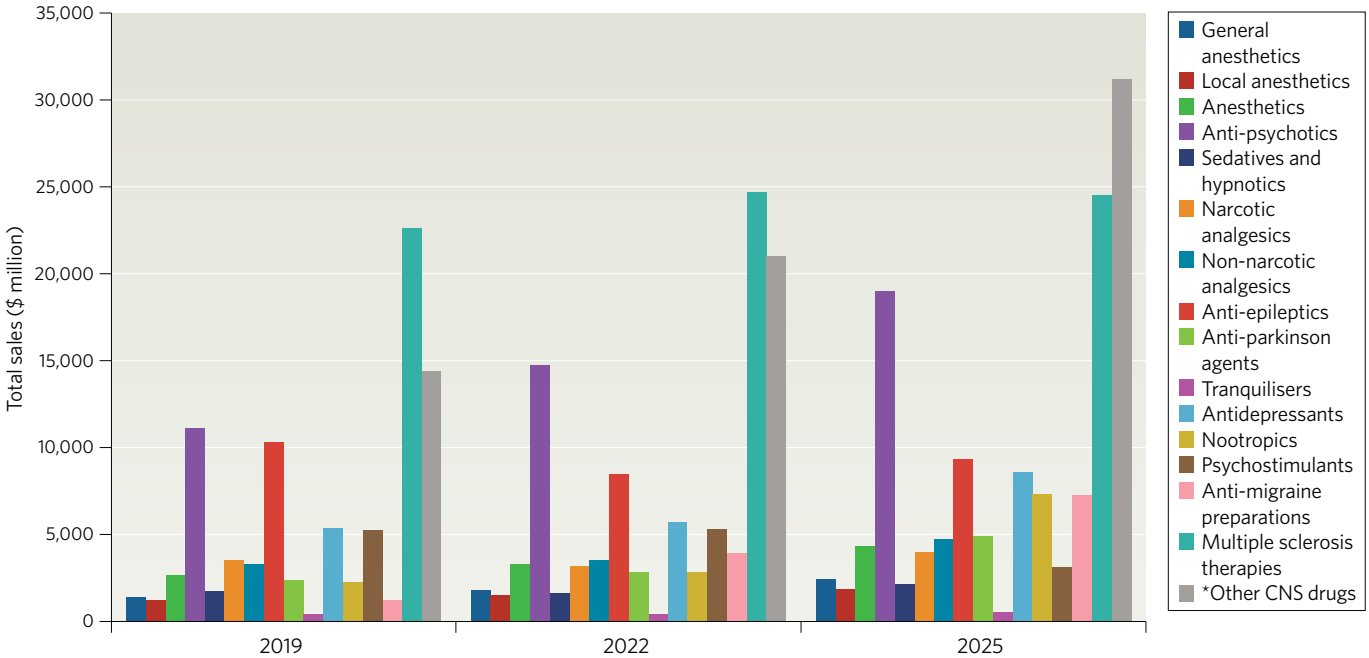

Fig.1 | Central nervous system market overview. Total sales and forecasts from 2019–2025, broken out by subcategory. *Other CNS products includes drugs that fall outside of primary classifications at the time of report generation. Source: EvaluatePharma, July 2020.

Methodology box

This analysis used data extracted from EvaluatePharma (data extracted in July 2020). Company and product sales forecasts are Evaluate Consensus Forecasts, and represent an unweighted average of up to six forecasts from equity analyst research. Historical sales, R&D pipelines and product classifications are based on company-disclosed information. Licensing deals data reflects notable in-licensing deals where the deal value was publically disclosed, and includes transactions between dedicated drug makers only – diagnostics and medtech transactions are excluded.

Pharmaceuticals' Parkinson disease anti-psychotic Nuplazid (pimavanserin) has the greatest forecasted growth in sales: $2.5 billion.

Anti-epileptics account for 12% of the market, coming fourth (Fig. 1). Antidepressants and psychostimulants each took 6% of CNS market share, coming joint fifth, but the two markets are forecasted to trend in the opposite direction in the next few years. Antidepressant product sales are set to rise from $5.2 billion to $8.6 billion between 2019 and 2025 (Fig.1), boosted by sales of recently approved novel products such as Rexulti (brexpiprazole). Sales of psychostimulants, in contrast, are set to fall from $5.2 billion to $3.2 billion over the same period, owing largely to a decline in sales ($2.3 billion) of Takeda's Vyvanse (lisdexamfetamine dimesylate), which is used to treat attention-deficit hyperactivity disorder and is anticipated to lose patent protection in 2023.

Top CNS companies

Of the top ten companies in the CNS market in 2019, Biogen was the clear leader, with 10% of the market (Fig. 3) and 4 of the top 15 top-selling products, including 3 for MS (Fig. 2a). Although Biogen looks likely to retain its top-ranking position in 2022, Roche is forecast to overtake it in 2025 owing largely to predicted sales of $7.7 billion for its CD20-targeted mAb Ocrevus for MS (Fig. 2b). Novartis is also expected to climb the ladder to capture a top 4 slot by 2025, with its recently approved gene therapy for spinal muscular atrophy (SMA), Zolgensma (onasemnogene abeparvovec), as well as its rival CD20-targeted mAb for MS, Arzerra (ofatumumab), which was filed for approval in the USA and the European Union in early 2020.

Johnson and Johnson is expected to fall from second position in 2019 to third in 2025, although its overall sales increase in the period. Pfizer, which largely exited from internal R&D in the CNS area in 2018, is anticipated to drop from third in 2019 to fifth in 2025, with a loss of sales from the off-patent Lyrica (pregabalin; $2.6 billion) compensated for by an increase in sales ($3.4 billion) for its transthyretin amyloid polyneuropathy treatment Vyndaqel (tafamidis meglumine) (Fig. 2b).

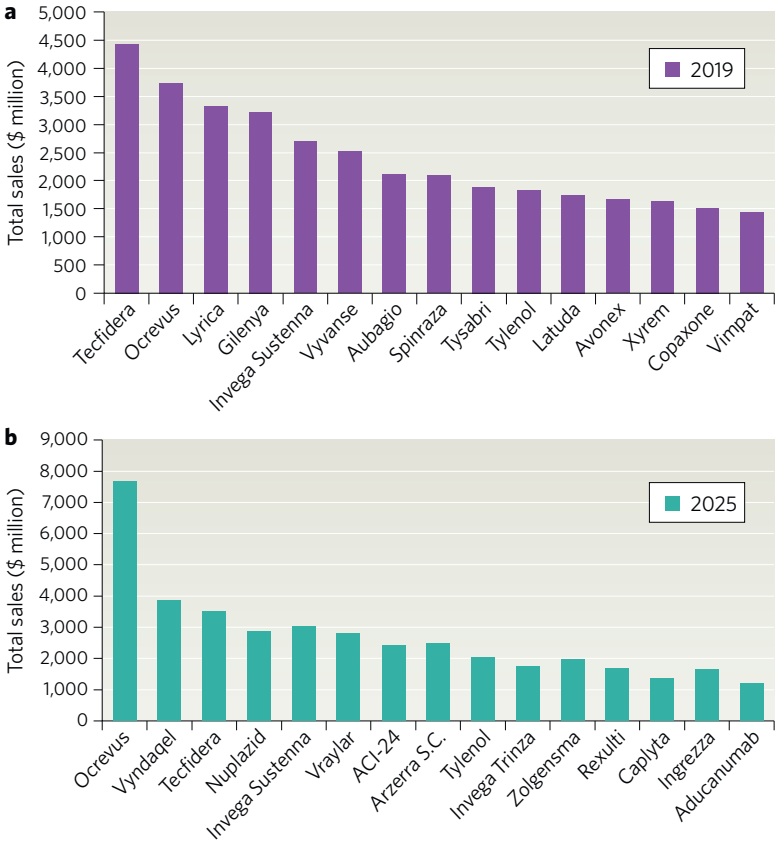

Fig. 2 | Top central nervous system products by sales. a, in 2019 and **b**, forecasted sales for 2025. Source: EvaluatePharma, July 2020.

Recent deals

Recent deals in the CNS area (Table 1) highlight growing interest in gene therapy approaches, encouraged by the US Food and Drug Administration (FDA) approval of Zolgensma for SMA in 2019. In February 2020, for example, Biogen announced a $2.72 billion licensing deal with Sangamo Therapeutics to develop and commercialize gene regulation therapies based on Sangamo's zinc

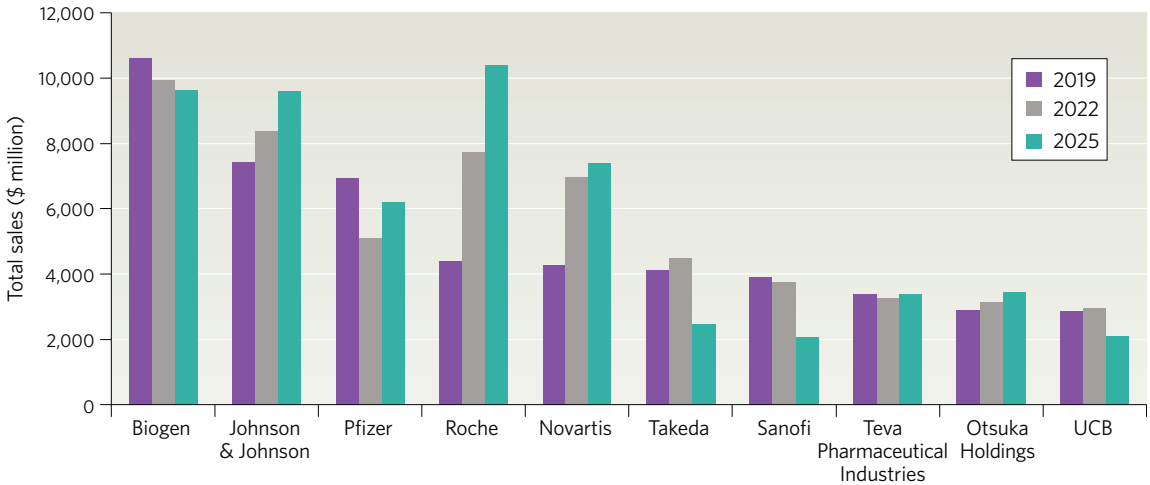

Fig. 3 | Top companies in the central nervous system market. Companies are ranked by 2019 sales, with forecasted Rx and OTC sales growth/rankings to 2025 also shown. Source: EvaluatePharma, July 2020.

Table 1 | Top 10 CNS licensing deals, based on total deal value, from January 2019 to July 2020

Partner/product source	Partner/licensee	Date	Deal type	Deal value ($ million)	Upfront payment ($ million)	Deal summary
Sangamo Therapeutics	Biogen	February 2020	In-licensing	2,720	350	Biogen signs licensing deal with Sangamo Therapeutics to develop gene therapies for neurological disorders based on Sangamo's zinc finger platform.
Voyager Therapeutics	Neurocrine Biosciences	January 2019	In-licensing	1,865	165	Neurocrine Biosciences collaborates with Voyager Therapeutics to develop and commercialize gene therapy programs based on AAV vectors, including VY-AADC for Parkinson disease.
Xenon Pharmaceuticals	Neurocrine Biosciences	December 2019	In-licensing	1,730	30	Neurocrine Biosciences and Xenon Pharmaceuticals collaborate to develop epilepsy therapies, including the sodium channel inhibitor XEN901, which has now entered phase 1.
Centrexion Therapeutics	Lilly	May 2019	In-licensing	988	48	Lilly secures rights to Centrexion's non-opioid pain therapy CNTX-0290, a small-molecule somatostatin receptor type 4 agonist that is in phase 1.
Pfizer	Biogen	January 2020	In-licensing	710	75	Biogen announces deal to acquire PF-05251749, a phase 1-stage modulator of circadian rhythms that is being developed to treat neurological symptoms associated with disorders such as Alzheimer and Parkinson disease.
StrideBio	Takeda	March 2019	In-licensing	710	30	Takeda signs deal with Stride Bio to develop AAV-based therapeutics to target Friedreich's Ataxia and two undisclosed targets. Takeda will advance any pre-clinical candidates manufactured by StrideBio and its AAV capsid development technology.
SK Biopharmaceuticals	Arvelle Therapeutics	February 2019	In-licensing	530	100	Arvelle Therapeutics announces licensing deal to develop and commercialize SK Biopharmaceuticals' anti-epileptic drug Cenobamate in Europe.
Oncodesign	Les Laboratoires Servier	March 2019	In-licensing	360	3	Servier partners with Oncodesign to develop therapeutics for Parkinson disease based on their LRRK2 kinase inhibitors. Servier has the option to license one or several candidates and will provide funds for whole project.
Alivio Therapeutics	Purdue Pharma	January 2019	In-licensing	275	15	Purdue Pharma joins forces with startup Alivio Therapeutics to develop their candidate ALV-107 as a non-opioid therapy for interstitial cystitis/bladder pain syndrome.
Corbus Pharmaceuticals	Kaken Pharmaceutical	January 2019	In-licensing	200	27	Kaken signs deal to license Corbus Pharmaceutical's Lenabasum for commercialization in Japan for the treatment of systemic sclerosis and dermatomyositis.

AAV, adeno-associated virus. Source: EvaluatePharma, July 2020.

finger platform to treat Alzheimer disease, Parkinson disease and other neurological diseases. The deal included an upfront payment of $350 million and up to $2.37 billion in milestone payments. In January 2019, Neurocrine Biosciences signed a similar deal with Voyager Therapeutics to develop and commercialize a series of gene therapy programs for neurodegenerative diseases, including VY-AADC for Parkinson disease. Neurocrine agreed to provide funding for ongoing development of each program, as well as $165 million upfront, to Voyager and up to $1.7 billion in milestone payments.

Biogen also signed another of the top 10 deals (Table 1), agreeing to pay Pfizer $75 million upfront and up to $635 million in milestones for PF-05251749, a drug candidate intended to improve behavioral and neurological symptoms in disorders by modulating circadian rhythms. This adds diversity to Biogen's investments in the failure-stricken area of Alzheimer disease, where its amyloid-targeted mAb aducanumab is now being considered for approval by the FDA. The agency's decision, expected by early next year, could have big implications not just for Biogen but for the CNS field overall.