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White Paper

IQVIA™ PHARMA DEALS

Review of 2017

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TABLE OF CONTENTS

INTRODUCTION

DEAL ACTIVITY REMAINS SLOW AS VALUATIONS RISE

Deal activity in the life sciences sector slowed in 2017 as soaring valuations deterred potential purchasers and licensees and biotech companies had a number of financing options available to them. Indeed, venture capital (VC) interest in biotech increased over the course of 2017 and the IPO market was stronger for companies in biotechnology-related industries than in the previous year. With the Nasdaq Biotechnology Index returning to 2015 levels, the M&A market in 2017 was subdued, with only a small number of big pharma companies signing multibillion-dollar deals. Licensing activity was less constrained, with both the mean upfront payment and mean total deal value for licensing deals increasing from 2016 to 2017.

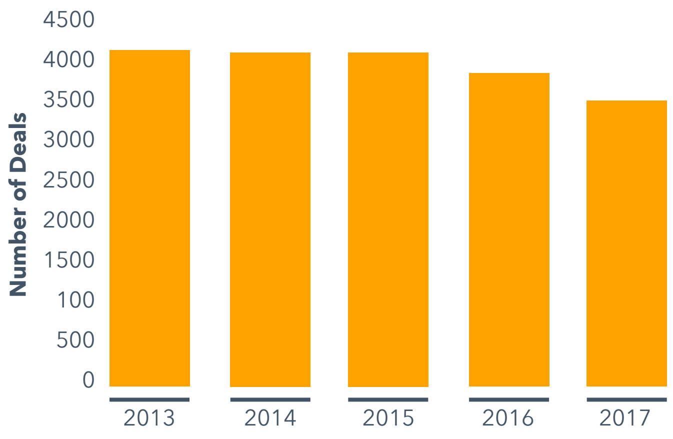
Johnson & Johnson (J&J) was the leading pharmaceutical dealmaker in terms of deal volume, taking the top position from AstraZeneca which fell down the rankings. The UK company's high-profile partnership with Merck & Co. for the co-development and commercialisation of Lynparza™ (olaparib) for multiple cancer types broke records in 2017 with its US$1.6 B upfront payment. The year also saw Chinese biotech companies out-license coveted immuno-oncology assets in return for significant sums.

Oncology remained the leading therapeutic area for partnering deals, although there was an interesting upturn in CNS dealmaking. On average, upfront payments for collaborative R&D alliances fell from 2016 to 2017, although mean deal values increased thanks to a number of broad collaborations laden with biodollars.

STRONG INVESTOR APPETITE FOR BIOTECH GIVES COMPANIES MULTIPLE OPTIONS

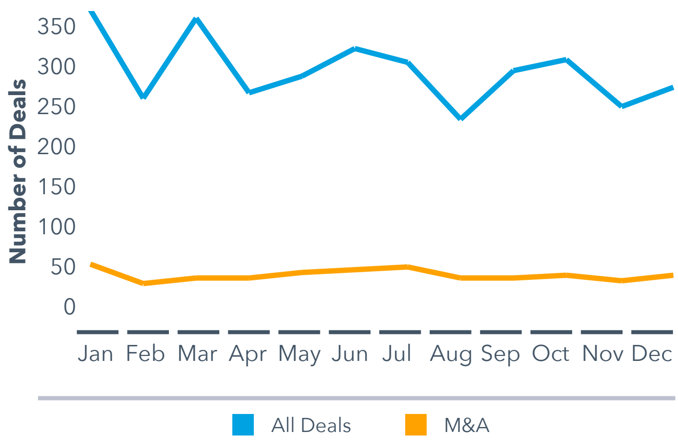
Deal activity in the life sciences sector, which slowed in 2016, showed no sign of acceleration in 2017. A review of the IQVIA Pharma Deals database of publicly disclosed deal activity reveals that the number of agreements signed, excluding standalone research grants, decreased by approximately 9% from 2016 to 2017 (Figure 1). After plateauing from 2013 to 2015, deal activity is now at its lowest level for 5 years. This downturn is partly a consequence of continuing political uncertainty, with potential acquirers waiting for US tax reforms to materialise before deciding on M&A strategy. Another factor contributing to the decline in deal volume is the fact that biotech companies had a number of financing options available to them in 2017, including staying independent and retaining rights to their pipeline programmes for longer. 2017 was a record-breaking year for global VC funding, with VCs investing US$10 B in biotechnology-related industries during the year[i], boosted by mega-deals such as Illumina spin-off GRAIL's US$1.2 B Series B financing and Roivant Sciences' US$1.1 B Series A round. Indeed, there is a trend towards fewer but larger funding rounds. Moreover, the IPO market for biotech companies was notably more active in 2017 than it was the previous year. Newly streamlined pharmaceutical companies are increasingly focusing their resources on those therapy areas in which they are strongest, resulting in a concomitant narrowing of their partnering interests. These companies are also managing and financing significant portfolios of deals and alliances that have been accrued in recent years. Figure 2 shows that dealmaking slowed throughout the course of 2017.

Figure 1: Number of deals (excluding funding awards), 2013-2017.



Source: IQVIA™ Pharma Deals

Figure 2: Deals signed in 2017 by month.



Source: IQVIA™ Pharma Deals

Despite the continued low cost of debt for potential acquirers, the volume of M&A deals (defined here as Mergers, Business Acquisitions and Divestments, signed but not necessarily completed) announced in 2017 fell 8% from 2016 to 2017, in line with the overall downturn in total deal activity in the life sciences sector (Figure 3). At US$175.2 B, the aggregate total value of all M&A deals signed in 2017 was 19% lower than the equivalent figure for 2016 and a staggering 50% less than the high of US$349.8 B achieved in 2014. It must be noted that our analysis is based on potential total deal value figures which may include contingent consideration that might not be paid. The fall in aggregate total deal value was accompanied by a 12.5% decrease in the mean total deal value for M&A deals from US$981 M in 2016 to US$854 M in 2017 (Figure 4), although the median total deal value actually rose 5% from US$95 M in 2016 to US$100 M in 2017 (Figure1).

[i] *PwC/CB Insights Healthcare MoneyTree™ Reports Q1-Q4 2017*

The Nasdaq Biotechnology Index gained 18.7% over the course of 2017 to finish 20% shy of its peak in July 2015. Rising company valuations are no doubt making some companies think twice about M&A, which is looking increasingly expensive.

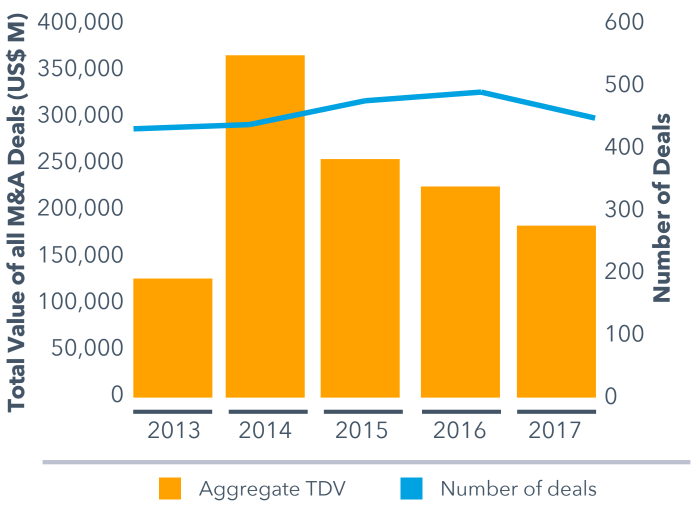
Table 1: Aggregate, mean and median values of M&A deals, 2016 vs. 2017.

	2016	2017	CHANGE
AGGREGATE VALUE OF ALL M&A DEALS	US$216,722 M	US$175,152 M	-19%
MEAN DEAL VALUE	US$981 M	US$854 M	-13%
MEDIAN DEAL VALUE	US$95 M	US$100 M	+5%

Source: IQVIA™ Pharma Deals

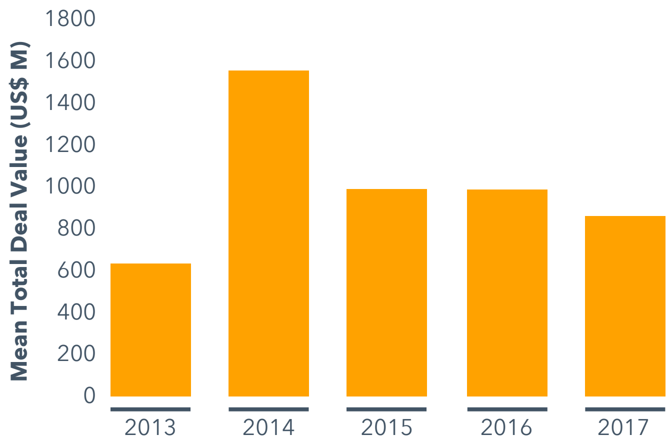
Big pharma was once again reluctant to engage in large-scale M&A in 2017, with only J&J, Gilead Sciences, Takeda Pharmaceutical and Novartis committing to multibillion-dollar upfront considerations. The largest M&A deal of 2017 was J&J's US$30.2 B cash purchase of the Swiss company Actelion for a premium of more than 80% (Deal no. 76351). The acquisition, J&J's largest pharmaceutical deal to date, bolstered the company's cardiovascular franchise at a time when it is facing biosimilar competition in the US on Remicade® (infliximab). The deal included Actelion's marketed and late-stage product portfolios and gave J&J an orphan drug franchise centred on therapeutics for pulmonary arterial hypertension with a strong growth profile. Actelion's early-stage research assets were not included in the acquisition, however, and have been spun off into a new company Idorsia Pharmaceuticals, in which J&J holds a 16% equity stake with the option to purchase an additional 16% via a convertible note (Deal no. 79615). After coming under intense shareholder pressure to sign a transformational deal to offset declining sales from its blockbuster hepatitis C virus (HCV) franchise, in August 2017 Gilead agreed to pay US$180 per share to acquire Kite Pharma for a total deal value of US$11.9 B (Deal no. 80732). The high-risk, high-reward deal, which was completed in October, gave Gilead access to Kite's chimeric antigen receptor T-cell (CAR-T) programmes, including its lead candidate axicabtagene ciloleucel, which has since been approved by the US FDA for refractory non-Hodgkin lymphoma.

Figure 3: Number and aggregate total value of M&A deals, 2013-2017.



Source: IQVIA™ Pharma Deals

Figure 4: Mean total deal value of M&A deals, 2013-2017.



Source: IQVIA™ Pharma Deals

Combined, the top M&A deals of 2017, as ranked by total potential deal value and recorded in the Pharma Deals database, had a total value of US$110.7 B, equivalent to 63% of the aggregate value of all M&A deals signed during the year (Table 2).
In contrast, the top M&A deals of 2016 had a combined value of US$120.5 B (Table 2). As was the case in 2016, only three of the top 10 acquisitions of 2017 had a deal value in excess of US$10 B. Moreover, only 23 M&A deals in 2017 had a value of between US$1 B and US$10 B, compared to 33 in 2016. As has been the case in recent years, the top 10 deals list spans a variety of industry sectors, including medical devices, life science consumables, service providers and generic, OTC and prescription pharmaceuticals. Interestingly, only two of the top 10 deals were signed in H2 2017.

The pursuit of economies of scale drove significant consolidation in the pharmaceutical services sector

Table 2: Top acquisitions of 2017 ranked by total deal value.

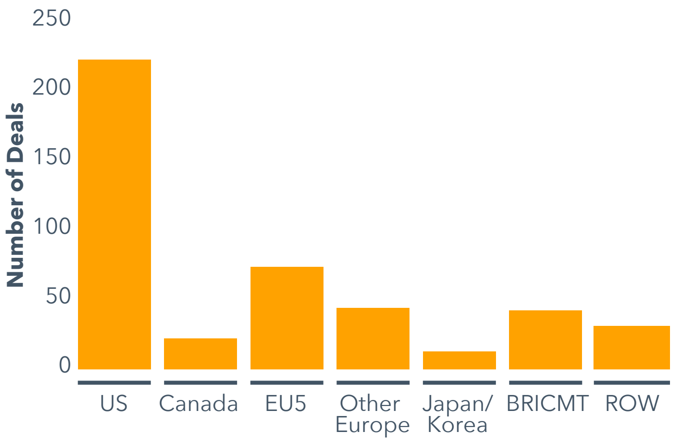
TOTAL DEAL VALUE	COMPANIES	DEAL DRIVER
US$30.2 B	Johnson & Johnson, Actelion	Orphan drug portfolio, diversification
US$24 B	Becton Dickinson, CR Bard	Minimally invasive devices in the areas of oncology, urology, vascular disease and surgery
US$11.9 B	Gilead Sciences, Kite Pharma	Engineered cell therapies, including axicabtagene ciloleucel under US regulatory review
US$8.7 B	Impax Laboratories, Amneal Pharmaceuticals	Expanded generics product portfolio and diversified generics pipeline
US$7.2 B	Thermo Fisher Scientific, Patheon	Entry into contract development and manufacturing organisation (CDMO) market
US$6.4 B	Avantor, VWR	Expanded offering in life sciences consumables and services
US$6.1 B	Cardinal Health, Medtronic	Medtronic's Patient Care, Deep Vein Thrombosis and Nutritional Insufficiency Businesses
€5.3 B (US$6.1 B)	Bain Capital/Cinven, Stada Arzneimittel	Generic and OTC pharmaceutical products, advancing growth strategy
US$5.2 B	Takeda Pharmaceutical, Ariad Pharmaceuticals	Marketed and clinical-stage oncology assets
US$5 B	Pamplona Capital Management, Parexel International	Strengthened position in biopharmaceutical services market

Source: IQVIA™ Pharma Deals

in 2017. A number of multibillion-dollar deals were announced, the largest of which was Thermo Fisher Scientific's US$7.2 B (including US$2 B in net debt) acquisition of Dutch contract development and manufacturing organisation (CDMO) Patheon (Deal no. 78787), another deal that will diversify Thermo Fisher's business away from its core focus areas of diagnostic tools and laboratory equipment. Other high-value M&A deals involving service providers in 2017 include the US$4.6 B merger of INC Research and inVentiv Health (Deal no. 79009) and Pamplona Capital Management's takeover of Parexel International in a deal valued at approximately US$5 B, including debt (Deal no. 79230). Parexel had come under pressure to explore a sale from activist investors who argued that the company's profit margins had consistently lagged behind those of its peers. No doubt driven by increasing downward pressure on generic drug prices, in October 2017 Impax Laboratories agreed to merge with Amneal Pharmaceuticals in an all-stock transaction valued at approximately US$8.7 B in enterprise value that will create the 5th largest generics business in the US (Deal no. 81932).

Figure 5 presents an analysis of M&A deals signed in 2017 by the territory of the target company. Acquisitions of US-based companies dominated the M&A landscape in 2017, with companies located in one of Europe's five largest markets (France, Germany, Italy, Spain and the UK) comprising the next largest group. Almost 70% of the EU5 M&A deals involved the acquisition of companies located in Germany or the UK. 61% of the deals for target companies located in BRICMT countries – namely Brazil, Russia, India, China, Mexico and Turkey – involved Chinese companies being acquired.

Figure 5: M&A deals in 2017 by target company territory.



Source: IQVIA™ Pharma Deals

J&J AHEAD OF THE PACK IN DEAL SPEND AND DEAL VOLUME

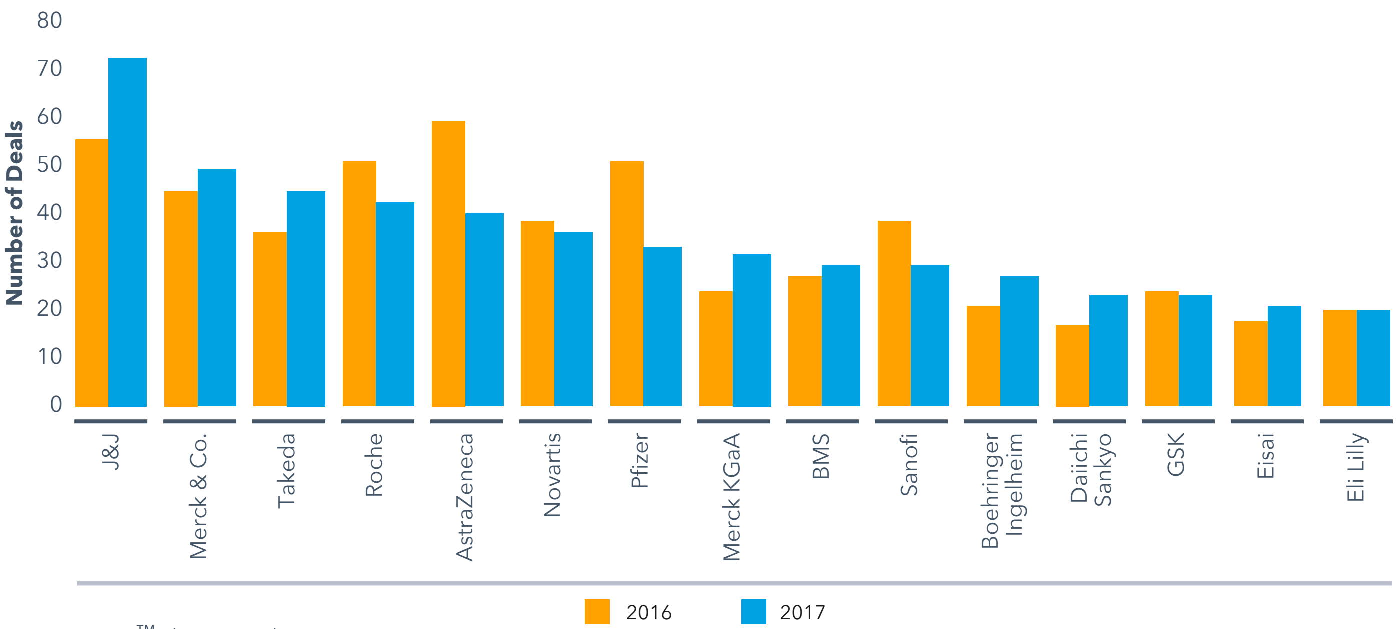
J&J overtook AstraZeneca in 2017 to assume the title of the most prolific pharmaceutical dealmaker with 72 publicly disclosed deals, up 31% from the 55 deals announced the previous year (Figure 6). As ever, the company's deal activity was as diverse as its portfolio of businesses and included a number of acquisitions of medical device companies, numerous early-stage research collaborations and the divestment of its Codman Neurosurgery business for US$1.045 B to Integra LifeSciences (Deal no. 78726). Merck & Co. takes second place in the deal activity rankings with 49 deals, followed by Takeda, Roche and AstraZeneca with 44, 42 and 40 deals, respectively. 17 of Merck's deals were clinical trial collaborations testing Keytruda® (pembrolizumab) in combination with oncology assets of various types. Outside of immuno-oncology, Merck optioned KalVista Pharmaceuticals' plasma kallikrein inhibitor KVD001, which is under development for the potential treatment of diabetic macular oedema, in a deal worth up to US$761 M (Deal no. 81684), and in-licensed Teijin Pharma's preclinical antibody candidate targeting the tau protein for the potential treatment of Alzheimer's and other neurological diseases (Deal no. 78830). AstraZeneca's deal activity fell 32% from 2016 to 2017, although the company still managed to find legacy or non-core assets to partner or divest after executing its externalisation strategy with particular gusto in 2016. Indeed, the company raised more than US$3 B in upfront cash in 2017 thanks to deals with TerSera Therapeutics (Deal no. 76937), Sanofi Pasteur (Deal no. 77236), Recordati (Deal no. 78744), Grünenthal (Deal no. 79067), Merck & Co. (Deal no. 80095), Aspen (Deal no. 81758) and Mereo BioPharma (Deal no. 82222). Pfizer's deal activity also fell in 2017 and could best be described as unremarkable, with the exception of licensing deals signed with Sangamo Therapeutics (Deal no. 78596) and Basilea Pharmaceutica (Deal no. 79188).

J&J was also the leading company in terms of deal spend, thanks in major part to its acquisition of Actelion and with a smaller contribution from partnering deals such as its drug discovery collaboration with PeptiDream (Deal no. 78022) and a bispecific antibody platform licensing deal with Zymeworks (Deal no. 82333). Its pharmaceutical deals were typically biased towards the early stages of development.

Figure 7 presents an analysis of the leading companies as ranked by the aggregate total potential deal value of each company's deals in 2017, excluding those deals where the company is itself receiving payment e.g. out-licensing agreements or divestments. Financials associated with the exercise of options granted in earlier years or with the extension/amendment of previous deals are excluded from the analysis. As licensing and collaborative deals are included in the analysis, the total deal spend is unlikely to be wholly realised in many cases. Each of the 20 companies pledged to spend more than US$3 B on deals in 2017. With the exception of Merck & Co., many of the top positions are occupied by companies that are also to be found in the top M&A deals list.

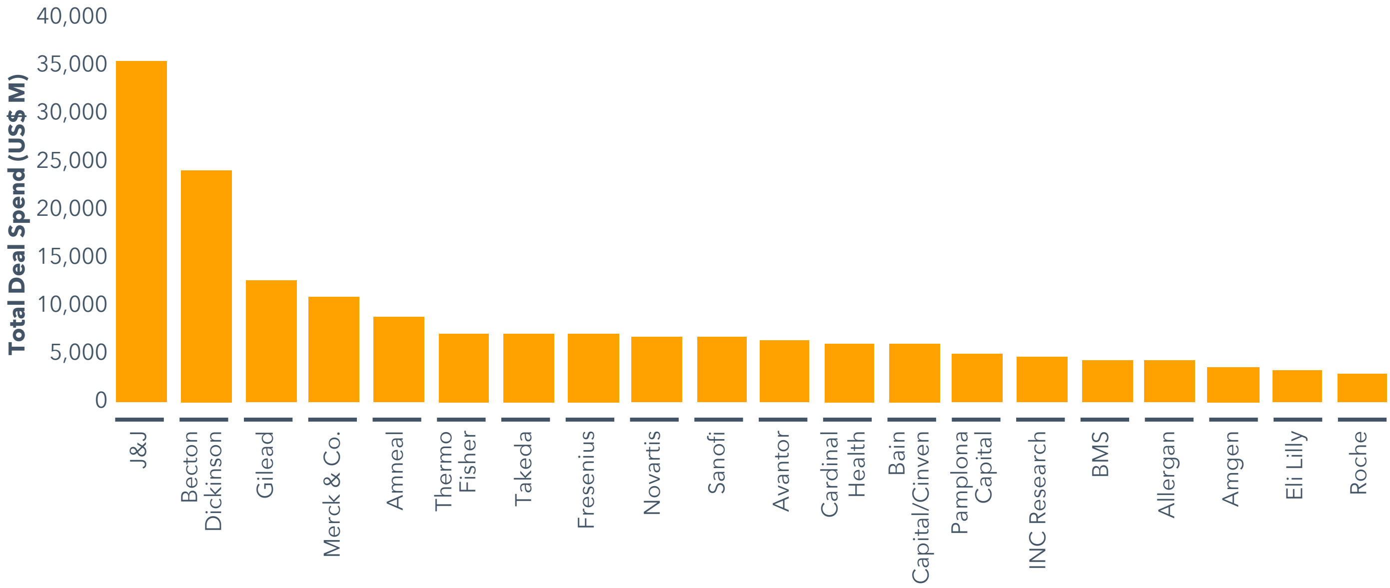
J&J overtook AstraZeneca in 2017 to assume the title of the most prolific pharmaceutical dealmaker with 72 publicly disclosed deals, up 31% from the 55 deals announced the previous year

Figure 6: Most prolific dealmakers, 2016 vs. 2017.



Source: IQVIA™ Pharma Deals

Figure 7: Top 20 companies ranked by aggregate total value of all disclosed deals in 2017 (excluding out-licensing deals and divestments by such companies).

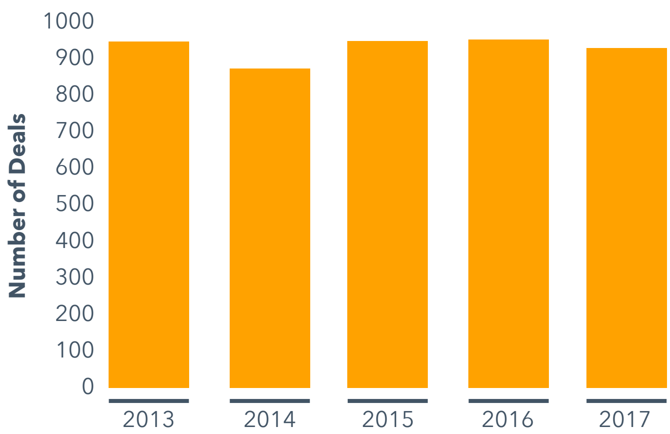


Source: IQVIA™ Pharma Deals

LICENSING ACTIVITY DIPS BUT VALUES RISE

Licensing activity in the life sciences sector has fluctuated around the 900 deals per year mark in recent years, with the number of licensing agreements announced in 2017 down 2% on 2016, a less pronounced decline than that in overall deal activity (Figure 8). In 2017, the mean total deal value, excluding royalties, for licensing deals with disclosed financial information reached its highest level for 5 years, rising 28% from 2016 to 2017 to reach US$360 M, helped by Merck & Co.'s US$8.5 B deal with AstraZeneca to co-develop and co-commercialise Lynparza™ (olaparib) for multiple cancer types. This increase was accompanied by an increase in the median total deal value of all licensing deals (arguably a better measure of the 'average'), from US$95 M in 2016 to US$114.5 M in 2017. While licensing deal values are frequently inflated by an assortment of milestone payments relating to multiple products and/or indications that may never be developed or to inaccessible sales targets, cash upfront payments

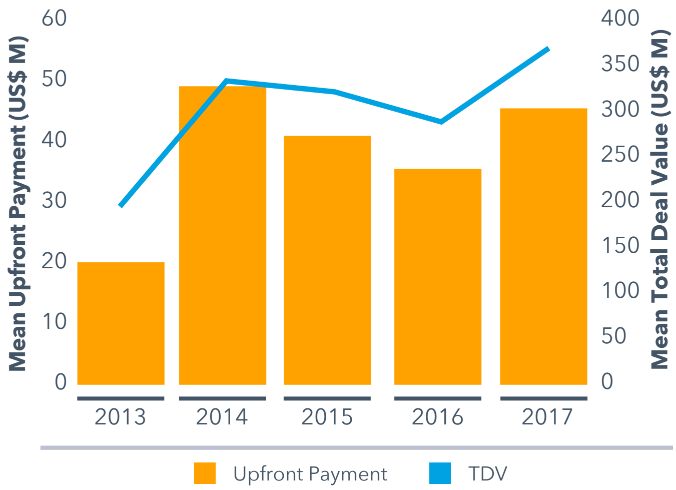
Figure 8: Number of licensing deals, 2013-2017.



Source: IQVIA™ Pharma Deals

offer a more informative means of assessing licensing deal terms. The mean cash upfront payment for licensing deals signed in 2017 was US$44.6 M, an increase of 28% on the figure achieved in 2016 but still 7% down on the high of US$48 M reached in 2014 (Figure 9). Interestingly, however, the median cash upfront payment for licensing deals recorded

Figure 9: Mean total deal value and mean upfront payment for licensing deals, 2013-2017.



Source: IQVIA™ Pharma Deals

in the Pharma Deals database, which was US$10 M in 2015 and US$11.2 M in 2016, actually fell to US$8 M in 2017. Indeed, the mean upfront payment for 2017 is heavily influenced by the record-breaking US$1.6 B upfront fee that Merck paid AstraZeneca for Lynparza. If this is removed from the dataset, the mean upfront payment for 2017 falls to US$34.2 M. Many analysts were perplexed as to why AstraZeneca would want to give away half of the value of one of its most valuable oncology assets in return for a short-term boost to its externalisation revenue. Significantly, AstraZeneca announced the Merck collaboration on the same day that it reported that its crucial MYSTIC combination trial of Imfinzi™ (durvalumab) and tremelimumab had failed to reach its primary endpoint on progression-free survival as a first-line therapy for non-small-cell lung cancer; an announcement that sent its share price crashing by 15%.

It must be noted that our licensing deal financial analysis excludes terminated deals, such as Immunomedics' failed partnership with Seattle Genetics for its solid tumour therapy candidate IMMU-132 (Deal no. 76719), and licensing payments made as part of settlement deals resolving patent or contractual disputes. Indeed, 2017 saw two high-profile and high-value settlement deals: Biogen's US$1.25 B deal with Forward Pharma settling patent litigation relating to Tecfidera® (dimethyl fumarate) (Deal no. 76240); and Merck & Co.'s US$625 M settlement with Bristol-Myers Squibb (BMS) and Ono Pharmaceutical resolving patent litigation relating to Keytruda (Deal no. 76237).

The highest upfront payments in 2017 were achieved by coveted oncology drugs and non-core big pharma assets. Table 3 presents the top 10 partnering deals of 2017 as ranked by upfront consideration (including both cash and equity investments). Settlement deals and product acquisitions are excluded from the analysis. Significantly, two of the top 5 deals as ranked by upfront consideration involved Chinese biotech companies as licensors. The July licensing agreement between Celgene and BeiGene for ex-Asia rights to the PD-1 (programmed cell death-1) inhibitor BGB-A317 in solid tumours is the second-ranked partnering deal of 2017, taking into account its US$263 M cash upfront payment and a US$150 M equity investment, and the largest overseas licensing deal to date for a drug originating in China (Deal no. 79662). The deal also includes almost US$1 B in milestone payments and saw BeiGene acquire Celgene's commercial operations in China and assume commercial responsibility for Celgene's approved therapies in the country as well as its pipeline candidate CC-122. While BGB-A317 is unlikely to challenge in the crowded PD-1 monotherapy market, the deal means that Celgene will no longer need to rely on other companies' checkpoint inhibitors for its solid tumour combination trials.

The highest upfront payments in 2017 were achieved by coveted oncology drugs and non-core big pharma assets. Significantly, two of the top 5 deals involved Chinese biotech companies as licensors

Table 3: Top partnering deals (excluding settlements and product acquisitions) of 2017 by upfront consideration.

TOTAL DEAL VALUE	UPFRONT PAYMENT	COMPANIES	INTEREST AREA	DEVELOPMENT PHASE
US$8500 M	US$1600 M	AstraZeneca, Merck & Co.	Co-development and co-commercialisation of Lynparza™ (olaparib) for multiple cancer types and selumetinib	Launched, Phase III
US$1493 M	US$413 M (US$263 M in upfront cash + US$150 M equity investment)	BeiGene, Celgene	BGB-A317 in all fields of treatment, other than haematology, in the US, Europe, Japan and rest of world outside Asia	Phase I
US$1550 M	US$400 M	Loxo Oncology, Bayer	TRK (tropomyosin receptor kinase) inhibitors larotrectinib and LOXO-195 for patients with TRK fusion cancers	Phase II, Phase I/II
US$350 M +	US$350 M	Genscript Biotech/Legend Biotech, Janssen Biotech	LCAR-B38M, a chimeric antigen receptor T-cell (CAR-T) drug candidate that specifically targets the B-cell maturation antigen	Phase I/II
US$710 M	US$300 M	Bristol-Myers Squibb, Biogen	BMS-986168, an anti-tau antibody with potential in Alzheimer's disease and progressive supranuclear palsy	Phase I
US$300 M	US$300 M	AstraZeneca, Recordati	Seloken®/Seloken® ZOK and associated Logimax® fixed-dose combination in Europe	Launched
US$320 M	US$250 M	AstraZeneca, TerSera Therapeutics	Commercial rights to Zoladex® (goserelin acetate implant) in the US and Canada	Launched
US$230 M	US$230 M	Vertex Pharmaceuticals, Merck KGaA	Worldwide rights to two clinical-stage programmes targeting DNA damage repair and two preclinical programmes	Phase II, Phase I, Preclinical
US$225 M	US$205 M	Alector, AbbVie	Collaboration to advance immune therapies for Alzheimer's disease and other neurodegenerative disorders	Discovery
US$1655 M	US$175 M (US$75 M upfront option payment + US$100 M equity investment)	Ionis Pharmaceuticals/ Akcea Therapeutics, Novartis	Option and collaboration agreement for AKCEA-APO(a)-LRx and AKCEA-APOCIIILRx	Phase II, Phase I

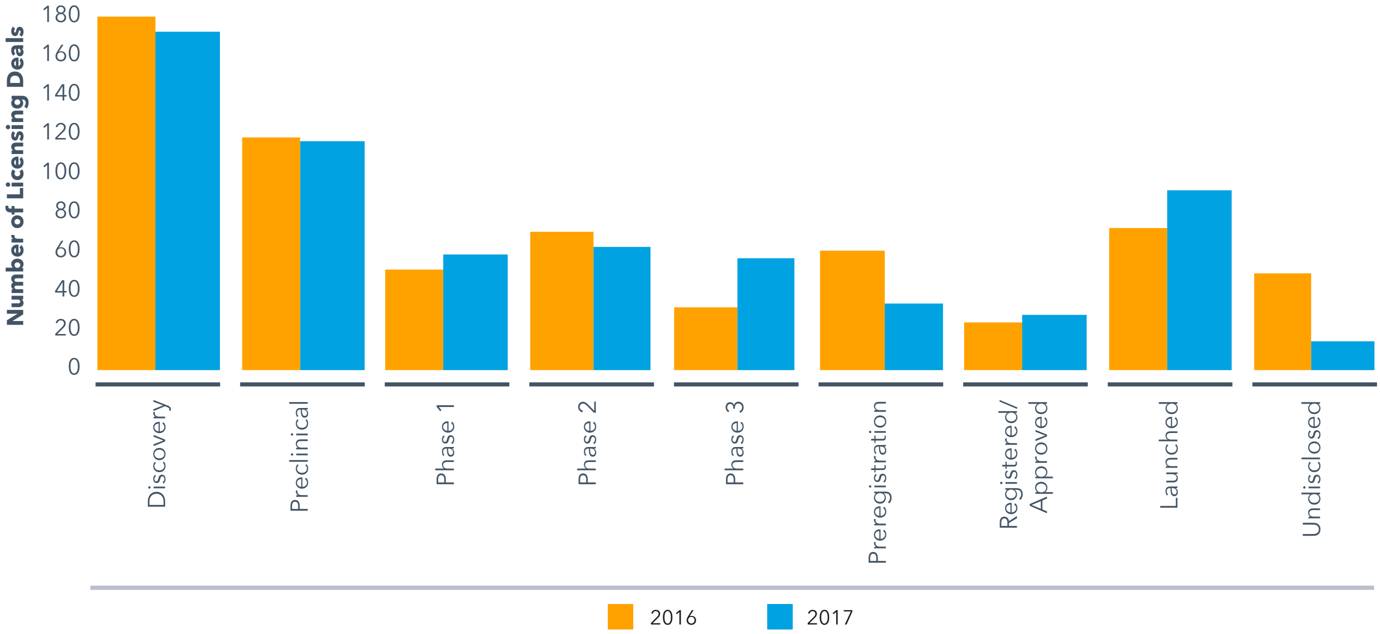
Figure 10 presents an analysis of licensing activity for therapeutic programmes in 2016 and 2017 by development stage. Where deals concern multiple assets or assets in different stages of development for different indications, the highest achieved development phase has been selected for the analysis. The level of licensing activity for preclinical programmes was maintained from 2016 to 2017, while licensing at the discovery stage fell 5% over the same period. Deals involving licensing options, which continue to be popular for early-stage assets, are excluded from the analysis, however. Despite the level of licensing activity being in decline, the number of licensing deals for Phase I and Phase III assets actually increased from 2016 to 2017. Comparatively few of the Phase III licensing deals signed in 2017 involved global rights being granted, however, with the majority being regional or single territory deals. More deals were also seen for approved and launched products in 2017, most of which were regional, single territory or generic deals.

An analysis of upfront payments for licensing deals by development stage, restricted to those deals granting rights in major markets, reveals that on average Phase I assets commanded the highest upfront payments in 2017 (Figure 11). The mean upfront payment for Phase I licensing deals in 2017 was US$83.2 M, an increase of 150% on the equivalent figure for 2016, with six Phase I deals having upfront payments in excess of US$100 M. While the mean upfront payment for Phase II assets increased 30% from 2016 to 2017 to US$65.6 M, it failed to break the US$80 M mark as it did in both 2014 and 2015. The most striking feature of Figure 11 is the 78% drop in the mean upfront payment for Phase III assets from 2016 to 2017. There was limited big pharma participation in licensing at the Phase III development stage in 2017, perhaps suggesting that competition is driving such companies to access external assets of interest at an earlier stage of clinical development.

ONCOLOGY REMAINS THE LEADING THERAPY AREA

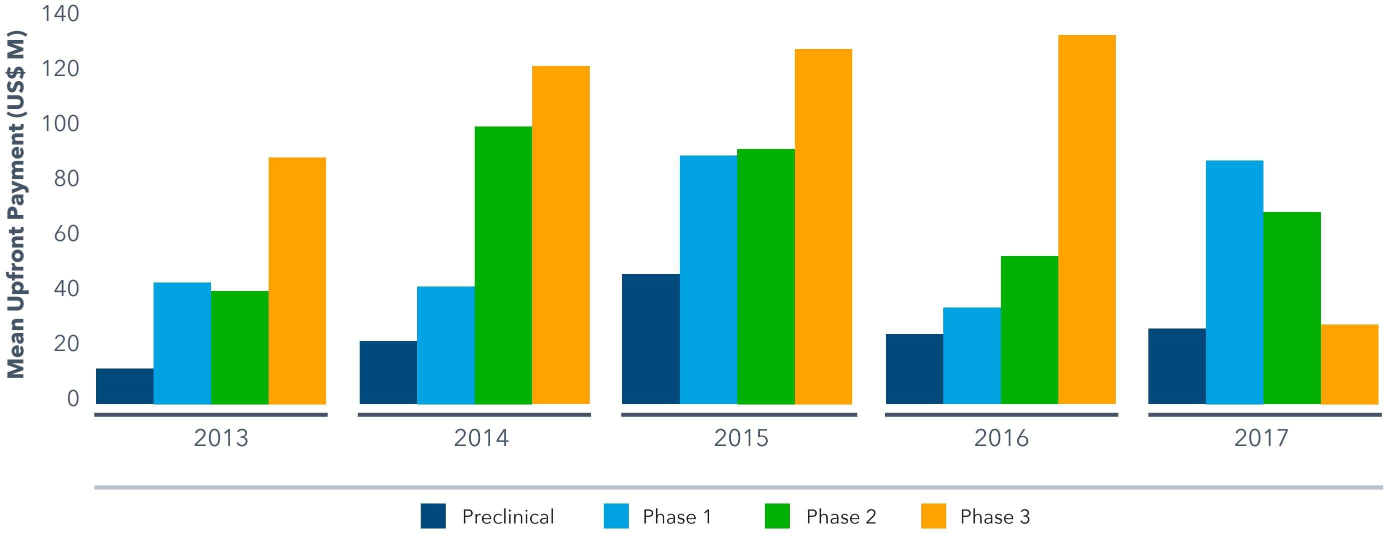
As it has done ever since the Pharma Deals database began in 1996, oncology represents the principal therapy area for dealmaking in the life sciences sector by a considerable margin, with more than 30% of the deals signed in 2017 that were ascribed an indication

Figure 10: Therapeutic licensing deals by development stage, 2016 vs. 2017.



Source: IQVIA™ Pharma Deals

Figure 11: Mean upfront payment for licensing deals by development stage, 2013-2017.

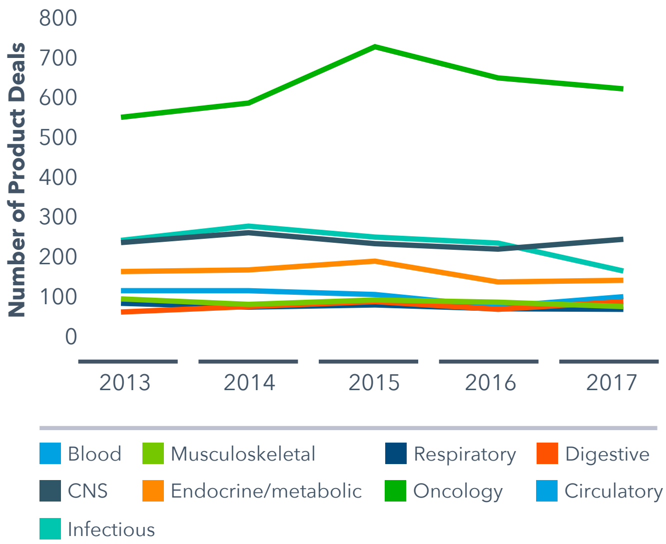


Source: IQVIA™ Pharma Deals

involving therapeutics, diagnostics or medical devices for cancer. Figure 12 presents an analysis of product deals (including product acquisitions, licensing, option to license, co-development and collaborative R&D deals) by indication area. More than twice as many product deals in 2017 included oncology as a therapeutic area than did CNS, the second most popular therapy area for dealmaking. Infectious and parasitic diseases, endocrine, nutritional and metabolic diseases and diseases of the circulatory system comprised the third, fourth and fifth most popular therapy areas for deals signed in 2017, respectively. In a potentially worrying development for the therapy area, however, the number of product deals involving infectious and parasitic diseases fell 29% from 2016 to 2017, outpacing the overall decline in deal activity in the life sciences sector notably.

Within the oncology field, the highest value deals were mainly in the intensively competitive immuno-oncology sector and were mostly directed at early-stage programmes. Noteworthy alliances include Eli Lilly's collaboration with German biotech CureVac to develop up to five mRNA cancer vaccines that target neoantigens across multiple tumour types (Deal no. 81930), which is potentially worth up to US$1803 M, and Halozyme Therapeutics' US$105 M upfront

Figure 12: Number of product deals by therapeutic area, 2013-2017.



Source: IQVIA™ Pharma Deals

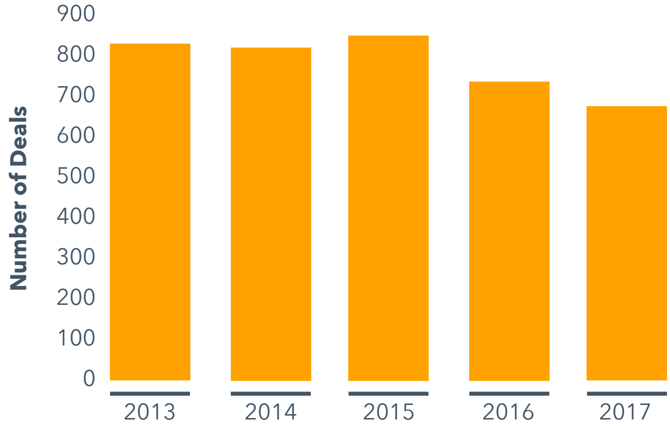
collaboration and licence agreement with BMS to develop subcutaneously administered BMS immuno-oncology medicines using Halozyme's Enhanze® drug delivery technology (Deal no. 81115). Continuing a trend seen in recent years, the key players in the immuno-oncology field established multiple clinical trial collaborations in 2017 to test various combinations of immuno-oncology assets in various tumour types. Beyond cancer immunotherapy, deal activity in oncology in 2017 was also directed towards the development of companion diagnostics. Targeted therapeutics being developed for genetically defined cancers were of considerable interest to certain companies, with Bayer paying US$400 M upfront to license co-exclusive rights to larotrectinib and LOXO-195, Loxo Oncology's franchise of highly selective TRK (tropomyosin receptor kinase) inhibitors for patients with TRK fusion cancers (Deal no. 82399), and Roche buying rival precision medicine specialist Ignyta for US$1.7 B in order to gain ownership of entrectinib, an orally bioavailable CNS-active tyrosine kinase inhibitor in Phase II development for tumours that harbour ROS1 or neurotrophic TRK fusions (Deal no. 83140).

The volume of product deals concerning CNS diseases increased 10% from 2016 to 2017, although big pharma participation was limited with a number of companies having exited R&D in this field. High-value CNS deals in 2017 include Mitsubishi Tanabe Pharma's US$1.1 B acquisition of NeuroDerm, a clinical-stage company developing drug-device combinations to address unmet needs of Parkinson's disease patients with novel formulations of existing therapies (Deal no. 79910) and Eli Lilly's US$960 M acquisition of CoLucid Pharmaceuticals (Deal no. 76198). With the acquisition Lilly gained lasmiditan, an oral migraine therapy in Phase III development that, if approved, could represent the first novel mechanism for treating acute migraine in 25 years. Interestingly, Lilly had originally developed lasmiditan and out-licensed it to CoLucid back in 2006 when pain was not an area of focus for the company (Deal no. 23153). In November 2017 and as part of a deal worth up to US$805 M, Sanofi paid US$40 M upfront to license global rights to Principia Biopharma's Phase I Bruton's tyrosine kinase inhibitor PRN2246, which can permeate the blood-brain barrier and modulate immune cell and brain cell signalling and which has potential in the treatment of multiple sclerosis and other CNS diseases (Deal no. 82277).

BROAD ALLIANCES DRIVE UPTURN IN MEAN VALUE FOR R&D DEALS

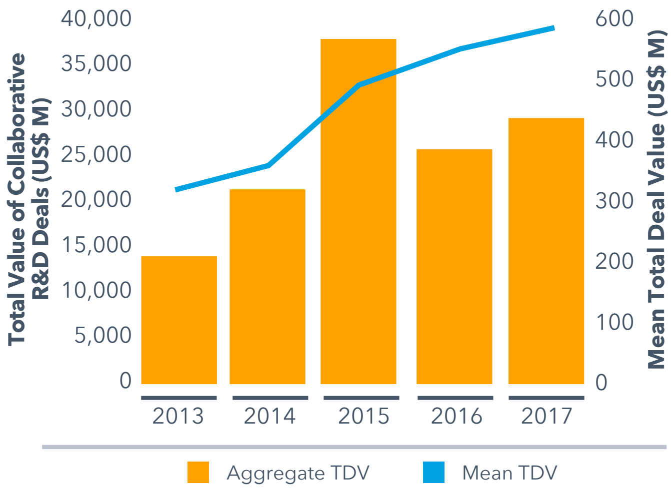
Mirroring the overall decline in life sciences deal activity, the level of disclosed collaborative R&D dealmaking (defined here as discovery or preclinical-stage deals that involve two or more parties actively collaborating on R&D) fell by 9% from 2016 to 2017 (Figure 13). This drop reflects increasingly focused partnering strategies, the multitarget and/or multi-indication nature of many R&D alliances as well as the ongoing resource and capital that is being directed towards alliances established in previous years. The aggregate total deal value, excluding royalties, of collaborative R&D deals (excluding multicomponent deals where it is not possible to split out the financial terms of the research collaboration element) reached its highest level in 2015, reaching an unprecedented US$36.9 B, before returning to more typical levels in 2016 and then rising 13% in 2017 (Figure 14). Despite these fluctuations in aggregate value, the mean total deal value, excluding royalties, of those collaborative R&D deals with disclosed financial terms rose by 6% in 2017 to US$571 M, with 12 deals having a headline value in excess of US$1 B. Therefore, although fewer collaborative R&D deals were signed in 2017, on average they were of higher potential total deal value. In most cases, these high

Figure 13: Number of collaborative R&D deals, 2013-2017.



Source: IQVIA™ Pharma Deals

Figure 14: Aggregate value and mean total deal value of collaborative R&D deals, 2013-2017.



Source: IQVIA™ Pharma Deals

potential deal values were inflated by biodollars linked to multiple targets or programmes and are unlikely to be realised in their entirety.

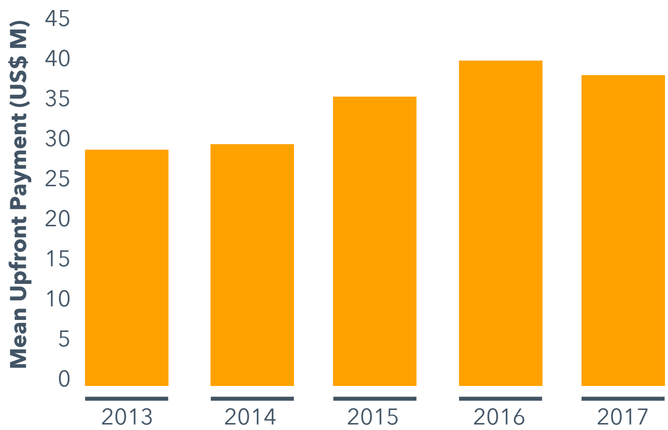
Because collaborative R&D deals are typically heavily backloaded in their deal structures, it is often more informative to consider trends in the upfront payments for such deals. Indeed, the mean upfront payment for collaborative R&D deals actually fell 5% from 2016 to 2017 to US$37.6 M, with only two deals having upfront payments exceeding US$100 M, compared with four deals in the previous year (Figure 15). Interestingly, the collaborative R&D deal with the largest upfront payment in 2017 was in the CNS field: AbbVie's US$205 M upfront, option-based collaboration with Alector to develop and commercialise immune therapies to treat Alzheimer's disease and other neurodegenerative disorders (Deal no. 82136).

Many big pharma companies are willing to sign new deals in their therapeutic areas of interest but also remain focused on advancing the collaborations they have established in recent years. Indeed, it must be noted that our 2017 analyses only include new deals that were signed in 2017 and not amendments or extensions of deals that were signed in previous years. A number of big pharma companies deepened their relationships with existing partners in 2017.

The mean upfront payment for collaborative R&D deals actually fell 5%

In return for a US$195 M cash upfront payment, Celgene exercised an option granted to it under a 2014 collaboration with Forma Therapeutics to evaluate additional therapeutic candidates in the areas of protein homeostasis, inflammation & immunology and neurodegeneration (Deal no. 57989), while BMS paid US$200 M upfront to extend its existing collaboration and licence agreement with CytomX Therapeutics focused on Probody™ therapeutics to include up to six additional oncology targets and two non-oncology targets (Deal no. 59009) and also exercised its option to extend the research term of its immuno-oncology discovery collaboration with Five Prime Therapeutics (Deal no. 57658).

Figure 15: Mean upfront payment for collaborative R&D deals, 2013-2017.



Source: IQVIA™ Pharma Deals

Table 4 presents the top 10 collaborative R&D deals of 2017 as ranked by total potential deal value. Once again, immuno-oncology features heavily on the list. It is also interesting to note that the majority of the deals relate to biological therapies, with bispecific antibodies, gene therapies, cell therapies, RNA-based therapeutics and engineered peptides all included.

Table 4: Top therapeutic collaborative R&D deals of 2017 by total potential deal value.

TOTAL DEAL VALUE	UPFRONT PAYMENT	COMPANIES	INTEREST AREA	DEVELOPMENT PHASE (NO. PROGRAMMES/ TARGETS)
US$2905 M	US$50 M	Assembly Biosciences, Allergan	Microbiome gastrointestinal development programmes	Preclinical, Discovery (4)
€2431 M (US$2803 M)	€23 M (US$26.5 M)	Ablynx, Sanofi	Nanobody®-based therapeutics for various immune-mediated inflammatory diseases	Discovery (up to 8)
US$2157.5 M	US$45 M	Pieris Pharmaceuticals, AstraZeneca	Inhaled biologic molecules leveraging the properties of Pieris' Anticalin® proteins	Preclinical, Discovery (up to 5)
US$1865 M	US$105 M	Halozyme, Therapeutics, Bristol-Myers Squibb (BMS)	Development of subcutaneously administered BMS immuno-oncology medicines using Halozyme's Enhanze® drug delivery technology	Discovery (up to 11)
US$1803 M	US$50 M	CureVac, Eli Lilly	mRNA cancer vaccines based on CureVac's RNActive® technology	Discovery (up to 5)
€1705 M (US$1779 M)	€30 M (US$31 M)	Pieris Pharmaceuticals, Servier	Bispecific therapeutic programmes in immuno-oncology, including PRS-332	Preclinical, Discovery (up to 8)
US$1668 M	US$60 M (US$40 M cash + US$20 M equity investment)	CytomX Therapeutics, Amgen	Probody™ T-cell engaging bispecific pharmaceutical or biologic products targeting epidermal growth factor receptor and certain oncology targets	Preclinical, Discovery (up to 4)
US$1150 M	Undisclosed	PeptiDream, Janssen Pharmaceuticals	Macrocyclic/constrained peptides against multiple metabolic and cardiovascular targets	Discovery (multiple)
US$1100 M	Undisclosed	PeptiDream, Bayer	Macrocyclic/constrained peptides against multiple targets of interest selected by Bayer in areas such as oncology and cardiology	Discovery (multiple)
US$1030 M	US$30 M	Immatics Biotechnologies, Amgen	Next-generation T-cell engaging bispecific immunotherapies targeting multiple cancers	Discovery (2 inferred)

Source: IQVIA™ Pharma Deals

Three collaborative R&D deals signed in 2017 had headline values in excess of US$2 B, led by Allergan's research, development, collaboration and licence agreement with Assembly Biosciences for the worldwide rights to four microbiome gastrointestinal development programmes, which is potentially worth up to US$2905 M if all programmes included in the deal are successfully developed and commercialised for multiple indications (Deal no. 76029). The agreement, aimed at expanding Allergan's therapeutic presence in gastroenterology, provided the company with worldwide rights to preclinical compounds ABI-M201 and ABI-M301, targeting ulcerative colitis and Crohn's disease, as well as two additional compounds to be identified by Assembly for irritable bowel syndrome. Ablynx's €2.4 B (US$2.8 B) alliance with Sanofi focused on developing and commercialising Nanobody®-based therapeutics for the treatment of various immune-mediated inflammatory diseases (Deal no. 79819) set the scene for the company's subsequent 2018 acquisition announcement while Pieris Pharmaceuticals' US$2.16 B partnership with AstraZeneca to develop novel inhaled drugs for respiratory diseases, including the IL-4 (interleukin-4) Anticalin® PRS-060 (Deal no. 78564), followed a broad immuno-oncology discovery collaboration with Servier (Deal no. 75962).

OUTLOOK FOR 2018

In December 2017, the US government passed legislation to reform the US tax code which is expected to drive the repatriation of cash held overseas and have a positive influence on VC investment. Opinions are conflicted as to the impact of US tax reform on dealmaking in the life sciences sector with some industry observers expecting tax savings to fuel increased M&A activity and others suggesting that US companies may take a more conservative approach and channel repatriated cash towards share buybacks or dividends. Interestingly, January 2018 saw the announcement of M&A deals collectively worth more than US$35 B, equivalent to 20% of the aggregate value of all the M&A deals signed in 2017, led by Sanofi's purchases of Bioverativ (Deal no. 83447) and Ablynx (Deal no. 83534) for US$11.6 B and €3.9 B (US$4.8 B), respectively, and Celgene's deals to acquire Impact Biomedicines (Deal no. 83298) and Juno Therapeutics (Deal no. 83503) for up to US$7 B and US$9 B, respectively. Whether these deals mark the start of a period of buoyant M&A activity remains to be seen, with bolt-on acquisitions more likely for many large companies rather than mega-mergers. With many potential takeover targets trading at a premium, acquisitions remain costly for big pharma. For some companies, strategic need outweighs cost, however. Indeed, Sanofi secured Ablynx with a €45 per share bid that was almost 50% higher than the unsolicited €30.50 per share offer that Novo Nordisk made for the company.

Biotech companies are experiencing almost unprecedented access to capital, with the outlook for both VC and IPO activity in 2018 looking positive after a strong 2017. This could exert a slight downward pressure on deal activity, as partnering is now one of several financing options available to early-stage companies. This will be balanced, however, by the need of pharmaceutical companies to address dwindling growth rates and pipeline weaknesses. As a result of increasingly focused partnering strategies and following much streamlining, big pharma companies continue to be selective in the types of deals they choose to pursue. Oncology deals will remain popular, with particular interest being taken in immunotherapy and addressing niche patient populations, as will deals giving access to platform technologies relating to next-generation biologics following the significant regulatory strides made by cell and gene therapies in 2017. Valuations for unpartnered drug candidates with strong efficacy profiles that address unmet medical needs are likely to climb higher in 2018, driven by low supply and high demand. Finally, Chinese companies are expected to rise in prominence in the dealmaking market and may become the subject of cross-border M&A deals.

BIOGRAPHIES

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Heather has more than 10 years of experience in providing intelligence and insight to the pharmaceutical industry and was previously a Senior Advisor at PharmaVentures, specialising in providing expert opinion on the structure and pricing of pharmaceutical licensing transactions. During this time, she also developed expertise in forecasting and product valuation, competitive landscaping, market analysis and transfer pricing. Heather graduated from the University of Oxford with a Master's degree in Molecular and Cellular Biochemistry and holds a Diploma in Financial Management from the ACCA.

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