

大成 DENTONS

LS & Pharmaceuticals Industry Report

December 2020
Europe Insight and Intelligence

LS & Pharmaceuticals

Market overview

This report offers a high-level overview focused mainly on the pharmaceutical industry, related capital events – incl. investments in biotech and medtech companies – FDI flows, the biggest players in the field, and the key trends in life sciences.

The ageing population on the developed markets and the growing access to healthcare on the emerging markets constitute important global demand drivers.

Pharmaceutical products fall into several categories that differ in terms of product development, supply chain management, marketing activities and regulatory compliance: patented, generics, and OTC medications.

While the global pharmaceutical market is dominated by multinational corporations headquartered in the US and Western Europe, the biggest player in the generic

drugs business is India, with a 20% share in global supply of generic medicines by volume.

As patents expire, brand drugs need to compete with generics. On top of that, there is a lot of competition between different types of products. Chemically synthesised pharmaceuticals compete with advanced therapy products, such as cell therapy, immunotherapy and gene therapy. Biologic medical products need to compete with biosimilars, i.e. products similar to already approved biologics (e.g. in anti-rheumatics a loss of 1.9% in CAGR is expected by 2026 as a biosimilar competitor has already entered the EU market and in the US biosimilar competition is expected to start from 2023 onwards).

In 2019, global pharmaceutical sales – i.e. patented drugs, generics and OTC products combined – reached



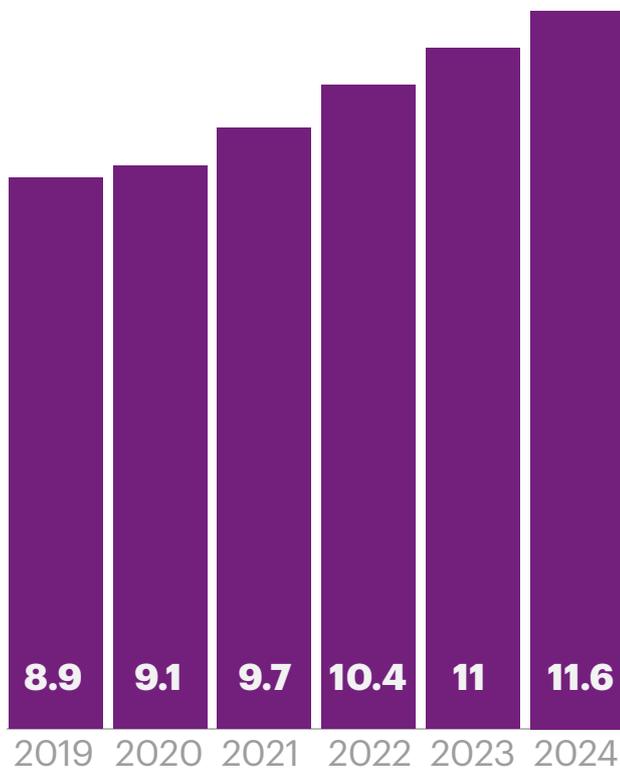
\$1.2trn, which accounts for 13.5% of global healthcare expenditure (Fitch's data). Starting from 2020, the share is expected to begin shrinking. The sales are forecast to dip slightly throughout 2020 – as the Covid-19 pandemic delayed treatments and procedures, resulting in fewer prescriptions – and then return to growth.

Between 2019 and 2024 the overall global healthcare market will expand at a CAGR of 5.6% at constant exchange rates, reaching \$11.6trn in 2024.

Meanwhile, the pharmaceutical market will develop more slowly, at a CAGR of 3.7%, growing from \$1.2trn in 2019 to \$1.4trn in 2024. But some segments of the pharma market are growing at a much faster rate. For example, due to some highly anticipated drug launches the prescription drug market is forecast to grow at a 6.5% CAGR from 2019 to 2024, with orphan drugs (intended for the treatment of rare diseases) as the fastest growing subsegment (+11%, from \$127bn sales in 2019 to a forecast \$214bn in 2024).

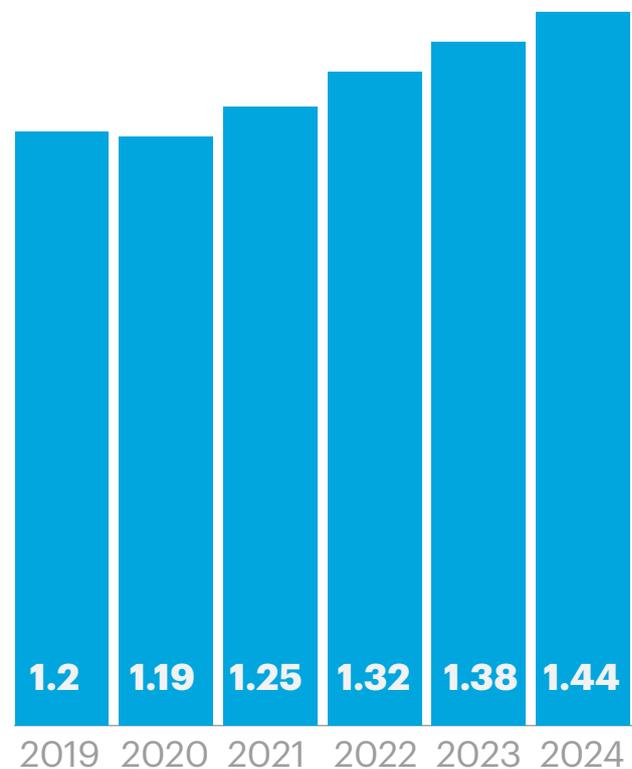
Global expenditures forecast

Fitch, 2019-2024, in \$trn



Global pharmaceuticals market forecast

Fitch, 2019-2024, in \$trn



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Life sciences megatrends

Digital transformation

Internet of Things and disruptive technologies are increasingly penetrating the LS industry.

AI is gaining traction in many fields of LS. Among other applications, it is improving diagnostics by recognising patterns too subtle to be detected by the human eye, it can accelerate drug development by mining large pools of data, and it can improve site and patient selection in clinical trials.

Connected technologies facilitate the adoption of digital health solutions – remote consultations, remote patient monitoring, digital clinical trials.

The Covid-19 pandemic is set to accelerate this trend further and governments are likely to improve the regulatory framework for such solutions.

Digital transformation means that more tech players – who have extensive expertise in using data and analytics – are likely to enter the health market or form alliances with incumbents (the Microsoft-Novartis partnership on AI development is an example of this trend).

Personalised diagnosis and healthcare

With growing and ageing populations, healthcare systems will need to focus on proactive prevention and cost-efficient solutions, hence the evolution towards predictive, preventive and precision care. The digitisation of the sector and health wearables are also driving this shift.

An evolution towards more personalised diagnosis and treatment is an opportunity for innovative LS companies, including those committed to immunotherapy (especially immuno-oncology is a major focus for LS majors), gene therapy, genetic testing, cell therapy, digital health solutions.

Direct-to-consumer genetic testing is expected to grow in popularity, giving individuals more information, but this development is likely to be a developed market phenomenon.

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Winners & losers of healthcare transformation

WINNERS

Innovators

Personalised healthcare networks(Health coaches and home-based care)

Providers of solutions to aid non-institutional chronic disease management and improve independence among elderly patients

Tech and telecom companies(creating new disruptive competition)

DNA testing companies

e-Health companies(e.g. patient-monitoring systems, telerehabilitation, telecare and mobile applications)

Medical IoT and smart devices (wearables) providers

Companies active in immunosuppressants and oncology

(CAGR of +14.5% and +11.5% from 2019 to 2026, respectively)

Biosimilar producers

LOSERS

Traditionalists

Traditional healthcare channels(such as hospitals and clinics)

Small and niche drugmakers

Public health providers

Companies active in anti-rheumatics due to biosimilars entering the market(CAGR of -1.9% from 2019 to 2026)

Manufacturers of drugs treating non-life-threatening diseases in the early trial phase

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Pharmaceuticals market overview – US and Canada

US

The US is the largest market in all three core sub-sectors of the pharmaceutical industry: OTC, patented and generic drugs. In 2019, sales grew 2.1% y/y, reaching \$369bn (for comparison – Japan, the second largest market, recorded \$95bn in drug sales in the same period).

As a result of the Covid-19 pandemic, the sales in 2020 are expected to slow down and gain only 0.4% due to delayed procedures and treatments. This may be exacerbated by a high proportion of the population without healthcare coverage, which can increase even further in the wake of the economic crisis.

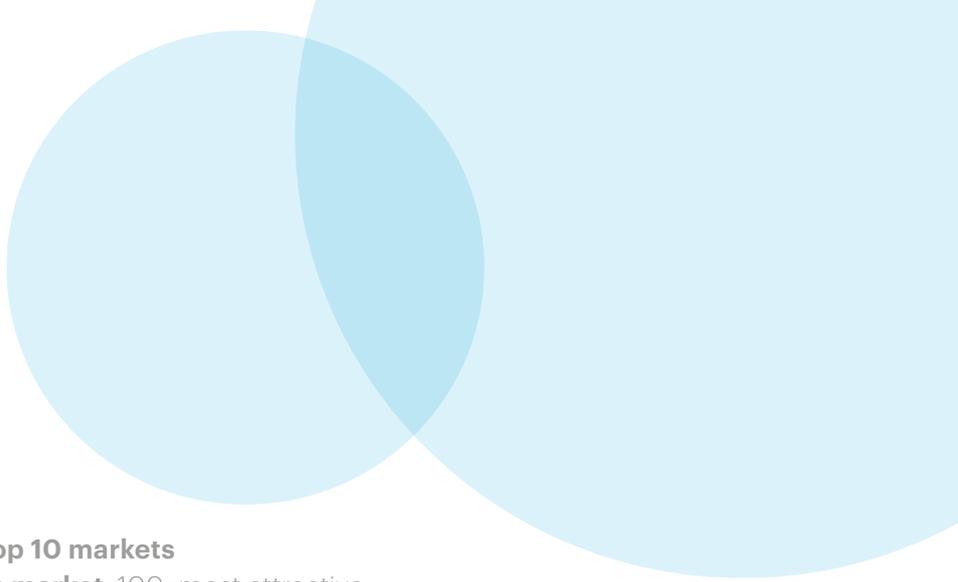
Still, with limited pricing restrictions, a world-class R&D base, and strong IP regime, the US is the most attractive pharmaceutical market in the world according to Fitch, with a risk and reward index of 86.1.

Its growth rate may be moderate, but it has top scores in nearly all index components, the key ones being market expenditure, spending per capita, pricing regime, patent protection and protectionism.

Canada

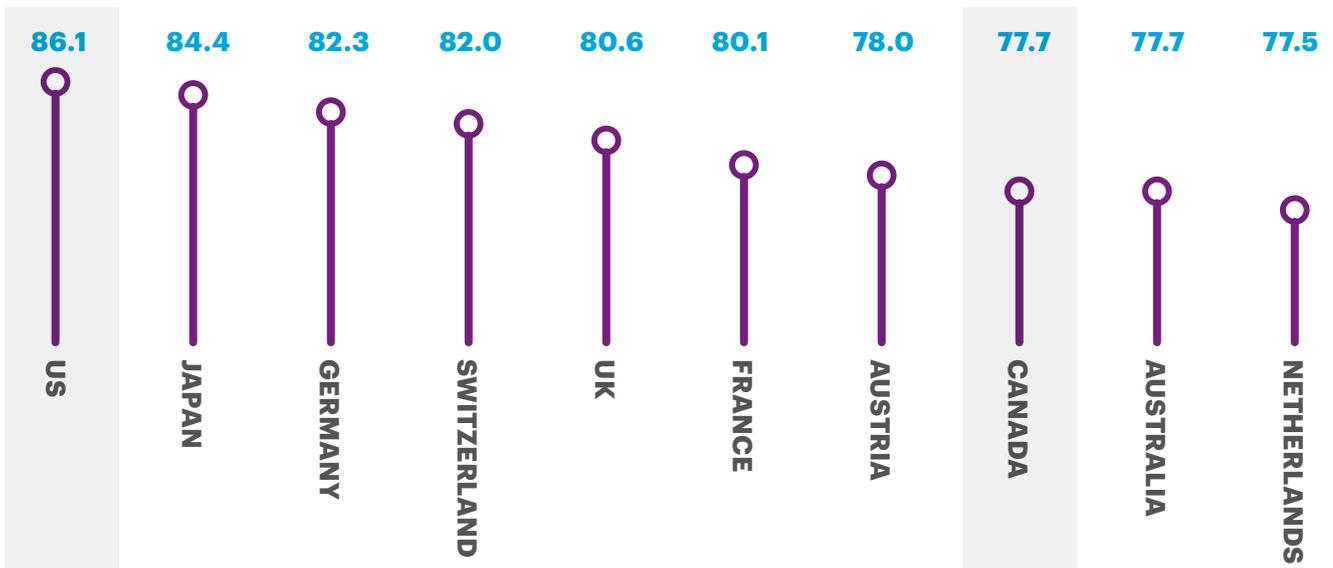
In 2019, pharmaceutical sales in Canada amounted to \$24bn and in 2020 they are expected to grow 0.1% in USD terms (4.9% in local currency). But the revenues will be under pressure, as the country has started introducing changes to its price regulation.

Nevertheless, Canada remains one of the most attractive pharmaceutical markets in the world. With a Fitch risk and reward index at 77.7, it is one of the top 10 markets globally. Canada can also boast one of the most transparent regulatory environments and it has a strong generic drug market, with prices generally higher than the international average.



Fitch's Risk and Reward Index 2020 – top 10 markets

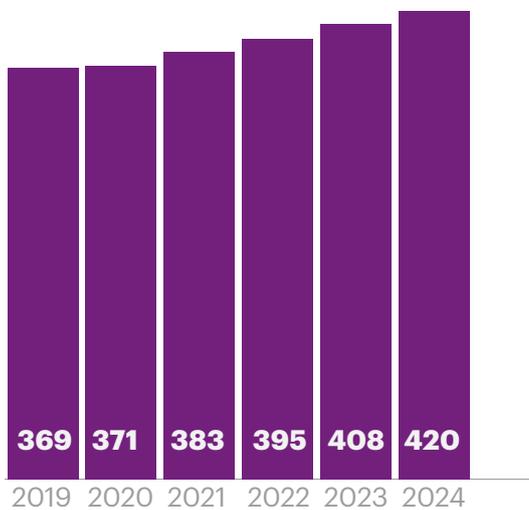
Fitch, 0=least attractive, **Pharmaceuticals market**, 100=most attractive



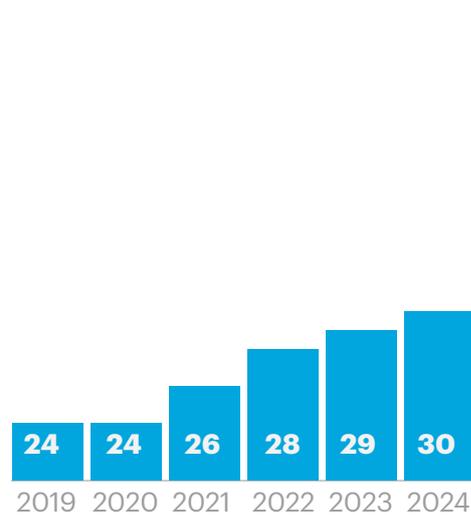
US and Canada 2019 sales and forecast to 2024

Fitch, in \$bn

US



Canada



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R&D in pharmaceuticals and impact of Covid-19

R&D

The pharmaceuticals industry is characterised by high R&D spending (\$186bn globally in 2019), which translates into the innovative character of this business. However, the global CAGR of R&D spend in 2019-2026 is expected to be slower than it was in 2012-2019 (3.2% vs. 4.6%). At this rate, in 2026 global R&D spending should each \$233bn.

The average costs of bringing a new drug to the market vary from \$1.3bn to \$2.8bn and the process may take up to 15 years. Thus, proper IP protection is crucial.

Once patents expire, it is a risk for patent owners' sales, as companies manufacturing branded drugs derive ca. 80% of their revenue from patents.

In recent years, the industry has been strongly focused on R&D work in immuno-oncology, i.e. developing drugs that harness the immune system to fight

tumours, as oncology has the biggest projected market share and global sales among all therapies.

Top 10 therapy areas by projected market share

Evaluate, 2026 forecast, in %

Oncology	21.7
Anti-diabetics	4.7
Immunosuppressants	4.3
Vaccines	3.9
Anti-rheumatics	3.5
Anti-virals	3.0
Sensory organs	2.4
Bronchodilators	2.3
Dermatologicals	2.2
MS therapies	1.7
Anti-hypertensives	1.6

Covid-19

Among the diverse consequences of the pandemic, three major topics stand out:

- Slowdown in drug & medical devices sales – due to the pandemic patients delayed appointments and hospitals postponed elective procedures, which translated into fewer prescriptions and delayed treatments. While the outbreak led to increased expenditure on healthcare, it is reducing the uptake of high margin products such as patented pharmaceutical and innovative medical devices as healthcare resources are re-directed to treating Covid-19 patients. In the longer term, the recession is likely to eat into healthcare budgets of both governments and individuals.
- Protectionism – the pandemic laid bare the dependence on Chinese suppliers of active pharmaceutical ingredients and it is likely to trigger protectionist attempts to source more ingredients and drugs locally. In August 2020, the president of the US issued an executive order requiring the federal government to purchase certain drugs from US manufacturers rather than overseas suppliers and the French government said in June 2020 that it planned to relocate paracetamol production to the country within 3 years.
- New alliances – in the face of a global pandemic, rival pharma companies have partnered up to find synergies and accelerate the work on the Covid-19 vaccine. Covid R&D Alliance has brought together the likes of Astra-Zeneca, Bayer, Bristol-Myers Squibb, Gilead Sciences, GSK, Novartis, Pfizer, Roche, Sanofi, Takeda, and others.



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Latest industry and company news

March

- Sanofi launches European pharmaceutical ingredients (API) company in Europe to reduce its reliance on China.
- India invests \$2bn in three drug production hubs, also to reduce its reliance on China.
- Astra-Zeneca, Bayer, Bristol-Myers Squibb, Gilead Sciences, GSK, Novartis, Pfizer, Roche, Sanofi, Takeda, and others establish a partnership to fight Covid-19.
- FDA issues new regulations for Competitive Generic Therapies to accelerate the development and registration of new generic drugs.

May

- The US awards Phlow Corporation a \$810m contract to manufacture drugs and APIs for fighting Covid-19 so as to limit dependence on Chinese and Indian supply chains.
- Germany introduces regulations that give the government the power to block foreign takeovers of domestic healthcare firms.
- Boehringer Ingelheim acquires Canadian Northern Biologics to strengthen its immuno-oncology business.
- Gilead Sciences establishes a 10-year \$1.6bn partnership with Arcus Biosciences to co-develop next-generation cancer immunotherapies.

April

- Bayer partners with Population Health Research Institute on Covid-19 research in Canada.
- Sanofi and Luminostics team up to develop a Covid-19 testing app.
- Blackstone backs Alnylam Pharmaceuticals, a pioneer in the field of RNA interference (RNAi) medicines with an up to \$2bn investment.
- Gilead Sciences signs a 4-year \$1.5bn collaboration deal with Second Genome on biomarker and inflammatory bowel disease drug discovery.

June

- Canada outlines new patented drug pricing regulations, which may result in a reduction in patented medicine expenditure by \$10bn over 10 years.
- Roche sells non-exclusive rights to cancer technology, cell therapy and bispecific antibody technology to Chinese Innovent Biologics.
- Sanofi partners with Chinese biotech Alphamab for breast cancer R&D.
- Royalty Pharma goes public in a \$2.5bn IPO on Nasdaq (biggest US IPO in H1 2020).
- Legend Biotech, subsidiary of Chinese Genscript Biotech Corporation, goes public in a \$424m IPO on Nasdaq.

July

- Boehringer Ingelheim and Roche launch R&D collaboration initiatives in China.
- GSK signs a \$1bn deal with CureVac (backed by Bill & Melinda Gates Foundation) for developing five messenger RNA-based vaccines and monoclonal antibodies.
- Sanofi gets the first insulin aspart biosimilar approval in Europe.
- AstraZeneca signs a \$6bn global development agreement with Daiichi Sankyo for an antibody drug conjugate ADC DS-1062 to treat cancer.
- Precision medicine company Relay Therapeutics goes public in a \$400m IPO on Nasdaq.

September

- Gilead Sciences acquires cancer drugmaker Immunomedics for \$21bn.
- Merck & Co. enters into a \$4bn cancer drug development deal with Seattle Genetics.
- AbbVie signs a \$2bn deal with China's I-Mab for a cancer drug candidate.
- France fines Novartis and Roche \$530m in an ongoing eye drug dispute.
- Pfizer acquires a 9.9% stake in the Hong Kong-based CStone Pharmaceuticals for \$200m, gaining exclusive rights to commercialize CStone's cancer immunotherapy in mainland China.

August

- The US earmarks \$9bn to accelerate Covid-19 vaccine development. There are three potential candidates in the Phase III clinical trials: Moderna, Pfizer and BioNTech and AstraZeneca.
- Moderna, Pfizer and BioNTech sign an agreement with Canada to supply a Covid-19 vaccine.
- Johnson & Johnson and BARDA launch Blue Knight, a residency scheme for start-ups focused on addressing future health threats.
- Johnson & Johnson acquires Momenta Pharmaceuticals, a developer of novel therapies for immune-mediated diseases for \$6.5bn.
- Sanofi acquires Principia Biopharma for \$3.6bn to bolster its immuno-oncology segment.
- Perceptive Advisors launches start-up LianBio with the aim of marketing cancer and heart disease drugs to China.
- CureVac goes public in a \$213m IPO on Nasdaq. It develops an mRNA Covid-19 vaccine.

October & H1 November

- Pfizer and BioNTech announce their Covid-19 vaccine is 90% effective.
- Bristol-Myers acquires heart drugs developer MyoKardia for \$13bn.
- Bayer acquires biotech firm AskBio for \$4bn.
- Nestle completes the acquisition of Aimmune Therapeutics for \$2bn, to gain full ownership of the first US-approved peanut allergy treatment.
- Novo Nordisk acquires Emisphere Technologies for \$1.8bn.
- Samsung Biologics partners with Chinese biotech GeneQuantum Healthcare to develop an antibody drug conjugate for cancer treatment.
- Atea Pharmaceuticals goes public in a \$300m IPO on Nasdaq.
- Kronos Bio goes public in a \$250m IPO on Nasdaq.

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Top 1,000 companies

There are more than 40,000 companies active in the LS & Pharma sector, globally. The market is dominated by publicly-listed multinational companies from the US and Western Europe.

At the beginning of September 2020, the combined market capitalisation of the largest 1,000 companies exceeded \$6tn. The American Johnson & Johnson, Swiss Roche and American Merck & Co. topped the list.

Nearly 40% of the top 1,000 companies are based in APAC, with more than half of it in China alone. Largest companies from the region include CSL Limited, Chugai Pharmaceutical and Jiangsu Hengrui Medicine.

North America and Europe are home to 35% and 20% of global businesses, respectively. Ca. 5% of the companies are based in South America and MEA.

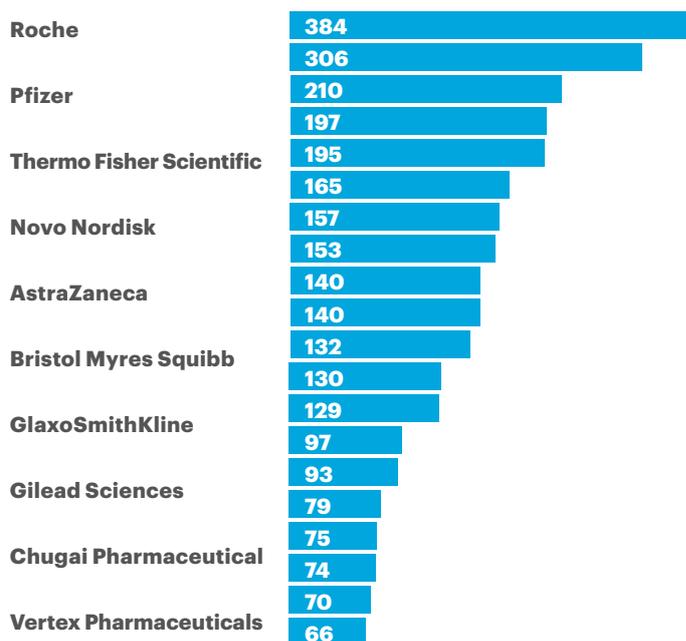
Most companies focus purely on the commercialisation of medicines (human and/or animal), but some are involved also in other businesses, usually medical devices.

Biotechnology companies account for 44% of the top 1,000 list compared with 49% share of conventional drugmakers. Roche, Merck & Co. and Amgen are the leading biologic companies with a combined 30% market share.

Roche is also the biggest spender on R&D (\$10.5bn in 2019), followed by Johnson & Johnson (\$8.8bn) and Merck Co. (\$8.7bn).

Top 20 LS & Pharma companies by market cap

S&P Capital IQ, Dentons analysis, in \$bn



Geographic distribution of LS & Pharma companies

S&P Capital IQ, Dentons analysis



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Foreign direct investment flows

Between 2016 and July 2020, foreign direct investments* (FDIs) in the area of LS & Pharma amounted to nearly \$68bn and created more than 156,800 jobs, globally.

Capital investments peaked in 2018, when they reached \$17bn. Over the period under review, average annual FDI spend stood at ca. \$15bn.

In the first half of 2020, companies already invested \$7.2bn in LS & Pharma-related creating 14,500 jobs. One of the largest announcements this year was the \$1bn expansion of the Japanese Fujifilm Diosynth Biotechnologies' plant in Denmark due by 2023.

Europe is responsible for 45% of FDIs. German, UK and Swiss companies have invested \$19bn since 2016. North America (30%) is the second with most of the capital coming from the US (\$16.5bn).

APAC accounts for 21% of FDIs, primarily from Japan, China and India.

Europe has also attracted most of global FDIs (\$25bn) mainly to the UK, Germany and France. The US has won almost \$20bn investments over the same period, while China \$7bn.

Sector-wise, LS & Pharma-related FDIs were mostly made in pharmaceuticals (\$35bn), biological products (\$23bn), and botanical medicine (\$5bn).

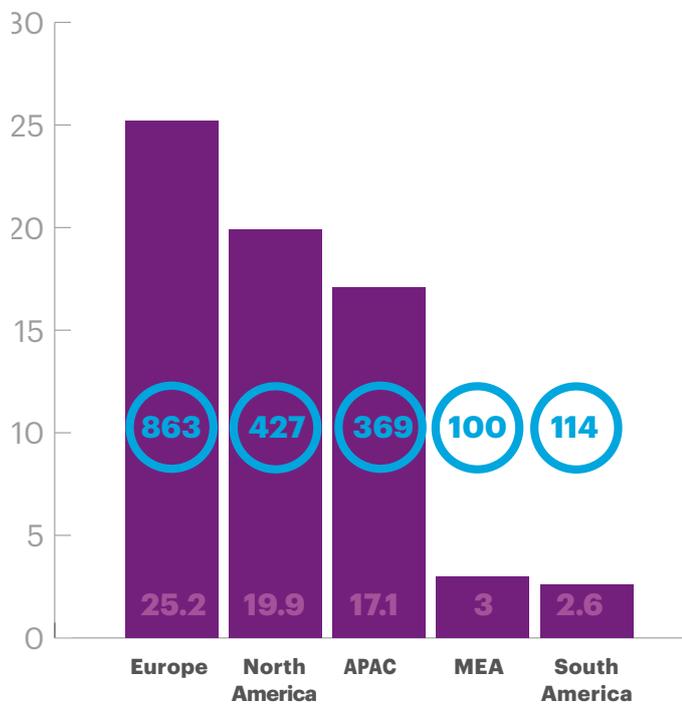
With 49 projects worth \$3.7bn, the US Merck & Co. has been the biggest global foreign investor since 2016, followed by Swiss Roche and French Sanofi.

**Cross border investments in a new physical project or expansion of an existing project in the LS area. Each project has been cross-referenced against multiple sources.*

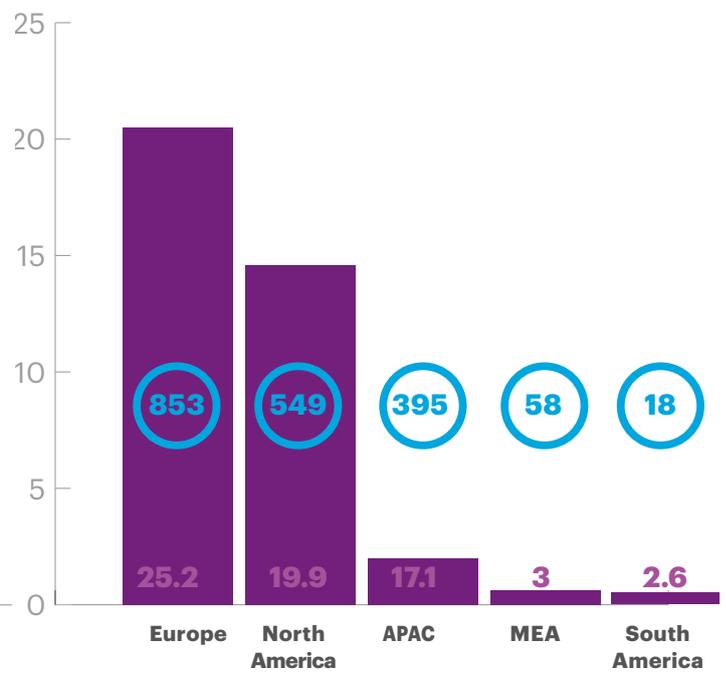
LS & Pharma-related global FDI flows

fDi Markets, Dentons analysis, between 2016 and July 2020 in  \$bn and  no of projects

Capital destination



Capital source



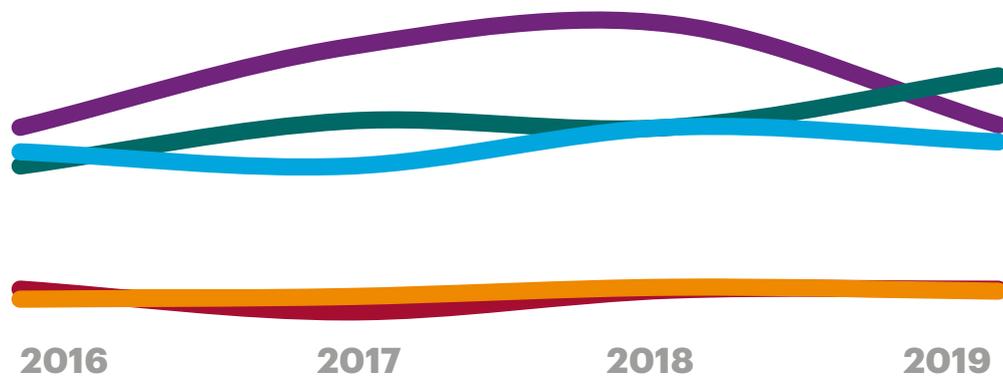
LS & Pharmaceuticals

Foreign direct investment flows

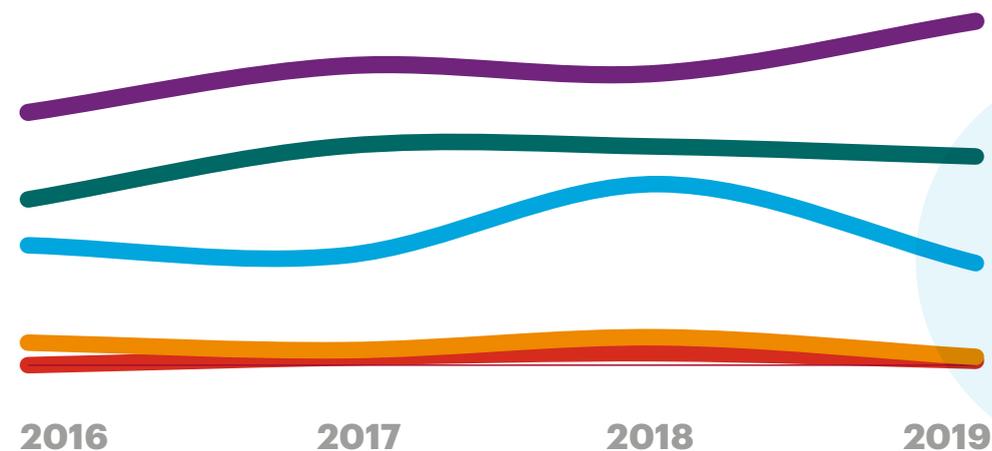
Top 20 FDI investors in LS & Pharma

fDi Markets, Dentons analysis, between 2016 and July 2020, in \$bn

Capital destination



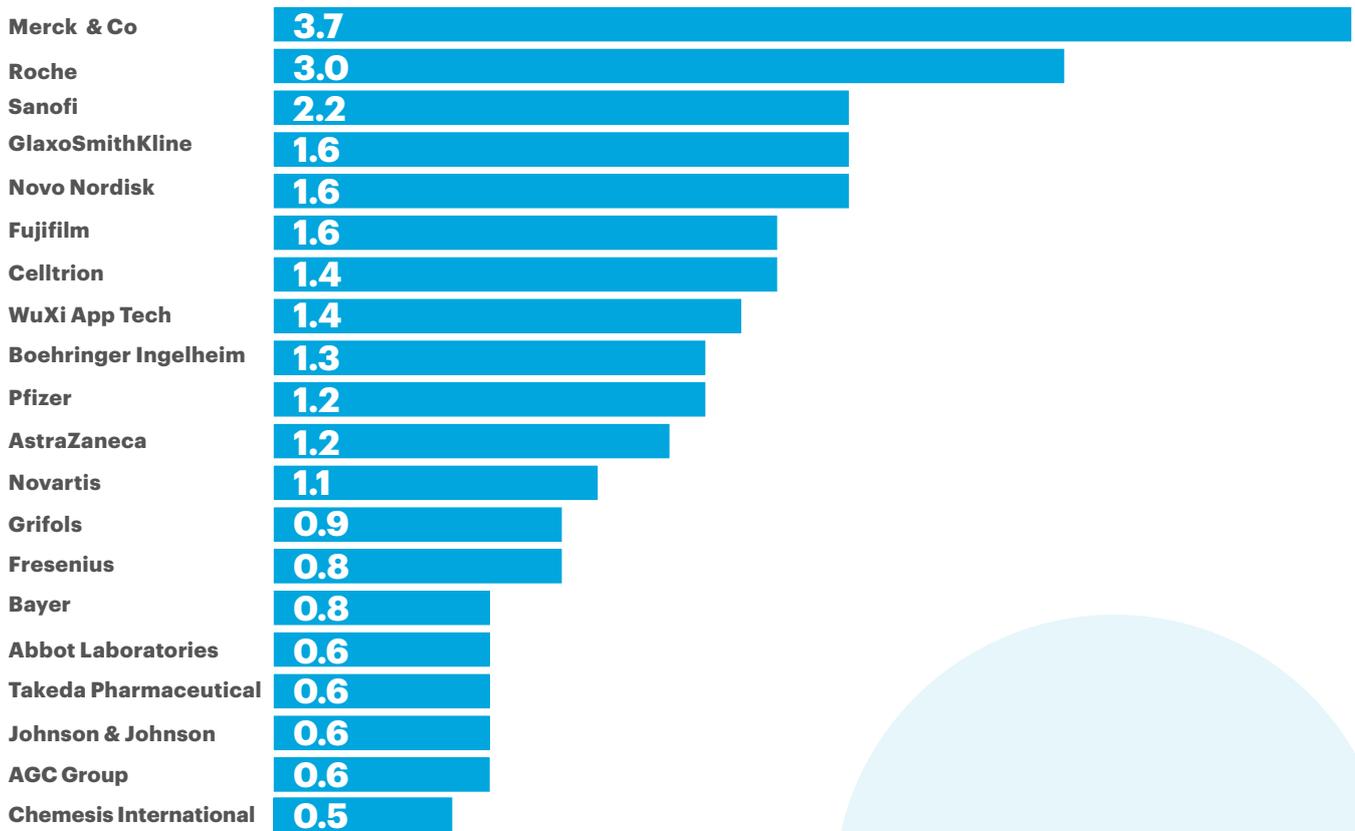
Capital source



● APAC ● Europe ● North America ● MEA ● South America

Top 20 FDI investors in LS & Pharma

fDi Markets, Dentons analysis, between 2016 and 2019, in \$bn



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Venture capital flows

Nearly \$120bn has been invested globally into early stage LS & Pharma companies* via VC financing over 2016 and mid-September 2020.

Annual VC activity peaked in 2018, when it reached the \$30bn mark in 1,494 deals. The drop in 2019, was primarily driven by a 20% drop in the US – by far the largest market with a 67% share globally.

From the start of 2020 to mid-September 2020, global VC financing pool stood at \$25.1bn, which is just \$1.2bn short of total 2019.

The activity in APAC, the second largest market, has been steadily growing over the past years – from \$2.1bn in 2016 to \$5.8bn at the end of 2019. This year is about to see another record with VC deal value passing \$6bn mark.

Europe accounts for 13% of the global VC activity. The key markets include UK, Switzerland, France and Germany.

Out of the top 20 companies with the most VC financing 14 come from the US. Topping the list is GRAIL, which attracted more than \$2.7bn for developing a technology enabling early cancer detection and identification. German BioNTech and US Moderna, both well-advanced in works on the Covid-19 vaccine, are also on the list.

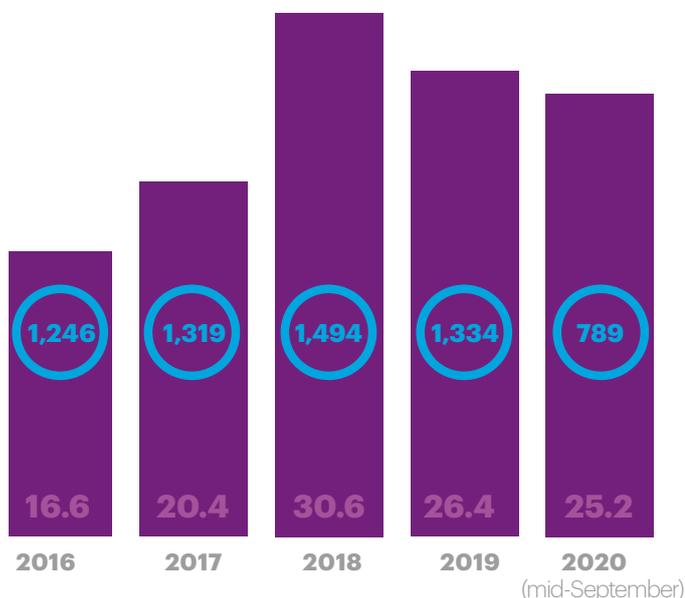
Similarly, 18 out of the top 20 most active investors are from the US. OrbiMed Advisors has pursued 139 VC deals, the largest number since 2016. The firm currently manages over \$13bn of investments.

Most popular subsectors include healthtech solutions and drug manufacturing, but investors are also eyeing companies that allow for a shift to low-carbon economy.

**Financing provided by venture capital firms or funds to start-ups, and early-stage companies.*

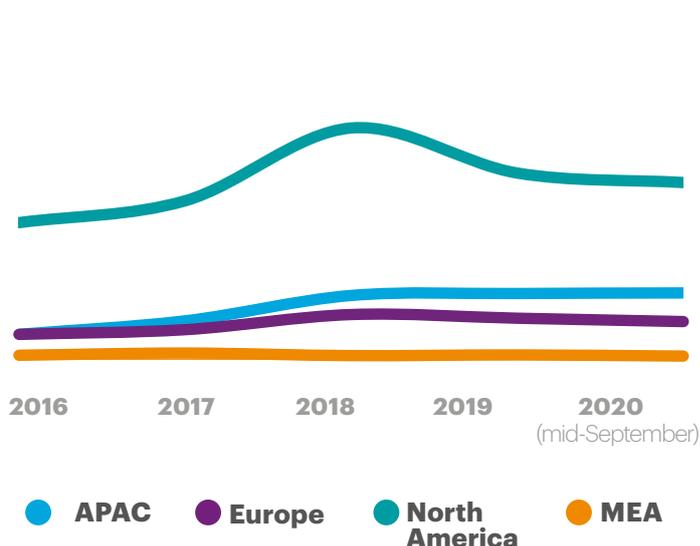
LS & Pharma-related global VC flows

Prequin, Dentons analysis, between 2016 and mid-September 2020, in \$bn and no. of deals



LS & Pharma-related global VC flows

Prequin, Dentons analysis, between 2016 and mid-September 2020, by target HQ office, in \$bn

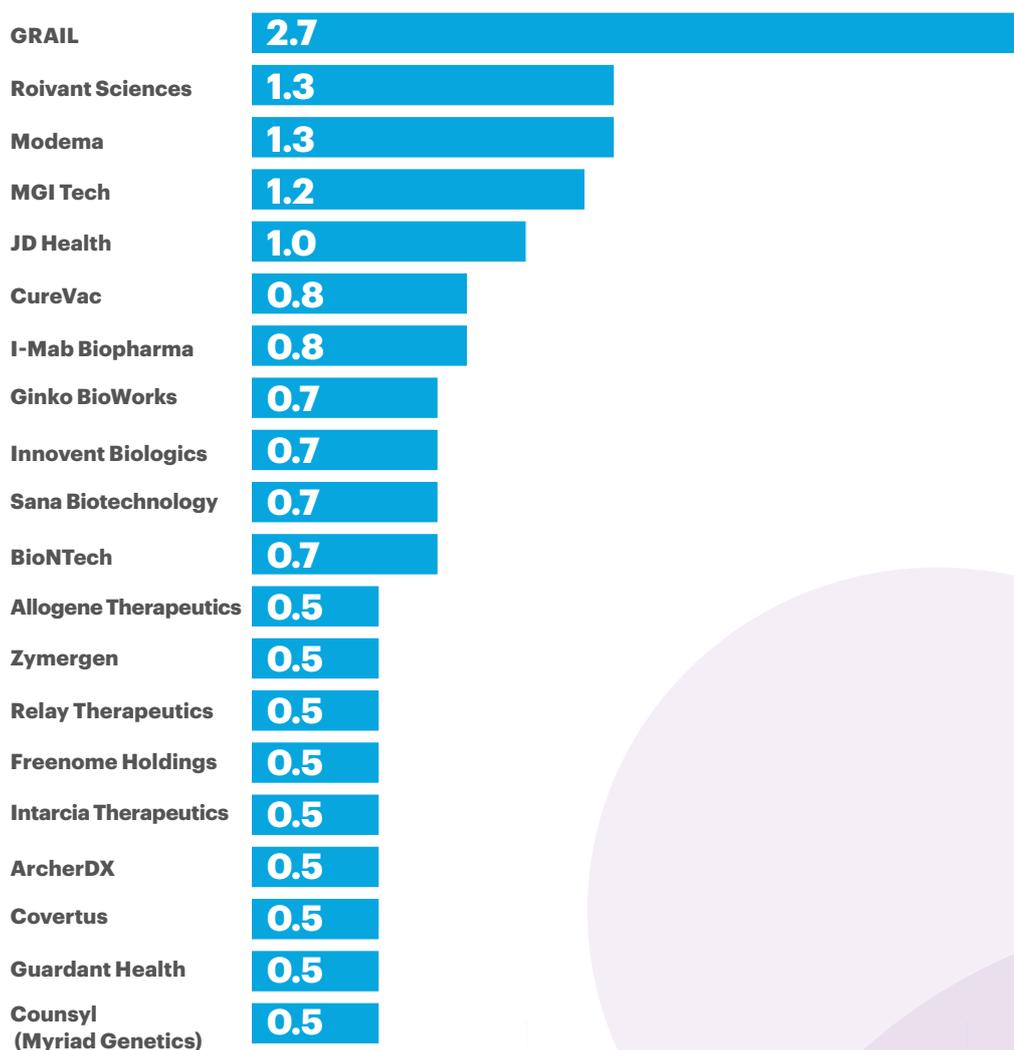


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Venture capital flows

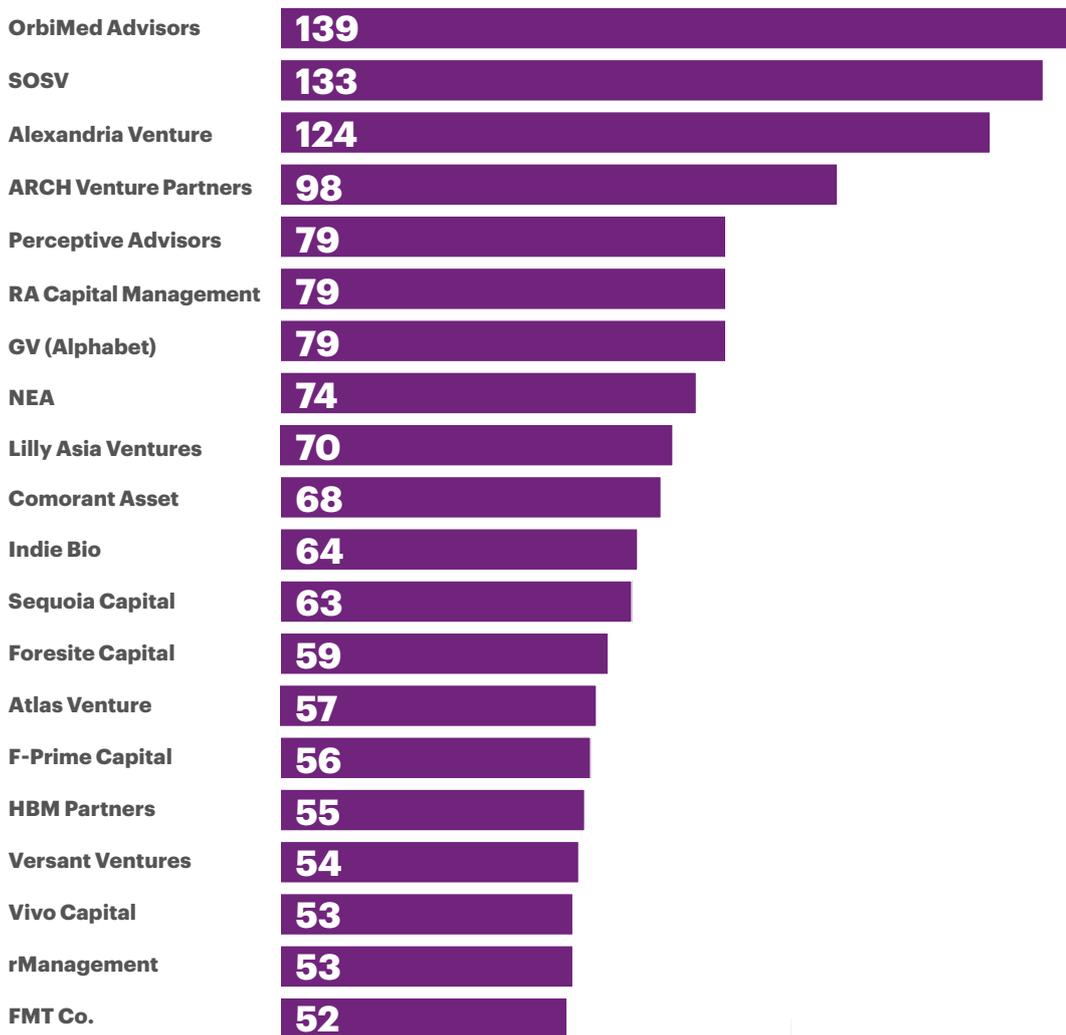
Top 20 LS & Pharma companies with most VC financing

Prequin, Dentons analysis, between 2016 and mid-September 2020, in \$bn



Top 20 VC investors in LS & Pharma

Preqin, Dentons analysis, between 2016 and mid-September 2020, in no. of deals



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Mergers & acquisitions

The LS sector is characterised by large and frequent M&As. Global deal value between 2016 and August 2020 exceeds \$2tn within total volume of 12,871 transactions*.

Dealmaking has been thriving over the past years – from 2,622 transactions worth \$425bn in 2016 to a record 2,881 totalling \$672bn in 2019.

There have been 1,924 M&A deals in a year to August 2020, worth at least \$165bn (the real figure is much higher due to a large proportion of deals with undisclosed value).

The US, China, Japan and Western Europe dominate the LS & Pharma-related M&A landscape. The US alone accounts for 30% of global deal volumes and 60% of total value. Canada enjoys a 4% and 2% share, respectively.

Sixteen of the top 20 deals involved targets from the US. Switzerland was second with three, and the last target was a British company.

Topping the list is the US cancer drugmaker Celgene, which was bought by Bristol Myers Squibb for \$87bn in 2019. The largest deal from Europe was the purchase of the UK rare diseases specialist Shire by Japanese Takeda for \$66bn in 2018.

Most acquisitive companies (with more than 20 M&A deals since 2016) are Luxembourg-based Eurofins Scientific and American Johnson & Johnson.

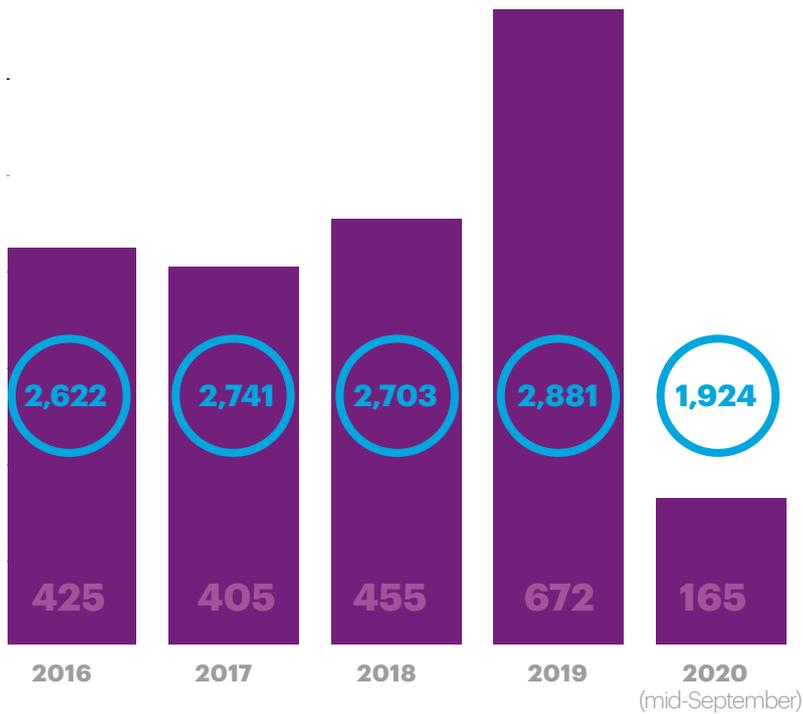
M&A activity is driven largely by the interest in biotech firms (in H1 2020 deal volumes rose nearly 25%, while in medtech and pharmaceuticals they declined 15% and 8%).

Big Pharma is primarily focusing on mid-size biotech companies that specialise in cell and gene therapy, oncology and next-generation biologics.

**Completed and pending M&A deals with a target and/or acquirer in LS & Pharma. Ca. 40% of deals had undisclosed values.*

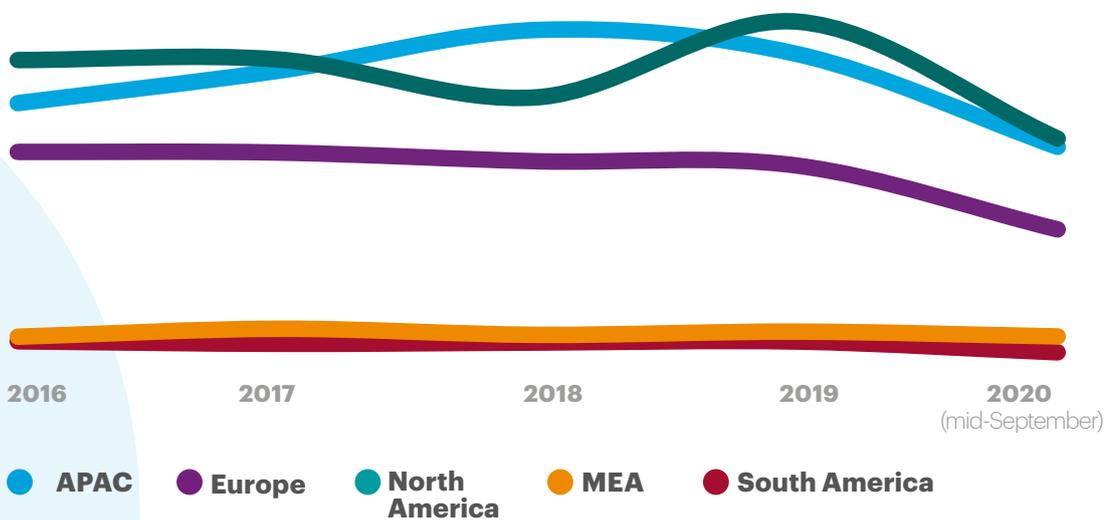
LS & Pharma-related global M&A flows

Dealogic, Dentons analysis, between 2016 and August 2020, in ■ \$bn and ○ no. of deals



LS & Pharma-related global M&A activity

Dealogic, Dentons analysis, between 2016 and August 2020, by target HQ, by no. of deals

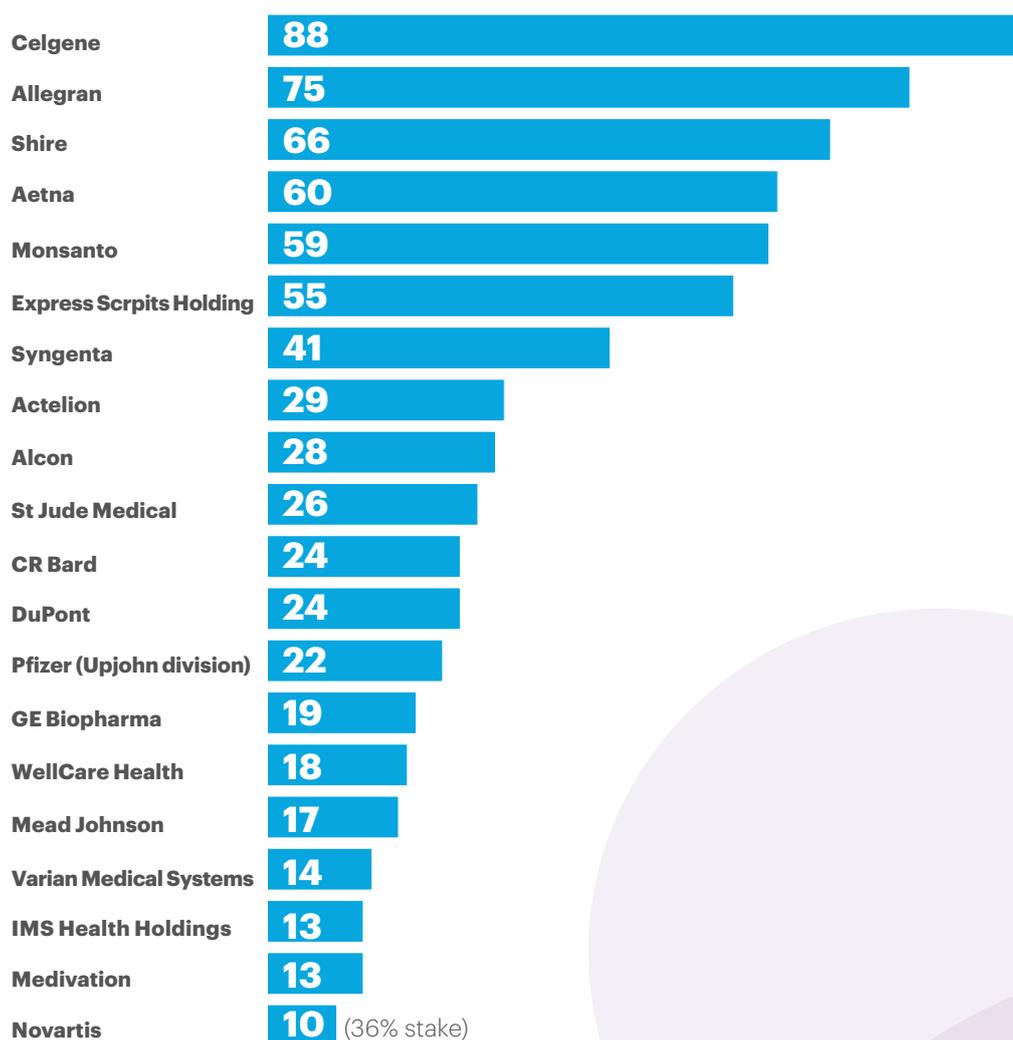


LS & Pharmaceuticals

Mergers & acquisitions

Top 20 LS & Pharma companies with most VC financing

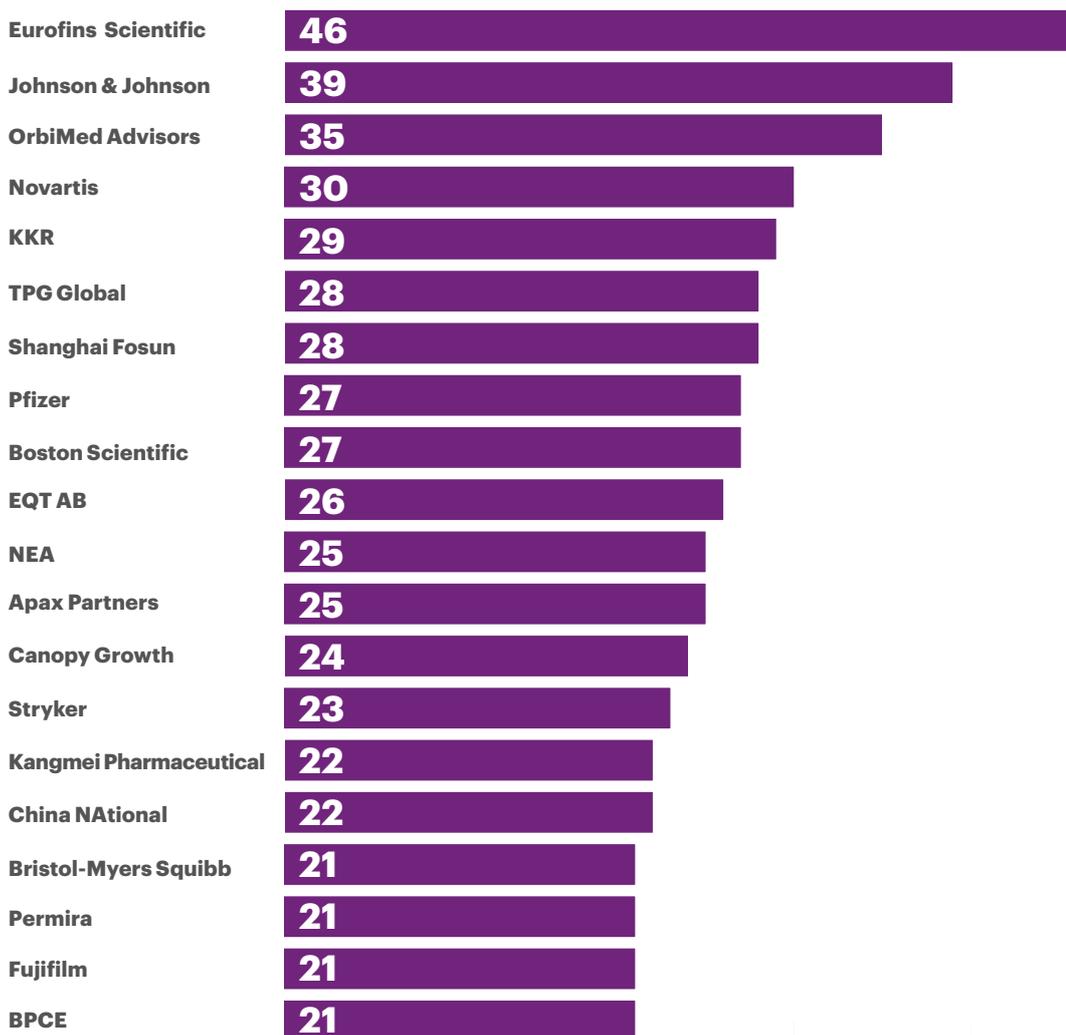
Preqin, Dentons analysis, between 2016 and mid-September 2020, in \$bn



**with more than 20 deals since 2016*

Top 20 LS & Pharma companies with most VC financing

Preqin, Dentons analysis, between 2016 and mid-September 2020, in \$bn



Key Contact:



Paola Pozzi-Dazza

Director of Marketing and Communication,
Life Sciences, IP&T and Sovereign Advisory
D + 33 1 42 68 92 72
paola.pozzi@dentons.com

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