European biotechs take a seat at the biotech funding table in 2019. Credit: Antikwar / iStock / Getty Images Plus

Europe's biotech renaissance

European biotech companies continued to raise unprecedented amounts of capital last year. Can they survive what are likely to be leaner times ahead?

Last year was a big year for life science start-ups in Europe. Overall, the private biotech sector raised a record-breaking $3.3 billion in private money. This is almost 35% more than was raised in the previous record year 2018. 2019 also saw new kinds of investors pile into biotech, bringing yet more sources of capital and driving up valuations. Both the funding and the partnering environments were healthy. Biotech looked "as de-risked as it could be, in terms of exit options," said Jeffrey Tong, partner at US venture capital firm Third Rock Ventures, speaking in early February 2020.

Then a risk not in any investor's model sent stock markets across the world plummeting while dealmaking dries up, as the coronavirus threat compels entire nations to shut down. Some observers were concerned, even before the coronavirus outbreak, that an influx of funding from a diverse set of investment sources from around the world could have created a glut of new companies — too many to sustain in the long term.

But the industry's macro-drivers, unmet need, continue to be strong — perhaps even more so during what is billed as the worst pandemic in a century. Indeed, Amsterdam-based investment firm LSP raised a $620 million life sciences fund in March 2020 — the largest ever in Europe, it claims. Even if the funding bonanza does not last, many more of Europe's biotech startups are strong enough to survive what may be leaner times ahead.

Fewer deals, more blockbusters

Looking globally, 2019's headline numbers beat even 2018's strong performance, albeit not by much. Global biotech venture funding in 2019, at $18.8 billion, was just up from the $17.0 billion raised in 2018 (Box 1 and Fig. 1a), and global initial public offering (IPO) proceeds of $11.5 billion as well just topped 2018's bumper $11.4 billion (Fig. 1b). The total value of mergers and acquisitions (M&As) surpassed 2018's $1.3 trillion (Table 1), and 2019's tally (52) of private financing rounds worth >$100 million — so-called 'mega-rounds' — topped the previous year's (50). This reflects expanding fund sizes among existing venture capital companies (VCs) and interest in biotech from new kinds of investors, including private equity, sovereign wealth funds and family offices.

The ten-year-long IPO window stayed open in 2019 and brought the biggest ever European biotech listing, when Denmark's Genmab raised $582 million on the Nasdaq in July, just shy of Moderna's $600 million record haul in 2018. "As more private

Box 1 | The data

This year's feature data were pulled from BioCentury's BCIQ database, rather than Dow Jones, which has provided the data for all our previous annual features on the private biotech sector. BCIQ has a somewhat different set of options for filtering financial data from Dow Jones; to focus exclusively on private investment going solely into startups and private companies, for this feature, we have filtered out PIPEs (private investments in public equity). Thus, the data presented here are not comparable with those in previous *Nature Biotechnology* features on the private biotech sector. We find that the trends differ from that seen when PIPEs are included, which is how these values have been widely reported. Readers should note that our quarterly Data Page on biotech sector finance encompasses all funding, including PIPEs.

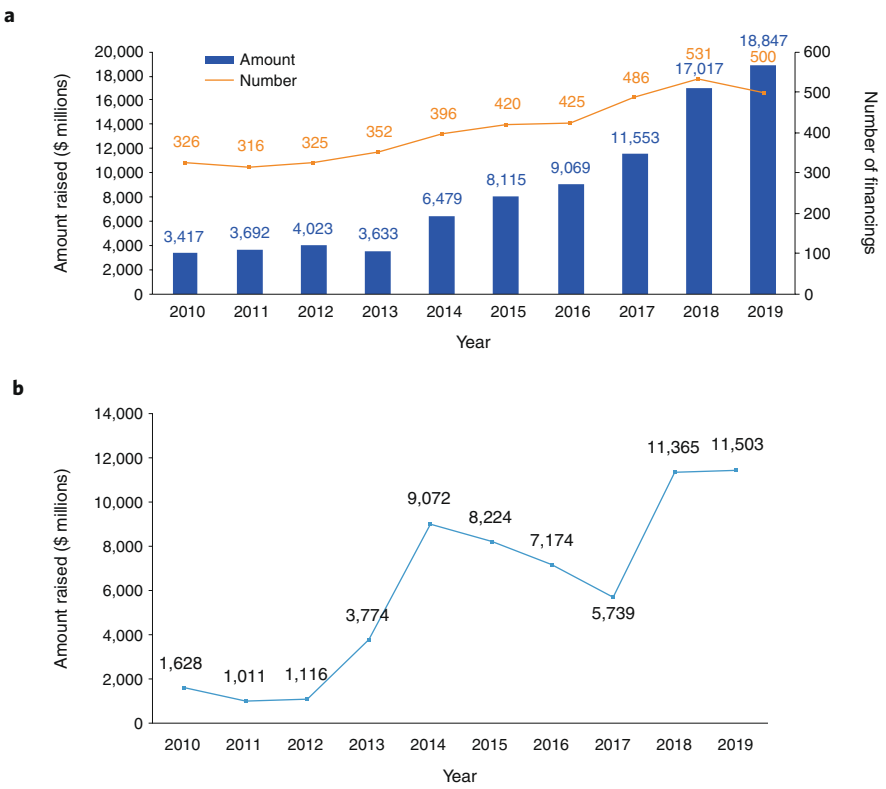

Fig. 1 | Money flowing into biotech 2019. a, Global VC investment in biotech. **b**, Global IPO financings. Source: BCIQ BioCentury Online Intelligence.

funding goes in [to biotech], so IPO sizes are also up. Median IPO valuations this year are north of $400 million; post-IPO valuations have never been as high," said Atlas Venture partner Bruce Booth.

The number of biotech acquisitions and licensing deals has been declining over the past two years, according to consultants Evaluate. But median M&A premiums paid for research-stage drug developers, at 97%, reached their highest level in five years in 2019, Evaluate calculates. It was a similar story in licensing, where the average up-front payments for programs at all stages, from preclinical to phase 3, increased over 2018. The median up-front payment for preclinical assets rose from $12 million to $20 million, Evaluate reports.

These data signal that pharmaceutical firms are willing to place their bets earlier as they seek to avoid the higher prices, and intense competition for assets, that emerge later on in development.

Fringe benefits from China's rise

European biotech has continued to benefit from increasing interest from Chinese investors. Overall, Chinese biotech — and biotech investors — continued to search for lucrative investment vehicles outside of mainland China. Last year, however, funding into US biotechs slowed, primarily due to the US-China trade war that kicked off in mid-2018, and updated rules on Chinese investment into US companies. This hit Chinese-led series B rounds in US companies particularly hard during the first half of 2019, according to data from Bay Bridge Bio. The uncertainty has been increasingly driving Chinese investors' gaze towards European biotech as an attractive target for investment. Several experts predict that Europe's biotechs may benefit from the United States–China standoff. This, combined with the considerable discounts for which high-quality science can be purchased in Europe compared with the United States, has continued to attract Chinese investment to European biotech. For example, in September, Milan-based Genenta Science raised €13.2 million ($14.5 million) in a series C round from Shanghai-based Qianzhan Investment Management.

Meanwhile, Chinese biotech is maturing, as the country prioritizes building a homegrown innovation-driven sector. That should, post-coronavirus, continue to drive licensing activity — and funding — for European and US biotechs as Chinese companies seek out innovative drug candidates to develop and commercialize in China. In June 2019, for example, Deciphera Pharmaceuticals received $20 million up front and up to $185 million in milestone and royalty payments from Shanghai-based Zai Labs, for development and commercialization rights in Greater China to the multikinase inhibitor ripretinib.

Ups and downs in Europe's biotech sector

Notwithstanding the continued dismal performance of European public markets — just seven IPOs happened in 2019, raising less than $500m in total, half the prior year's tally — 2019 has been the strong year for European private biotech funding, representing a milestone since the sector's nadir in capitalization 10 years ago (Fig. 2).

The continuing upward trend in the amount of private money raised by the biotech sector reflects a maturing local VC landscape (Table 2), a growing — if still inadequate — pool of management talent, and a growing inflow of US and Asian capital, according to Graziano Seghezzi, managing partner at Sofinnova Partners, an early-stage European VC. "We're creating more companies, and capitalizing them better," he says.

As biotech valuations got frothy in the United States and Asia, those foreign investors were drawn in by often more

Neil Woodford of the now defunct Woodford Equity Income Fund. Credit: Jeff Gilbert / Alamy Stock Photo

competitive valuations in Europe and supported by more-experienced local investors who have gotten better at identifying and curating early-stage science. European biotechs raised about 15% of overall series A money — about the same as in 2018. At the country level, the United Kingdom stood out in 2019, attracting almost three times as much venture capital as biotechs in France or Germany, according to Informa — about $870 million in total. The United Kingdom also outstrips its European neighbors in company creation, housing more than a third of all European biotechs seeded since 2012. Several UK private and public biotechs were badly hit by the collapse of investment manager Neil Woodford's funds, however. Woodford, once held up as a local hero in supporting riskier companies, was unable to support investor withdrawals from his fund because he overloaded his portfolio with too many illiquid stocks — stocks, like those of many private biotechs, that don't change hands very much.

Fortunately, the United Kingdom's investor base has broadened over the past ten years, with foreign investors featuring prominently in the largest of 2019's financings. US-based RA Capital led personalized cancer medicine company Achilles Therapeutics' £100 million ($121 million) B round in September; longevity-focused Juvenescence, which raised £82 million ($100 million), attracted US-based Explorer Equity Group alongside IDO Investments, an Oman-based VC supported by the Gulf state's sovereign wealth fund.

Overseas investors are likely to continue to play a key role supporting European biotech. In 2019 it became clear that Europe's weakness is now later-stage funding — a shift from five years ago, when early-stage money was the problem. Back then, "people thought you were crazy if you were doing early-stage in Europe," says Seghezzi, given a traditionally risk-averse mentality.

US exits and new technology

This later-stage funding hole is also what drove the definitive emergence, in 2019, of Nasdaq as the public market of choice for European R&D-focused biotechs. Nasdaq's advantages over Europe's small national exchanges in terms of access to capital, specialist investors and liquidity had long been clear. IPOs represent an important path for exit of biotech startup investors, and European exchanges have long underperformed. By 2019, all but one of the top eight European biotech IPOs were on Nasdaq — including Genmab's mega-raise, the hefty $148 million October 2019 IPO by German cancer immunotherapy company BioNTech, and $55 million raised by France's Innate Pharma. (The eighth, Ascelia Pharma, was on Stockholm's Nasdaq.) There was not a single biotech IPO on the United Kingdom's AIM. "The US capital market is nine or ten times larger than that in the UK, with a nearly endless list of specialized healthcare funds," says Andrew Oakley, CFO at UK-based chimeric antigen T (CAR-T) cell company Autolus Therapeutics, which raised $150 million on Nasdaq in 2018, bypassing a local IPO.

Indeed, it is not only established European companies like Genmab that are flocking to Nasdaq. Startups in novel, fast-moving fields need Nasdaq to raise money fast enough to remain competitive — and to attract buyers and partners. For example, in 2019, UK group Bicycle Therapeutics, which is developing a new class of peptide-based therapies for cancer, raised $60 million in a direct-to-Nasdaq listing. UK gene-therapy venture Nightstar Therapeutics, which had joined Nasdaq in 2017, was acquired by Biogen for $800 million in early 2019 — at an almost 80% premium to Nightstar's listing price. Gene therapy continued to be red-hot in 2019 — marked by Roche's $4.8 billion purchase of Spark Therapeutics; Asklepios BioPharmaceutical's $235 million private financing; and Johnson & Johnson's $100 million pact in January 2019 with UK-based MeiraGTx, working on gene therapies for vision loss. (MeiraGTx is another Nasdaq pioneer, raising $80 million in a 2018 IPO; gene-therapy compatriot Orchard Therapeutics raised $186 million the same year.)

A changing investor profile

The continued rise of crossover investors during 2019 was another factor driving European biotechs toward Nasdaq. Crossover investors support companies with private (pre-IPO) and post-IPO funding. Since most crossover investors are in the United States, they support US listings.

BioNTech had raised a combined $600 million in two private funding rounds in 2018 and 2019 — both led by US crossover investors. (Fidelity Management led a $325 million series B in July 2019, which was billed as one of the largest private biotech rounds ever in Europe. Redmile Group led the $270 million series A in early 2018.) So the October 2019 listing came as no real surprise. Founded in 2008, BioNTech has a full suite of technologies, from mRNA to cell therapies and antibodies, and a host of big-name partners. Most of its pipeline is still in phase 1 or preclinical, however.

European biotech's reliance on later-stage US capital means that "European VCs' role is to catalyze that US interest and form substantial funding syndicates," according to Sander Slootweg, co-owner and managing partner at Naarden, Netherlands-based Forbion. Other local VCs still hold out a vision to "grow these companies ourselves," however, notes Sofia Ioannidou, a partner at Paris-based Andera Partners. Andera's Biodiscovery team participated in the $207.5 million A round of Swiss-based Arvelle Therapeutics in February 2019 — a company set up to develop and market epilepsy candidate cenobamate, discovered by South Korea's SK Life Sciences.

Europe's lack of specialist, long-term investors is in part down to the lack of role models. Europe has produced very few fully integrated, revenue-generating biotechs; Actelion (now part of Johnson & Johnson) and Genmab are among the exceptions.

Builders' boom

The landscape of willing buyers, prepared to buy earlier, continued to boost company-building venture capitalists like Arch Venture Partners, Flagship Pioneering and Third Rock in the United States and Sofinnova Partners in Europe, who together raised over $2.5 billion in new funding in 2019 (Table 3). These groups create companies from scratch, retaining a bigger piece of the equity as they approach

Table 1 | Top M&As 2017–2019

Year	Number	Total amount raised ($ millions)	Companies (role)	Upfront cash ($ millions)
2019	89	152,419	AbbVie (buyer)[a]	63,000
			Allergan (seller)	
			Bristol-Myers Squibb (buyer)	35,000
			Celgene (seller)	
			Array BioPharma (seller)	11,400
			Pfizer (buyer)	
			Novartis (buyer)	9,700
			The Medicines Company (seller)	
			Eli Lilly (buyer)	7,234
			Loxo Oncology (seller)	
2018	144	129,724	Shire (seller)	62,000
			Takeda Pharmaceutical (buyer)	
			Bioverativ (seller)	11,600
			Sanofi (buyer)	
			Celgene (buyer)	9,000
			Juno Therapeutics (seller)	
			AveXis (seller)	8,700
			Novartis (buyer)	
			GlaxoSmithKline (buyer)	5,100
			Tesaro (seller)	
2017	134	71,365	Actelion (seller)	30,000
			Johnson & Johnson (buyer)	
			Gilead Sciences (buyer)	11,900
			Kite Pharma (seller)	
			Patheon (seller)	7,200
			Thermo Fisher Scientific (buyer)	
			Akorn (seller)	4,300
			Fresenius (buyer)	
			Advanced Accelerator Applications (seller)	3,900
			Novartis (buyer)	

[a]Deal was announced in 2019. As *Nature Biotechnology* went to press, there were reports that the deal may be delayed by the coronavirus pandemic. Source: BCIQ BioCentury Online Intelligence

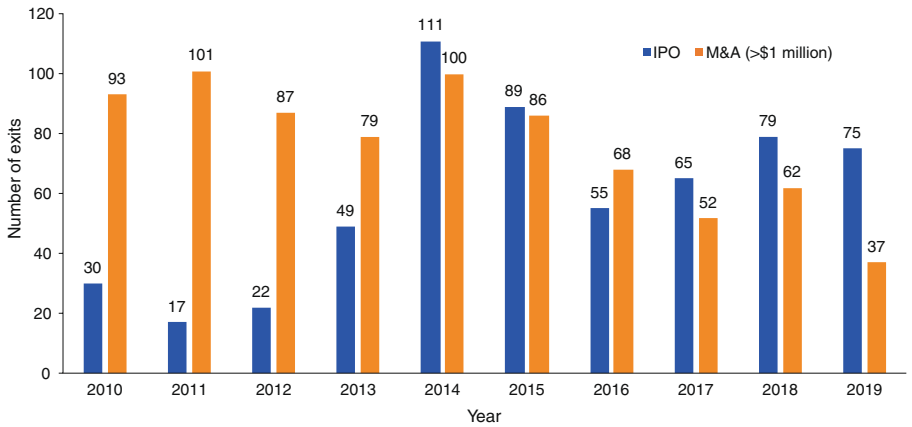

Fig. 2 | Private biotech company exits 2019. Source: BCIQ BioCentury Online Intelligence.

IPO or buyout — which is happening increasingly rapidly.

The mostly oversubscribed fund-raises proved investors' enthusiasm for the returns that this model has generated to date. Flagship helped build modified-RNA-focused Moderna. It was also behind Rubius Therapeutics, which engineers red blood cells to express therapeutic proteins. Rubius raised over $240 million in a 2018 IPO, despite having no clinical candidates.

The build-it-from-scratch model has also attracted other, traditionally later-stage investors, including Deerfield Management and RA Capital, which in 2019 launched a dedicated company-incubator project. Soaring biotech valuations, especially in the United States and China, meant it had become much more expensive to buy in at later stages, making it harder to achieve the kinds of returns that investors and their limited partners would like. Seeding opportunities means investors get to buy in cheaply.

Deerfield's hunt for early innovation within academia began in earnest in 2018, with a series of research collaborations. 2019 saw the group push into biotech real estate and manufacturing. In September 2019 it announced a $635 million plan to build a life sciences campus in New York City, and in January 2020 came a large-scale contract development and manufacturing facility for cell and gene therapies in Pennsylvania.

For RA Capital, 2019 was its first year engaging in biotech incubation "in a concerted way," with a dedicated group, according to managing director Josh Resnick, who leads early-stage investments and company creation. RA Capital launched seven companies in 2019, according to Resnick, though these remain in stealth mode. It drew heavily for due diligence on its TechAtlas — disease maps that combine biology, pipelines and the competitive landscape — to identify priority targets and unmet need.

Just as later-stage investors have moved upstream — not only large public investors, but also VCs like New Enterprise Associates (NEA) — so some early-stage investors have raised new, larger funds that enable them to support programs for longer and thereby retain more of the value on offer in this sellers' market. London-headquartered Medixci's €400 million ($439 million) fund, closed in July 2019 after just six weeks, will invest across discovery to late-stage clinical assets. Other VCs have morphed into crossover investors, supporting companies through and beyond IPO.

Mega-rounds beyond Europe

US private investment in biotech topped anything seen in the previous nine years,

Table 2 | VC investing

Number	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
China	6	3	2	3	11	14	25	38	46	55
Europe	106	101	108	118	124	132	136	129	134	134
United States	199	191	197	204	232	243	236	286	318	284
Amount ($ millions)										
China	71	66	35	28	125	494	607	996	2,037	3,008
Europe	1,010	853	897	1,072	1,582	2,677	2,209	2,631	3,230	3,258
United States	2,200	2,576	2,864	2,285	4,510	4,383	5,973	7,510	11,335	11,913
Totals	3,592	3,790	4,103	3,710	6,584	7,943	9,186	11,590	17,100	18,652

Source: BCIQ BioCentury Online Intelligence

Table 3 | Selected VC funds raised in 2019

Company	Name of fund	Amount raised ($ millions)	Date
Flagship	Special Opportunities Fund II	825	20 March
Third Rock	Fund V	770	6 June
Arch	Fund X	636	28 October
Sofinnova	Sofinnova Capital IX	360	17 October

and was four times the totals in China and Europe. Indeed, investors' continued largesse in 2019 translated into a chart-topping 52 mega-rounds. Eleven were A rounds (including FerGene, Anthos and Arvelle, which started life with clinical-stage assets from pharma; Table 4). Though slightly down from 2018, last year's totals still represented a more than tenfold increase in $100 million+ rounds over 2010 (from just four in 2010). Meanwhile, the average A round in 2019 cooled off to $28.3 million, down from $33.5 million in 2018 — still a ten-year high (Fig. 3).

Platform technologies, with the potential to generate multiple assets across a range of therapy areas, continued to draw in the big bucks last year, especially when accompanied by seasoned management (Table 5). Sana Biotechnology, for example, emerged in January 2019 with a reputed $800 million (or more) from Arch Venture Partners and F-Prime Capital Partners. The company's cofounders include former Juno Therapeutics execs Hans Bishop and Steve Harr (CEO), and Flagship Pioneering's Noubar Afeyan. Sana assembles a range of cell- and gene-engineering technologies, including manufacturing; its mission is to create and deliver engineered cells as medicines. Maze Therapeutics launched in February 2019 with $191 million from Third Rock Ventures, Arch Venture Partners and others to uncover genetic modifiers that may play a role across range of diseases.

Some people question whether these firms are raising too much money, potentially leading to undisciplined spending and outsized company valuations. "Many US companies have valuations that are too high and rounds that are too big vis-à-vis where they are in product development," opines Bibhash Mukhopadhyay, principal at VC firm NEA. But companies like Sana are not raising money in the standard, stepwise fashion through A, B and C rounds, says Afeyan. They're raising enough capital to take them all the way to a public offering. "Sana did not do a large series A. There won't be a Series B," he says. The company's technology arsenal includes methods of delivering genes and proteins to specific cell types, ex vivo genome editing, scaling-up of cell lines, and gene modifications to help protect transplanted cells from immune attack.

Maze's $191 million round was an outlier, in size terms, for Third Rock, acknowledges Tong. His justification: the breadth of the platform and a conviction that it will lead to multiple pipeline projects across several therapy areas. Precious few biotech companies have ever generated multiple marketed drugs from a single platform. But Tong claims that platform technologies today are much more tightly linked to specific product ideas and clinical applications than they were in the early 2000s, the last time platform companies were in vogue. "We have got much better at seeing how these can translate into medicines," he argues.

2019 also highlighted how the maturing biotech sector is drawing new kinds of investors, both to support established players

Table 4 | Mega A rounds of 2019

Company	Amount ($ millions)	Date	Region	Business
FerGene	570	25 November	Saint-Prex, Switzerland	Cancer gene therapy
Nuvation Bio	275	28 October	New York	Oncology
Anthos Therapeutics	250	27 February	Cambridge, Massachusetts	Targeted cardiovascular therapy
Century Therapeutics	250	1 July	Philadelphia, Pennsylvania	Stem cells and oncology
Arvelle Therapeutics	207.5	1 January	Zug, Switzerland	Central nervous system
Maze Therapeutics	191	27 February	South San Francisco, California	Functional genomics
ElevateBio	150	13 May	Cambridge, Massachusetts	Cell and gene therapy
Passage Bio	115.5	14 February	Philadelphia, Pennsylvania	Neurology, cell and gene therapy
Thrive Earlier Detection	110	30 May	Cambridge, Massachusetts	Diagnostic
Kronos Bio	105	18 July	San Mateo, California	Cancer
Talaris Therapeutics	100	18 April	Boston, Massachusetts	Cell and gene therapy, transplantation

Source: BCIQ BioCentury Online Intelligence

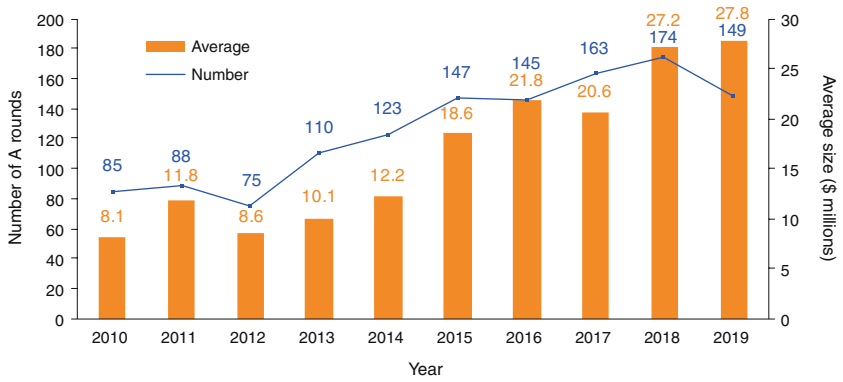

Fig. 3 | Average A round size over time. Source: BCIQ BioCentury Online Intelligence.

and to spawn new ones. Private equity (PE) — investment firms that typically buy, restructure and sell existing companies to make money — has begun to feature more prominently in the last year or 18 months, as this group of investors, hitherto more active within the broader healthcare space, seek some of the far-bigger returns shown to be possible within biotech. "Traditional PE has been absent from biopharma to date, mostly because they were not comfortable evaluating drug development," says Ben Thorpe, head of healthcare banking at Goldman Sachs. But now they've hired or accessed the required expertise and are putting money to work — big money.

KKR, for instance, held a 10% stake in BridgeBio Pharma, whose $400 million IPO in mid-2019 was, aside from Genmab's, the biggest for a therapeutics-focused company. Blackstone, which acquired life sciences investor Clarus in late 2018 as part of its bid for greater biopharma exposure, led several of 2019's mega-rounds, albeit of spinoffs with part-baked assets rather than discovery upstarts. It launched targeted cardiovascular therapy company Anthos with Novartis in February, with $250 million, and put $400 million into Ferring Pharmaceuticals spin-out FerGene in November 2019.

Family offices are also becoming more prominent in biotech, as these seek 'impact' investments and become more organized and able to access the necessary expertise. The Wild Family Office (of Swiss billionaire Hans-Peter Wild) participated in ADC Therapeutics' $303 million E round, along with private equity group Auven Therapeutics.

Even Warren Buffett's Berkshire Hathaway investment group, not renowned for biotech investing, in late 2019 reportedly took at $192 million stake in Biogen, which is awaiting FDA's verdict on its controversial Alzheimer's candidate aducanumab. "Biotech is maturing to a point where … many more people — crossover investors, specialized institutions, high net worth, sovereign wealth funds — are entering the space, looking for advantageous ways to deploy non-public money," says Flagship's Afeyan. In the past decade, gross internal return rates for biotech-focused venture capital funds have outperformed those in technology and software by almost 20 percentage points, according to data from Cambridge Associates and Correlation Ventures, compiled by Atlas Ventures' Booth. That's a sharp reversal from the 1990s.

Table 5 | Top ten rounds of 2019

Company	Financing type	Amount raised ($ millions)	Date completed
Verily Life Sciences	Not disclosed	1,000	3 January
FerGene	Not disclosed	570	25 November
ADC Therapeutics	Series E	303	9 July
Ginkgo Bioworks	Series E	290	19 September
Nuvation Bio	Series A	275	28 October
Anthos Therapeutics	Not disclosed	250	27 February
Century Therapeutics	Not disclosed	250	1 July
Asklepios BioPharmaceutical	Not disclosed	235	11 April
BioNTech	Series B	226	9 July
Tempus Labs	Beyond series E	200	30 May
MGI Tech	Not disclosed	200	13 May

Source: BCIQ BioCentury Online Intelligence

Too much of a good thing?

Not only European biotech, but biotech as a whole, was enjoying one of the richest periods in its 25-year history: a growing range of deep-pocketed private investors, including those from China; welcoming public markets, especially in the United States; and innovation-hungry big pharma willing to pay ever more generously for innovation. "The last eight quarters have been the biggest of all time in our industry," said Booth, speaking in early 2020.

But caution is creeping in, even pre-COVID-19. There are concerns over the impact of the forthcoming US election on drug pricing, along with the knock-on effect this could have on public markets and on individual biotech stocks. Perhaps a sign of the times was the launch in early 2020 by former Third Rock partner Alex Borisy of EQRx, which raised $200 million to develop new versions of existing drugs, which will be sold much more cheaply.

Meanwhile, the coronavirus outbreak is already impacting medicine supplies, the movement of people, Hong Kong's IPO market and China's relationship with the United States and the rest of the world. It likely has much further to run.

So although it may be tempting to assume that giant A rounds, $500 million IPOs and multi-billion-dollar valuations for preclinical companies is the new normal for biotech, "consternation is creeping in, caused by the thought that markets won't last forever and that the back end [of the market] may fall out," says NEA's Mukhopadhyay — a remark that would prove particularly prescient as *Nature Biotechnology* went to press in March 2020.

Granted, there are now multiple pillars supporting that back end — a wider range of later-stage investors, Big Pharma and public markets. But there are also "more [investor] companies doing company creation than ever have been," points out Sofinnova partner Maina Bhaman. That means more mouths to feed — and more competition.

Some of the company creators claim they have an edge. "On average, there are

Table 6 | Top licensing deals in 2019

Companies (role)	Deal	Date announced	Upfront cash ($ millions)
Amgen (licensor) BeiGene (licensee)	Amgen partners with BeiGene to expand oncology presence in China	31 October	2,700
AstraZeneca (licensee) Daiichi Sankyo (licensor)	Daiichi grants AstraZeneca worldwide commercialization and development rights to trastuzumab deruxtecan (DS-8201) to treat cancer	28 March	1,350
Roche (licensee) Sarepta Therapeutics (licensor)	Sarepta grants Roche exclusive, ex-US rights to develop and commercialize SRP-9001 to treat Duchenne muscular dystrophy	23 December	750
Alnylam Pharmaceuticals (licensor) Regeneron Pharmaceuticals (licensee)	Alnylam and Regeneron partner in a five-year deal to discover, develop and commercialize RNAi therapeutics	8 April	400
GlaxoSmithKline (licensee) Merck KGaA (licensor)	Merck KGaA grants GlaxoSmithKline rights to co-develop and co-commercialize bintrafusp alfa to treat cancer	5 February	343.6
Adaptive Biotechnologies (licensor) Genentech (licensee) Roche (other)	Adaptive Biotechnologies partners with Roche's Genentech unit to develop personalized and off-the-shelf T cell therapies to treat cancer	4 January	300
Akcea Therapeutics (licensor) Ionis Pharmaceuticals (other) Pfizer (licensee)	Akcea Therapeutics grants Pfizer exclusive, worldwide rights to develop and commercialize AKCEA-ANGPTL3-LRx to treat cardiovascular and metabolic diseases	7 October	250
AstraZeneca (licensor) Cheplapharm Arzneimittel (licensee)	Cheplapharm Arzneimittel purchases AstraZeneca's commercial rights to heart failure and hypertension drugs Atacand (candesartan cilexetil) and Atacand Plus (candesartan cilexetil and hydrochlorothiazide) in Europe	1 October	243
Clinigen (licensee) Novartis (licensor)	Novartis grants Clinigen exclusive, US rights to Proleukin (aldesleukin), giving Clinigen worldwide rights to the IL-2 therapy	13 February	180
AstraZeneca (licensor) Cheplapharm Arzneimittel (licensee)	Cheplapharm Arzneimittel purchases AstraZeneca's commercial rights to schizophrenia and bipolar disorder drugs Seroquel (quetiapine) and Seroquel XR in Europe and Russia	30 October	178
Dicerna Pharmaceuticals (licensor) Novo Nordisk (licensee)	Dicerna partners with Novo Nordisk to discover and develop novel therapies for the treatment of liver-related cardio-metabolic diseases using Dicerna's GalXC RNAi platform technology	18 November	175
CRISPR Therapeutics (licensor) Vertex Pharmaceuticals (licensee)	CRISPR grants Vertex exclusive, worldwide rights to its current and future intellectual property covering CRISPR–Cas9 technology, endonucleases, single- and double-cut guide RNAs and adeno-associated viral vectors to develop Duchenne muscular dystrophy and myotonic dystrophy type 1 gene editing therapies	6 June	175

Source: BCIQ BioCentury Online Intelligence

five or more companies doing exactly the same thing," claims Flagship's Afeyan, since intellectual property violation constraints don't generally kick in until an actual drug is launched. To avoid that competition, Afeyan's team at Flagship developed a process that steers clear of extrapolating ideas from academic literature, digging instead for innovation "far away from where others are." They try to leap to "possible realities that would, if they existed, create value," and then test those in the lab, he says.

Company creation may already be coming off the boil. Booth, in a January 2020 blog post, highlighted a "troubling" drop of nearly 50% since the start of 2019 in the number of biotech startups announcing first-round funding. Given strong overall venture funding, he writes, this suggests a shift from new company creation to supporting existing groups.

Those numbers don't capture new companies operating in stealth mode, however. And if the slowdown is real, it may not be a bad thing. It may simply reflect the natural bottlenecks to company creation: talent and time. Ideas and capital are emerging far quicker than the talent pool is expanding, notes Tong. He and Sofinnova's Bhaman say they have been consistent in their rate of company creation, averaging about three each year. "Company creation must happen at a steady pace, not in stops and starts. New companies should always be built if there are good ideas that can solve an unmet need; capital is not the constraint at that early stage," says Bhaman.

The commercial market — payers — may prove the ultimate bottleneck for biotech company creation. Series A rounds of $500 million mean that to make money, "you have to have high drug prices," says Daniel Mahony, co-head of Healthcare at London-based investment firm Polar Capital. Mahony, like most other investors, doesn't expect drug price legislation this year. But there will be continued pricing pressure, all the more so given coronavirus's likely impact on health systems, economies and household finance. Payers are also looking ever more closely at specialty medicines, including the gene and cell therapies that so many biotechs and their investors have flocked to.

Meanwhile, 2018's and 2019's bumper M&A deals mean that "not all of these VCs

will be bailed out by big pharma buyers — there aren't enough of them," Mahony warns. Large M&A deals were indeed missing so far as last year's deals are digested (though Gilead Sciences' $4.9 billion takeover of Forty Seven, announced in early March 2020, serves as a reminder that big biotech represents buyers, too). Yet pharmaceutical firms will not stop paying to fill their pipelines (Table 6); biotech accounts for a growing share of commercial-stage Investigational New Drug (IND) applications. The number of commercial INDs is up by 20% over the last five years, according to data from FDA and clinicaltrials.gov cited in Booth's 13 December year-in-review blog; yet the number of early clinical programs within Big Pharma over the same period has fallen by about the same amount, according to Clarivate Analytics' Centre for Medicines Research. "This highlights the increasingly important role of small and mid-cap biotechs in the early development of innovative medicines," says Booth in an accompanying webcast.

So far in 2020 there have been12 biotech IPOs on Nasdaq, and although coronavirus may be delaying some Hong Kong listings, the exchange's long-term position as a regional hub appears intact. Coronavirus has hit mainstream markets hard in what may be the start of a prolonged economic downturn. Yet R&D-focused biopharma companies should, in theory, remain relatively insulated from the worst of the economic malaise. Some are even benefiting as they step up to try to address the disease. Shares in Moderna have rocketed: on 16 March 2020, the first participant was dosed in a US National Institutes of Health-run phase 1 trial of the biotech's mRNA-based coronavirus vaccine candidate. Gilead is expanding phase 3 testing of its antiviral remdesivir. Johnson & Johnson, Sanofi and Pfizer (with partner BioNTech) are all working on vaccines against COVID-19; Sanofi also plans to test arthritis drug Kevzara (sarilumab), an interleukin-6 inhibitor developed in partnership with Regeneron, as a treatment for hospitalized patients with severe disease. Roche's coronavirus diagnostic test was among the handful approved in March by the FDA, through an Emergency Use Authorization.

Biotech's heyday looks unlikely to continue in 2020. But the sector could prove a safe haven for investors looking to escape the wider market turmoil. And, if coronavirus medicines do emerge, 2020 may also be the year that biotech reminds the wider world — not just investors — of the value it can deliver. ❐

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PATENTS

Antimicrobials

Recent patents related to new antimicrobial materials and methods of imparting antimicrobial activity to an article or product.

Patent number	Description	Assignee	Inventor	Date
US 10,584,191	A star polymer with light-activated enhanced antimicrobial functionality that can comprise a plurality of non-degradable copolymer arms comprising respective first ends and respective second ends. The respective first ends can be crosslinked to form a vinyl polymer core and the respective second ends can have antimicrobial functionality. Further, the polymer can comprise a singlet oxygen generator loaded within the vinyl polymer core. The singlet oxygen generator can generate a singlet oxygen species in response to light.	International Business Machines (Armonk, NY, USA)	Bakar MB, Hedrick JL, Piunova VA, Tek AT	3/10/2020
US 10,583,154	Non-mercurial preservatives, including antimicrobial polyamide polymers and octenidine, and methods of use thereof to produce preservative-containing multi-dose formulations. The preservative-containing multi-dose formulations exhibit resistance to one or more contaminating microorganisms and have advantageous properties with respect to long term stability of biological and small molecule active ingredients.	Boehringer Ingelheim Animal Health USA (Duluth, GA, USA), Genzyme (Cambridge, MA, USA)	Rigaut G, Loss-Dunod C, Parisot AGAL, Dhal PK	3/10/2020
US 10,582,711	A method for imparting to an article or product antimicrobial activity, including a step of applying an antimicrobial agent containing an antimicrobial polyaminosilane to the article or product. The antimicrobial polyaminosilane is prepared by subjecting an aminosilane monomer to a hydrolysis and condensation reaction. The antimicrobial polyaminosilane thus prepared is free of halide ions.	Leader Optronics Technology Co. (Tainan, Taiwan)	Huang Yu-H, Su S-H	3/10/2020
US 10,582,707	Extracts from *Persea* sp. (avocado) enriched in bioactive compounds that can be used as antimicrobial, antibacterial or spore-germination-inhibiting agents, the process for obtaining the extracts, acetogenins and isolated molecules, and methods for using the extracts enriched in bioactive compounds for providing antimicrobial, antibacterial or spore-germination-inhibiting effect.	Monterrey Institute of Technology and Higher Education (Monterrey, Mexico)	Hernandez-Brenes C, Garcia-Cruz MI, Gutierrez-Uribe JA, Benavides-Lozano JA, Rodriguez-Sanchez DG	3/10/2020
US 10,577,638	Systems, devices, products and methods for detecting and identifying microbial organisms in a sample, as well as testing antimicrobial susceptibility of microbial organisms.	Board of Regents, The University of Texas System (Austin, TX, USA)	Srinivasan A, Ramasubramanian AK, Lopez-Ribot JL, Frei CR	3/3/2020
US 10,577,395	Total synthesis and evaluation of key analogs of vancomycin containing single-atom changes in the binding pocket, as well as their peripherally modified, *N*-(hydrophobe-substituted) derivatives exemplified by a *N*-4-(4′-chlorobiphenyl)-methyl derivative and their pharmaceutically acceptable salts. Their evaluation indicates the combined pocket and peripherally modified analogs exhibit a spectrum of antimicrobial activity and potencies against both vancomycin-sensitive and vancomycin-resistant bacteria, and likely benefit from two independent and synergistic mechanisms of action.	The Scripps Research Institute (La Jolla, CA, USA)	Boger DL	3/3/2020
US 10,577,247	A hybrid nanomaterial consisting of graphene oxide nanomaterial covalently conjugated to cationic quaternized chitosan, a method of preparing the hybrid nanomaterial, an antimicrobial composition containing the hybrid nanomaterial, and use of the antimicrobial composition in inhibiting growth of microorganisms in an environment.	Nanyang Technological University (Singapore)	Chan BEM, Li P	3/3/2020
US 10,576,186	An antimicrobial medical device that includes a substrate having a metal surface that is made from a metal or metal alloy that may include stainless steel, cobalt and titanium. Disposed on the metal surface is a first antimicrobial oxide layer that includes an antimicrobial metal that may include silver, copper, zinc and combinations thereof. The atoms of antimicrobial metal in the first antimicrobial oxide layer are of a first concentration. The first antimicrobial oxide layer is positioned in a direction opposite that of the metal surface. The device further includes a second antimicrobial oxide layer that includes an antimicrobial metal that may be silver, copper, zinc and combinations thereof. The atoms of the antimicrobial metal present in the second antimicrobial oxide layer are of a second concentration. The first concentration and the second concentration are not equal.	Nanovis (Columbia City, IN, USA)	Hedrick M, Yao C	3/3/2020

Source: United States Patent and Trademark Office (http://www.uspto.gov).

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