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White Paper

IQVIA PHARMA DEALS

Half-Year Review of 2018

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INTRODUCTION

QUALITY OVER QUANTITY? DEAL ACTIVITY SLOWS BUT VALUES CLIMB HIGHER

While some dealmaking records were broken in H1 2018, overall deal volumes in the life sciences sector were depressed relative to H1 2017. While the number of M&A deals fell from H1 2017 to H1 2018, the aggregate, mean and median total deal values for these deals increased over this period, although this was much to do with Takeda Pharmaceutical's pending £46 B (US$62.3 B) acquisition of Shire.

M&A is now a less attractive option for early-stage companies who are able to access large funding rounds and which are seeing valuations climb higher thanks in part to an increasingly robust IPO market. Some major biopharmaceutical companies returned to M&A in H1 2018, with Novartis, Sanofi and Celgene signing multibillion-dollar deals.

Despite overall deal activity being constrained, the volume of licensing deals in H1 2018 was broadly similar to the level seen in H1 2017, but with a significant rise in aggregate, mean and median deal values. The mean upfront payment for licensing deals fell in H1 2018, however, perhaps suggestive of a shift to early-stage dealmaking and some risk aversion on the part of licensees. Johnson & Johnson (J&J) retained the title of the most prolific dealmaker, although Roche and AstraZeneca climbed up the rankings.

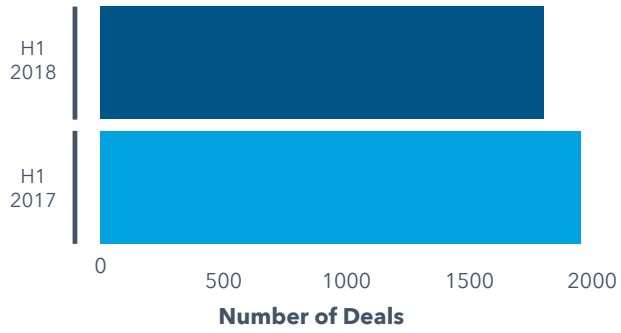
Oncology continued to be the most popular therapy area for dealmaking, with two of the top 3 partnering deals as ranked by upfront payment being co-development and co-commercialisation collaborations centered on key immuno-oncology assets. Oncology and rare diseases also dominated the M&A landscape.

Gene therapy deals rose in prominence in H1 2018, featuring in both the top 10 M&A and partnering deals lists. Appetite for collaborative R&D alliances was reduced in H1 2018, with a variety of deal structures being used for early-stage assets and both principal and partnering companies being able to demonstrate selectivity in the deals they chose to pursue, albeit for quite different reasons. Nevertheless, Biogen's April 2018 collaboration with Ionis Pharmaceuticals to develop antisense therapeutics for neurological diseases ranks as the largest collaborative R&D on record in terms of upfront consideration if both its US$375 M upfront payment and US$625 M equity investment are taken into account.

M&A MARKET COOLS THANKS TO STRONG FINANCING CLIMATE

The level of deal activity in the life sciences sector remains dampened relative to previous years. 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 8% from H1 2017 to H1 2018 (Figure 1). A significant factor contributing to this slowdown in deal activity is the buoyant financing market available to biopharmaceutical companies. Venture capital (VC) firms invested US$8.1 B in biotechnology-related industries during H1 2018[1], up 72% on H1 2017, thanks to two strong quarters of investment dollars, including an all-time quarterly high of US$4.1 B in H1 2018 buoyed by mega-deals such as Moderna Therapeutics' US$500 M raise. Moreover, investor sentiment towards public biotech companies is increasingly bullish, with biotechs now more able to access the public markets early in their life cycle. H1 2018[2] was a strong period for biotech IPOs, with 33 listings recorded in the US compared with just 17 in H1 2017, although short of the record 42 achieved in H1 2014 . Biotech companies now have a variety of funding options available to them and are able to retain rights to their pipeline programmes for longer, in the hope of achieving higher returns. From the perspective of larger pharmaceutical companies, the continuing uncertainty relating to future US government policy on drug pricing is also likely to have influenced dealmaking in H1 2018, although this may have been countered by the impact of the favourable US tax reforms which were announced in December 2017. Many biopharmaceutical companies have streamlined their operations and narrowed their therapeutic focus in recent years, and are now prioritising resources on a limited number of areas. This has undoubtedly had a knock-on effect on the biopharmaceutical dealmaking landscape, with major companies focusing on quality and not quantity when it comes to supplementing their pipelines.

Figure 1: Number of all deals (excluding funding awards), H1 2017 vs. H1 2018.



Source: IQVIA™ Pharma Deals

[1] PricewaterhouseCoopers, CB Insights Healthcare MoneyTree™ Reports Q1'18 and Q2'18
[2] The MTS US Biotech IPO Monitor, Edition 3

Table 1: Aggregate, mean and median values of M&A deals, H1 2017 vs. H1 2018.

All Deals

	H1 2017	H1 2018	CHANGE
AGGREGATE VALUE OF ALL M&A DEALS	US$116,773 M	US$161,180 M	+38%
MEAN DEAL VALUE	US$1283 M	US$1697 M	+32%
MEDIAN DEAL VALUE	US$143 M	US$201 M	+40%

Deals excluding Shire/Takeda

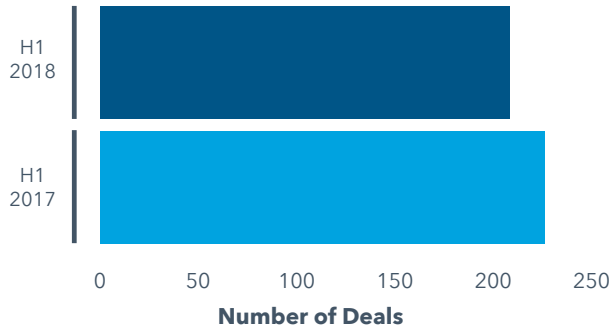
	H1 2017	H1 2018	CHANGE
AGGREGATE VALUE OF ALL M&A DEALS	US$116,773 M	US$98,842 M	-15%
MEAN DEAL VALUE	US$1283 M	US$1052 M	-18%
MEDIAN DEAL VALUE	US$143 M	US$196 M	+37%

M&A activity (defined here as including Mergers, Business Acquisitions and Divestments, signed but not necessarily completed) continued to slow in H1 2018, with the number of deals announced down 8% on H1 2017, mirroring the decline in overall deal activity in the life sciences sector (Figure 2). Significantly, however, at US$161.2 B, the aggregate total value of all M&A deals signed in H1 2018 was 38% higher than the US$116.8 B total value achieved in the same period the previous year (Table 1). Moreover, the mean total deal value for M&A deals increased 32% from US$1283 M in H1 2017 to US$1697 M in H1 2018, while the median total deal value increased 40% to US$201 M. The data set is distorted, however, by the inclusion of the Shire/Takeda Pharmaceutical mega-merger (Deal no. 85249). Indeed, if this £46 B (US$62.3 B) deal is excluded then the aggregate total deal value and the mean total deal value for M&A deals fell 15% and 18% respectively from H1 2017 to H1 2018.

M&A is less appealing to many early-stage companies at present owing to their ready ability to raise capital via alternative means. Moreover, the Nasdaq Biotechnology Index, which climbed 18.7% over the course of 2017, remains robust and high market capitalisations may continue to dissuade big pharma from pursuing all but the most attractive acquisition targets – companies with high-potential marketed or late-stage assets in key therapy areas or potentially novel technology platforms – which increasingly appear to be few and far between.

Table 2 presents the top 10 M&A deals of H1 2018 ranked by total potential deal value. Combined, these deals were worth a total of US$126.7 B, equivalent to 79% of the aggregate value of all M&A deals signed in this time period. In contrast, the top 10 M&A deals of H1 2017 had a combined value of US$96.9 B (a lesser figure than previously reported owing to the termination of Fresenius Kabi's proposed US$4.3 B acquisition of Akorn (Deal no. 78506)). Unlike in H1 2016 and H1 2017, the list covers a limited number of industry segments, with representation only from prescription and OTC pharmaceuticals. Indeed, H1 2018 saw a return to M&A for a number of big pharma and biotech companies after a period of absence.

Figure 2: Number of M&A deals, H1 2017 vs. H1 2018.



Source: IQVIA™ Pharma Deals

Takeda's proposed £46 B (US$62.3 B) cash and stock purchase of rare disease specialist Shire was the largest deal to be announced in H1 2018 by some considerable margin, accounting for 39% of the aggregate value of all M&A deals signed in the first 6 months of 2018. The deal, which somewhat impressively from the perspective of Shire is effectively a 50:50 merger, will catapult Takeda into the ranks of big pharma, with the combined group forecast to be the ninth largest pharmaceutical company in 2019 with sales of US$29.5 B, leapfrogging the likes of AstraZeneca and Bristol-Myers Squibb (BMS) (IQVIA™ Analytics Link). According to the Pharma Deals database, the acquisition is the sixth largest in the history of the pharmaceutical industry and the largest overseas purchase by a Japanese pharmaceutical company.

The level of deal activity in the life sciences sector remains dampened relative to previous years – the number of agreements signed, excluding standalone research grants, decreased by approximately 8% from H1 2017 to H1 2018.

Table 2: Top M&A deals of H1 2018 ranked by total deal value.

TOTAL DEAL VALUE	COMPANIES	DEAL DRIVER
£46 B (US$62.3 B)	Takeda Pharmaceutical, Shire	Increased footprint in US market,expanded portfolios in neuroscience and gastroenterology, rare disease franchise
US$13 B	GlaxoSmithKline, Novartis	Full ownership of consumer healthcare joint venture
US$11.6 B	Sanofi, Bioverativ	Haemophilia franchise, rare disease pipeline assets
US$9 B	Celgene, Juno Therapeutics	Cellular immunotherapy platform
US$8.7 B	Novartis, AveXis	Phase III gene therapy for spinal muscular atrophy
US$7 B	Celgene, Impact Biomedicines	Fedratinib, a Phase III Janus kinase 2 (JAK2) inhibitor for myelofibrosis
€3.9 B (US$4.8 B)	Sanofi, Ablynx	Nanobody® technology platform, strengthened pipeline in rare blood disorders
€3.4 B (US$4.2 B)	Procter & Gamble, Merck KGaA	Expansion of consumer health business
€3.03 B (US$3.5 B)	CVC Capital Partners, Recordati	Growth in orphan disease and speciality care markets
CAD3.2 B (US$2.5 B)	Aurora Cannabis, Medreleaf	Increased scale in medical cannabis market

Source: IQVIA™ Pharma Deals

Concerns have been raised over both the size and rationale of the deal, however. While arguably not a natural strategic fit, the Shire takeover will increase Takeda's exposure to the lucrative US market, where Shire has a strong presence, while strengthening its offerings in neuroscience and gastroenterology and adding a market-leading rare disease franchise and a robust late-stage pipeline of mainly high margin rare disease drug candidates. Takeda will be left with a hefty US$30.85 B debt pile, however, and the task of integrating two rather different companies and achieving the cash flow necessary to pay down the accompanying debt.

Novartis and Sanofi both returned to the top 10 M&A deals list in H1 2018 with multibillion-dollar acquisitions. Sanofi's purchase of haemophilia specialist Bioverativ, which was completed in March (Deal no. 83447), was the company's largest deal since its US$20.1 B takeover of Genzyme in 2011 (Deal no. 37246) and represented a much-anticipated return to large-scale M&A for the company after it missed out

on both Medivation and Actelion. Sanofi is in need of new growth drivers following the 2015 patent expiry of its lead asset Lantus® (insulin glargine), which is forecast to decline at a CAGR of -9.6% over 2017 to 2024 (Analytics Link) due to increased competition from biosimilars such as Merck & Co.'s Lusduna Nexvue™ and Boehringer Ingelheim and Eli Lilly's Basaglar® (Deal no. 38795). Later the same month, Sanofi agreed to pay €3.9 B (US$4.8 B) to acquire Nanobody® specialist Ablynx (Deal no. 83534). Ablynx's lead product caplacizumab, which is based on Ablynx's Nanobody platform, has since been recommended for approval by the EMA's Committee for Medicinal Products for Human Use (CHMP) for the treatment of acquired thrombotic thrombocytopaenic purpura. The two purchases signal Sanofi's intent to strengthen its rare disease portfolio, although concerns have been raised over the long-term future of Bioverativ's haemophilia franchise due to evolving treatment paradigms with the launch of Roche's Hemlibra® (emicizumab-kxwh) and the potential emergence of future gene therapies.

Two of the top 10 M&A deals of H1 2018 relate to the consumer healthcare sector. In the second largest deal of the period, Novartis exercised an option it had previously been granted (Deal no. 58332) requiring GlaxoSmithKline (GSK) to buy out the Swiss company's 36.5% stake in the consumer healthcare joint venture the two parties had formed in 2015 for US$13 B (Deal no. 86278). Further down the list, Procter & Gamble agreed to acquire the consumer health business of Merck KGaA for a purchase price of approximately €3.4 B (US$4.2 B) (Deal no. 84904). Just days after announcing the deal with GSK, Novartis agreed to spend US$8.7 B to acquire AveXis, a biotech company specialising in gene therapies for the treatment of rare neurological diseases (Deal no. 84716). AveXis' lead candidate is AVXS-101, a potential one-time gene therapy to treat life-threatening spinal muscular atrophy that is in Phase III development.

Celgene is another company that appears twice on the list of top 10 M&A deals thanks to its agreements to acquire Impact Biomedicines (Deal no. 83298) and Juno Therapeutics (Deal no. 83503) for up to US$7 B and US$9 B, respectively. Celgene paid US$1.1 B upfront to acquire Impact and thereby gain access to the Phase III Janus kinase 2 (JAK2) inhibitor fedratinib, which is being developed for the treatment of myelofibrosis and polycythaemia vera. The rest of the deal consideration is tied to regulatory approval and sales-based milestones. Fedratinib has an interesting history, having been discovered by TargeGen, a company later acquired by Sanofi in 2010 (Deal no. 36552). Sanofi discontinued development of the programme in 2013 after potential cases of Wernicke's encephalopathy (WE), a neurological condition linked to vitamin B deficiency, were reported in eight out of 877 patients in a clinical trial and the company deemed that the risk to patient safety outweighed the benefits of the drug. Impact acquired worldwide rights to fedratinib in 2016 (Deal no. 83346) and has since presented analysis suggesting that the drug did not increase WE risk. Just 3 weeks after the Impact deal, Celgene moved to position itself as one of the key protagonists in the chimeric antigen receptor T-cell (CAR-T) field by acquiring Juno in its largest ever deal, which represents a bold bet on the future of cell therapy. For Celgene, the Impact and Juno deals are attempts to secure the long-term growth of the company ahead of the patent expiry of its flagship drug Revlimid® (lenalidomide) in 2022. The company is under increased pressure to find new revenue drivers after the high-profile failure of GED-0301 for Crohn's disease due to unfavourable benefit/risk data in late-stage studies. Celgene expects Juno's CD19-directed CAR-T JCAR017 (lisocabtagene maraleucel) to be approved in the US in 2019 and to achieve potential global peak sales of approximately US$3 B.

Private equity interest in the pharmaceutical sector continued in H1 2018 with CVC Capital Partners acquiring a controlling stake in Italian pharmaceutical company Recordati for an enterprise value of €3.03 B (US$3.5 B) (Deal no. 86311) and Advent International entering into a share purchase agreement with Sanofi to acquire the company's European generics business Zentiva for €1.9 B (US$2.4 B) (Deal no. 85153).

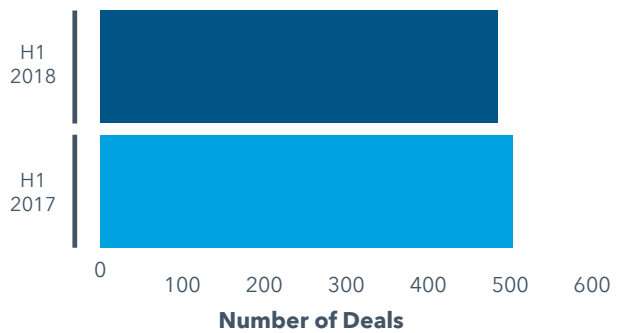
LICENSING DEALS ATTRACT HIGHER VALUES BUT LOWER UPFRONTS

The level of licensing activity in the life sciences sector fell only 4% from H1 2017 to H1 2018, a less marked decline than that in overall deal activity (Figure 3). Significantly, however, the aggregate potential total deal value of all licensing deals signed in H1 2018 was US$35.6 B, 41% higher than in H1 2017. Moreover, at US$346 M, the mean total deal value for all licensing deals in H1 2018 was 11% higher than the equivalent figure for H1 2017 (US$312.6 M), while the median total deal value (arguably a better measure of the 'average') rose by 41% to US$127 M (Table 3). While it is unlikely that many headline deal values that include a plethora of development and commercial milestone payments across multiple products or indications will ever be fully realised, non-contingent upfront payments offer a more useful measure of deal value trends. The mean upfront payment for all licensing deals dropped from US$62 M in H1 2017 to US$33.3 M in H1 2018, although significantly the median value increased by 33% to US$10 M. The mean upfront figure for licensing deals in H1 2017 is influenced by the inclusion in the data set of two high-profile and high-value settlement deals, notably 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 BMS and Ono Pharmaceutical resolving patent litigation relating to Keytruda® (pembrolizumab) (Deal no. 76237). If these two deals are excluded from the analysis then the mean upfront payment for H1 2017 falls to US$36.6 M, and H1 2018 compares more favourably.

The top 10 partnering deals by upfront payment in H1 2018, excluding settlement deals and product acquisitions, are shown in Table 4. It must be noted that not all of the listed deals are licensing deals, however.

The largest upfront payment in H1 2018 was the staggering US$1 B that BMS paid Nektar Therapeutics as part of a US$3.63 B development and commercialisation agreement centred on Nektar's lead immuno-oncology asset NKTR-214 which aims to test drug combinations that could increase the effectiveness of its immune checkpoint inhibitors (Deal no. 83869). The deal, which also saw BMS make a US$850 M equity investment in Nektar, comes

Figure 3: Number of licensing deals, H1 2017 vs. H1 2018.



Source: IQVIA™ Pharma Deals

Table 3: Aggregate, mean and median values of licensing deals, H1 2017 vs. H1 2018.

	H1 2017	H1 2018	CHANGE
AGGREGATE VALUE OF ALL LICENSING DEALS	US$25,324 M	US$35,644 M	+41%
MEAN TOTAL DEAL VALUE	US$313 M	US$346 M	+11%
MEDIAN TOTAL DEAL VALUE	US$90 M	US$127 M	+41%
MEAN UPFRONT PAYMENT	US$62 M	US$33.3 M	-46%
MEDIAN UPFRONT PAYMENT	US$7.5 M	US$10 M	+33%

Source: IQVIA™ Pharma Deals

Table 4: Top partnering deals (excluding settlements and product acquisitions) by upfront payment, H1 2018.

TOTAL DEAL VALUE	UPFRONT PAYMENT	COMPANIES	INTEREST AREA	DEVELOPMENT PHASE
US$3630 M	US$1850 M (US$1000 M cash upfront + US$850 M equity investment)	Nektar Therapeutics, Bristol-Myers Squibb (BMS)	Joint development and commercialisation of NKTR-214 in combination with Opdivo® (nivolumab) and Opdivo plus Yervoy® (ipilimumab)	Phase II
US$1270 M	US$1000 M (US$375 M cash upfront + US$625 M equity investment)	Ionis Pharmaceuticals, Biogen	Antisense drug candidates for neurological diseases	Discovery
US$5755 M	US$750 M (US$300 M cash upfront + US$450 M reimbursement for R&D expenses)	Eisai, Merck & Co.	Co-development and co-commercialisation of Lenvima® (lenvatinib mesylate), both as monotherapy and in combination with Keytruda® (pembrolizumab)	Launched, Clinical stage
US$2230 M	US$170 M (US$110 M cash upfront + US$60 M equity investment)	Wave Life Sciences, Takeda Pharmaceutical	Nucleic acid therapies for disorders of the CNS	Phase 1/2, Preclinical, Discovery
US$3150 M	US$150 M	Sangamo Therapeutics, Kite Pharma/ Gilead Sciences	Next-generation engineered cell therapies for cancer	Discovery
US$1880 M	US$150 M	Ionis Pharmaceuticals, Akcea Therapeutics	Inotersen and IONIS-TTR-LRx for transthyretin amyloidosis	Preregistration, Preclinical
US$2262.5 M	US$150 M (US$100 M cash upfront + US$50 M equity investment)	Prothena, Celgene	Therapies for a broad range of neurodegenerative diseases	Discovery
US$170 M	US$105 M	Spark Therapeutics, Novartis	Ex-US rights to ophthalmology gene therapy Luxturna™ (voretigene neparvovec)	Registered/ Approved
UNDISCLOSED	US$101 M (including an equity investment)	Vividion Therapeutics, Celgene	Small molecules that function through the ubiquitin proteasome system	Discovery
US$1000 M	US$100 M	Theravance Biopharma, Janssen Biotech	TD-1473 for inflammatory intestinal diseases	Phase I

Source: IQVIA™ Pharma Deals

a year after the two companies formed a clinical trial collaboration to evaluate NKTR-214 with BMS's Opdivo® (nivolumab) in Phase I/II clinical trials in various cancers, including renal cell carcinoma (RCC), non-small-cell lung cancer and bladder cancer (Deal no. 73711). The new collaboration will see the two companies jointly develop and commercialise NKTR-214 in combination with Opdivo and Opdivo plus Yervoy® (ipilimumab) in more than 20 indications across nine tumour types, with BMS having a period of exclusivity that extends to the later of commercial launch or 3 years after the closing date of the deal. It remains to be seen if this deal is a prelude to a potential takeover of Nektar by BMS.

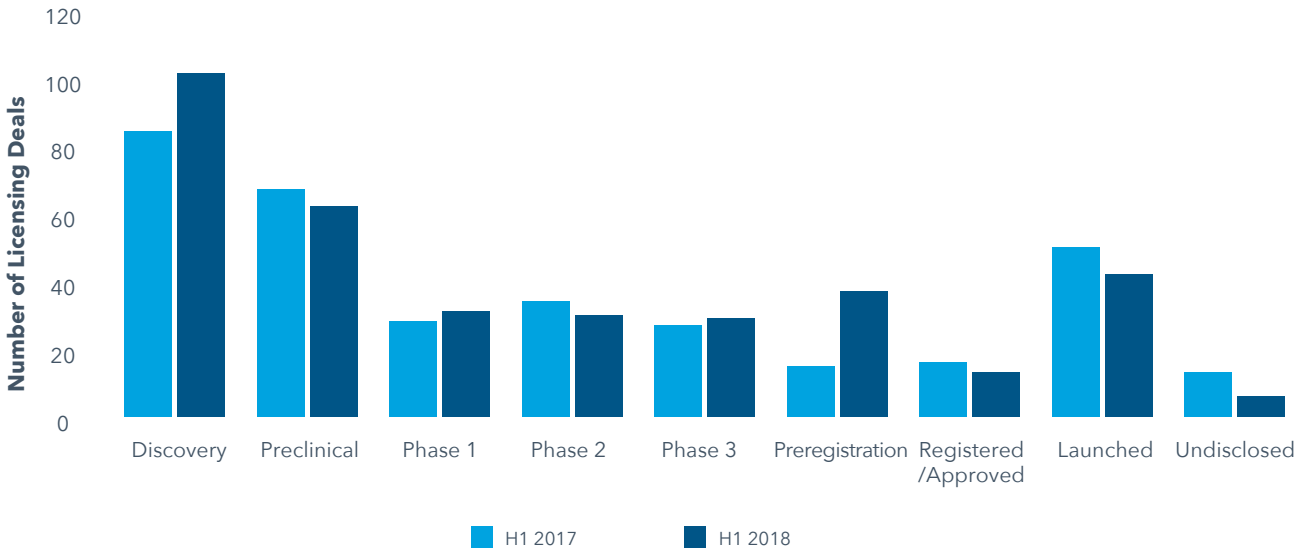
Another significant deal in the immuno-oncology field aiming to expand the use of an already marketed checkpoint inhibitor into new patient populations was the collaboration Merck & Co. established with Eisai to study the oral multireceptor tyrosine kinase inhibitor Lenvima® (lenvatinib mesylate), both alone and in combination with Keytruda, in 11 additional potential indications across six cancer types (Deal no. 84255). The global co-development and co-commercialisation deal follows encouraging results from the RCC cohort of a Phase Ib/II study of Lenvima in combination with Keytruda in which 63% of patients achieved an objective response rate after 24 weeks (Deal no. 63743). Merck paid Eisai US$300 M upfront and agreed to pay up to US$650 M for certain option rights through Eisai's 2020 fiscal year, US$450 M as reimbursement for R&D expenses, up to US$385 M in clinical and regulatory milestone payments and up to US$3.97 B in sales milestone payments. For Eisai, sales of Lenvima will no doubt benefit handsomely from Merck's commercial expertise and footprint. Moreover, the Japanese company will use the funds it receives under the deal to accelerate its R&D efforts in Alzheimer's disease and cancer.

In addition to acquiring AveXis, Novartis moved to broaden its footprint in gene therapy in H1 2018 by in-licensing ex-US rights to Spark Therapeutics' Luxturna™ (voretigene neparvovec), a one-time gene therapy to restore functional vision in children and adult patients with biallelic mutations of the *RPE65* gene (Deal no. 83547). Luxturna received US FDA approval in December 2017 but has since been a topic of controversy due to its high price tag of US$850,000.

There were 50 licensing deals for the Chinese market in H1 2018, up from 34 in H1 2017, with some US biotechs out-licensing regional rights to their drug candidates for not insubstantial fees. The largest Chinese licensing deal of H1 2018 in terms of total potential deal value was Agios Pharmaceuticals' US$424 M deal with CStone Pharmaceuticals for the development and commercialisation of ivosidenib in Mainland China, Hong Kong, Macau and Taiwan (Deal no. 86269). Ivosidenib is an oral, targeted inhibitor of the mutant isocitrate dehydrogenase-1 (IDH1) enzyme that received US approval in July for patients with relapsed or refractory acute myeloid leukaemia. In terms of upfront payment, the largest licensing deal for the Chinese market in H1 2018 was the partnership under which French biotech Adocia granted exclusive development and commercialisation rights to Tonghua Dongbao Pharmaceutical for the fixed-ratio insulin glargine and insulin lispro combination, BioChaperone® Combo, and ultra-rapid insulin, BioChaperone® Lispro, in China and other designated countries in return for US$50 M upfront (Deal no. 85007). Premixed insulins are the most popular insulin treatment in China and interestingly BioChaperone Lispro was formerly partnered with Eli Lilly (Deal no. 62537). In another sizeable deal covering the Chinese market, AstraZeneca sold the rights to Seroquel® (quietapine) and Seroquel XR® in the UK, China and other international markets to Luye Pharma in a deal worth US$538 M (Deal no. 85280).

Figure 4 presents an analysis of therapeutic licensing deals by development phase. Licensing activity at the discovery stage increased by 20% from H1 2017 to H1 2018 as companies remained keen to secure access to innovation at a very early development stage, although this increase was accompanied by a 7% dip in licensing activity for preclinical assets over the same time period. The level of licensing activity for Phase I assets rose 11% from H1 2017 to H1 2018, although

Figure 4: Therapeutic licensing deals by development stage, H1 2017 vs. H1 2018.



Source: IQVIA™ Pharma Deals

the number of licensing deals for Phase II assets fell 12% over the same time period. Big pharma mostly abstained from clinical-stage in-licensing deals in H1 2018, with exceptions including Janssen Biotech's US$100 M upfront deal with Theravance Biopharma for TD-1473, a Phase I gastrointestinal restricted pan-Janus kinase (JAK) inhibitor for the treatment of inflammatory bowel disease (Deal no. 83690), and Novo Nordisk's global licence to EpiDestiny's sickle cell disease programme, EPI01 (decitabine/tetrahydouridine), which is potentially worth up to US$400 M (Deal no. 84745).

Many of the Phase III licensing deals signed in H1 2018 were single territory or regional licensing deals, often including the Chinese market. One of the few major market Phase III licensing deals signed in H1 2018 was Vifor Fresenius Medical Care Renal Pharma in-licensing worldwide rights, excluding the US, Japan and South Korea, to Cara Therapeutics' product candidate CR845/difelikefalin to prevent, inhibit or treat itch associated with pruritus in haemodialysis and peritoneal-dialysis patients for US$50 M upfront (Deal no. 85540). The number of licensing deals concerning preregistration-stage assets more than doubled from H1 2017 to H1 2018. These deals were a diverse mix, including patent infringement settlement agreements, single territory licensing deals and licensing deals for generic/biosimilar products. Finally, there was a downturn in the number of licensing deals for registered/approved and launched products, most of which concerned territories outside the major markets and products late in their life cycle.

Licensing activity at the discovery stage increased by 20% from H1 2017 to H1 2018 as companies remained keen to secure access to innovation at a very early development stage.

J&J REMAINS THE MOST PROLIFIC DEALMAKER

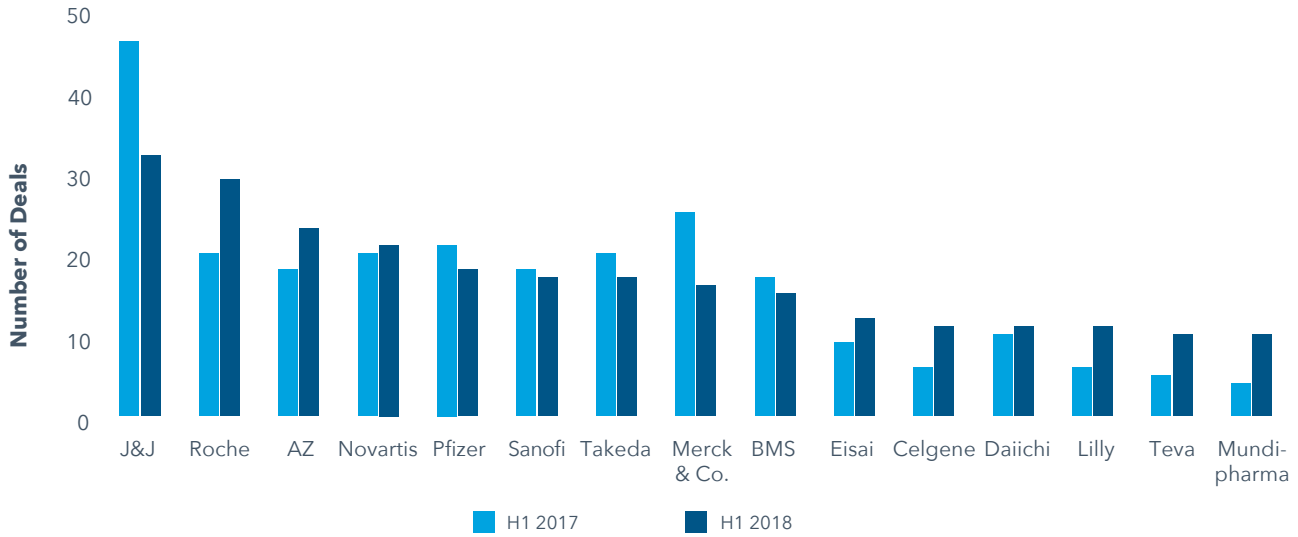
As it was in H1 2017, J&J was the most prolific dealmaker in the first 6 months of 2018 with 32 publicly disclosed deals, 14 less than the same period the previous year (Figure 5). Following closely behind in the rankings is Roche with 29 deals, a 45% increase on the company's deal volume in H1 2017. The Swiss company's most high-profile deal was its move to purchase the 43% of genomic profiler Foundation Medicine that it does not already own for US$2.4 B (Deal no. 86026). Further expanding its presence in personalised medicine, in April 2018 Roche acquired oncology data specialist Flatiron Health for US$1.9 B (Deal no. 83901).

Merck & Co. signed nine fewer deals in H1 2018 than it did in H1 2017, thus falling from second to eighth position in the deal activity rankings. 65% of the company's deals were in oncology and roughly one third were clinical trial collaborations testing Keytruda in combination with various oncology assets. The company announced one acquisition in H1 2018, agreeing to acquire Australian biotech Viralytics for AUD502 M (US$397 M), thereby gaining full rights to Cavatak®, a proprietary formulation of an oncolytic virus (Coxsackievirus type A21) that is being evaluated in multiple Phase I and Phase II clinical trials, including in combination with Keytruda (Deal no. 83928).

J&J's dealmaking was as diverse as ever in H1 2018, spanning a variety of industry sectors, development phases and therapy areas. The company continues to streamline its business, accepting a US$2.1 B binding offer from Platinum Equity for its LifeScan blood glucose monitoring business (Deal no. 84387) and receiving a US$2.8 B binding offer from Fortive for its Advanced Sterilization Products business (Deal no. 85910). However, it also signed a variety of pipeline-enhancing deals in H1 2018, including the acquisition of preclinical-stage oncolytic virus company BeneVir Biopharm in a deal potentially worth US$1.04 B (Deal no. 85147) and a collaboration with BMS for the development and commercialisation of the Factor XIa inhibitor BMS-986177, which is expected to enter Phase II clinical trials in H2 2018 for the study of secondary stroke prevention (Deal no. 84857).

AstraZeneca was the third most prolific dealmaker of H1 2018, with the company's deal volume up 28% on H1 2017. Its deals in H1 2018 were a mixed bag, including clinical trial collaborations centred

Figure 5: Most prolific dealmakers, H1 2017 vs. H1 2018.



Source: IQVIA™ Pharma Deals

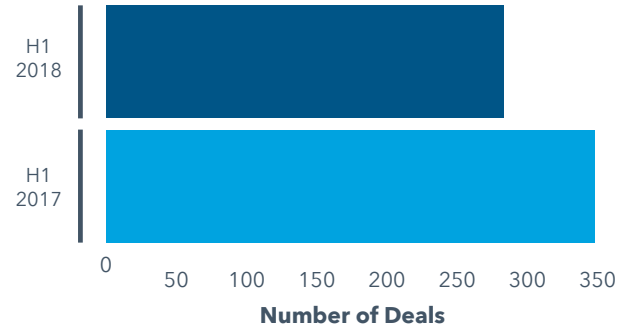
on durvalumab, the out-licensing of deprioritised programmes such as MEDI4945 for gout to Horizon Pharma (Deal no. 83370), contract research and manufacturing deals, early-stage research collaborations and an exclusive licence agreement with Compugen to enable the development of bispecific and multispecific immuno-oncology antibody products (Deal no. 84966).

R&D ALLIANCES FALL IN POPULARITY

The level of collaborative R&D dealmaking (defined here as discovery or preclinical-stage deals that involve two or more parties actively collaborating on R&D) in H1 2018 was down by 19% on the same period the previous year (Figure 6). This is a significant downturn and likely reflects a number of factors. Given the buoyant funding climate, many start-up companies are healthily financed at present and need not rely on signing partnering deals to help sustain their operations, or at least they are able to delay doing so. Many large and mid-sized biopharmaceutical companies are pursuing increasingly focused partnering strategies and are already directing significant resource and capital towards an array of broad, multitarget alliances established in previous years. While they remain keen on accessing innovation at an increasingly early stage of development, they are often happy to do so via option-based deal structures that leave responsibility for R&D in the hands of the biotech company or via straight licensing deals, as evidenced by the upturn in discovery-stage licensing deals. Such deals do not fall under the umbrella of Collaborative R&D. Another contributing factor is the fact that some research collaborations are only announced retrospectively, so the observed decline in collaborative R&D dealmaking may not be as pronounced as it currently appears.

In line with perceptions of a shift towards broader R&D alliances covering an increased number of targets or programmes, the aggregate total deal value for collaborative R&D deals increased by a significant 50% from H1 2017 to H1 2018, in part because there were more than twice as many deals with disclosed financials in H1 2018 than in the same period the previous year. While the mean total deal value for collaborative R&D deals fell by 31% in H1 2018 to US$462 M, the median total deal value actually increased by 20% to US$310 M (Table 5).

Figure 6: Number of collaborative R&D deals, H1 2017 vs. H1 2018.



Source: IQVIA™ Pharma Deals

Table 5: Aggregate, mean and median values of collaborative R&D deals, H1 2017 vs. H1 2018.

	H1 2017	H1 2018	CHANGE
AGGREGATE VALUE OF ALL R&D DEALS	US$12,022 M	US$18,009 M	+50%
MEAN DEAL VALUE	US$668 M	US$462 M	-31%
MEDIAN DEAL VALUE	US$259 M	US$310 M	+20%

Source: IQVIA™ Pharma Deals

Table 6: Selected Collaborative R&D deals, H1 2018.

TOTAL DEAL VALUE	UPFRONT PAYMENT	COMPANIES	INTEREST AREA	DEVELOPMENT PHASE (NUMBER OF PROGRAMMES)
€1130 M (US$1389 M)	€15 M (US$18.4 M)	OSE Immuno -therapeutics, Boehringer Ingelheim	Microbiome gastrointestinal development programmes	Preclinical (1)
US$1230 M	US$30 M	Pieris Pharmaceuticals, Seattle Genetics	Bispecific immuno-oncology treatments for solid tumours and blood cancers	Discovery (3)
US$1179 M	US$69 M	Voyager Therapeutics, AbbVie	Vectorised antibodies directed against tau for Alzheimer's disease and other neurodegenerative diseases	Preclinical (3)
US$1172.5 M	US$150 M (US$40 M cash + US$110 M equity investment)	Denali Therapeutics, Takeda Pharmaceutical	Therapies for neurodegenerative diseases utilising Denali's Antibody Transport Vehicle technology	Preclinical, Discovery (up to 3)
US$969 M	Undisclosed	Lodo Therapeutics, Genentech	Drug discovery utilising Lodo's metagenomics-based natural products platform	Discovery (undisclosed)

Source: IQVIA™ Pharma Deals

Selected collaborative R&D deals are profiled in Table 6.

The largest collaborative R&D deal of H1 2018 in terms of total potential deal value and the second largest in terms of upfront payment was Sangamo Therapeutics' US$3.15 B genome editing deal with Gilead Sciences' Kite Pharma to develop next-generation ex vivo cellular immunotherapies in oncology for both autologous and allogeneic use (Deal no. 83948). The collaboration, which saw Kite pay US$150 M upfront, represents a major endorsement of Sangamo's zinc finger nuclease (ZFN) genome editing technology and strengthens Gilead's position as a leading player in the engineered T-cell therapy field following its acquisitions of Kite (Deal no. 80732) and Cell Design Labs (Deal no. 82746). Of the US$3.15 B total deal value, approximately US$1.26 B relates to research, clinical development and first commercial sales milestones and approximately US$1.75 B relates to commercial milestones linked to the achievement of specified sales levels. For Sangamo, the Gilead deal was the second big pharma collaboration

the company announced in H1 2018 following its partnership with Pfizer for the development and commercialisation of potential gene therapy products that use zinc finger protein transcription factors to treat C9ORF72-linked amyotrophic lateral sclerosis and frontotemporal lobar degeneration (Deal no. 83234).

Biogen's 10-year option-based collaboration agreement with long-standing partner Ionis Pharmaceuticals to develop antisense drug candidates for a broad range of neurological diseases ranks as not only the largest collaborative R&D deal of H1 2018 in terms of upfront consideration, but also the largest collaborative R&D deal on record when you take account of its US$375 M cash upfront payment and the US$625 M equity investment Biogen made in Ionis at a 25% premium (Deal no. 85107). The front-loaded nature of the deal surprised some industry observers but Biogen estimates that only one successful commercial product is needed to generate a positive deal value. The two companies first partnered in 2012 in a collaboration that produced Spinraza® (nusinersen), a survival motor neuron-2 (SMN2)-directed antisense oligonucleotide indicated for the treatment of spinal muscular atrophy in paediatric and adult patients that generated sales of US$541 M in 2017 (Deal no. 44773). They also have two antisense drug candidates in clinical development, with the potential to advance up to seven more into the clinic within the next 2 years.

The plethora of development setbacks that continue to plague the Alzheimer's disease therapy area failed to deter a number of top 30 biopharmaceutical companies from signing early-stage R&D alliances in this field in H1 2018. In February, AbbVie paid Voyager Therapeutics US$69 M upfront as part of an option-based alliance to develop tau-targeted vectorised antibodies for the treatment of Alzheimer's disease and potentially other neurodegenerative diseases (Deal no. 84096). The aim of the collaboration is to develop a one-time treatment using Voyager's gene therapy platform to reduce tau build-up, which is thought to lead to impaired brain function. Rather than collaborating on research and development, some companies prefer to fund early-stage research at biotech companies via option-based deals that delay the co-development or licensing decision. One notable example in the central nervous system (CNS) field in H1 2018 is Prothena's partnership with Celgene to develop new therapies targeting three proteins implicated in the pathogenesis of several neurodegenerative diseases, including tau, TDP-43 and an undisclosed target (Deal no. 84740). For each of the programmes, Celgene has an exclusive right to license clinical candidates in the US at the drug IND filing.

The plethora of development setbacks that continue to plague the Alzheimer's disease therapy area failed to deter a number of top 30 biopharmaceutical companies from signing early-stage R&D alliances in this field in H1 2018.

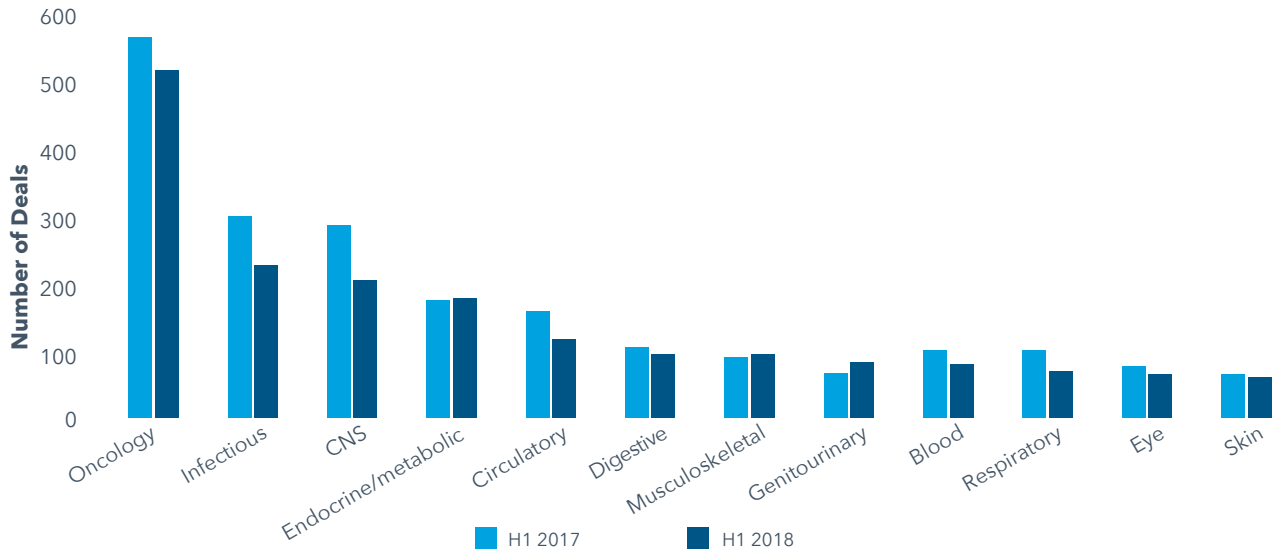
THE DOMINANCE OF ONCOLOGY CONTINUES

Oncology continues to reign as the principal therapy area for dealmaking in the life sciences sector, with nearly twice as many deals being signed in this therapy area in H1 2018 than infectious diseases, the second leading therapy area for dealmaking in H1 2018 (Figure 7). Of the deals signed in H1 2018 that were ascribed an indication, approximately 33% involved oncology, a slightly higher percentage than in H1 2017. Diseases of the CNS, endocrine, nutritional and metabolic diseases and diseases of the circulatory system comprised the third, fourth and fifth most prevalent therapy areas for deals signed in H1 2018, respectively.

The immuno-oncology field saw a return to high-profile dealmaking in H1 2018, with several deals already discussed in this White Paper featuring in the top deals lists thanks to their high upfront dollar considerations. While BMS and Merck & Co. looked to protect and extend their checkpoint inhibitor franchises, Celgene jumped to the forefront of the cellular immunotherapy field with its acquisition of Juno. In line with the evolution of the immuno-oncology market, partnership deals in this therapy area are increasing in complexity, as companies with coveted assets are able to retain significant co-development and co-commercialisation rights in deals that involve extensive clinical development programmes across multiple indications. A not insignificant proportion of the oncology deals signed in H1 2018 were clinical trial collaborations to test various combinations of immuno-oncology assets in various tumour types. Deals relating to biomarkers or companion diagnostics were also popular.

With many pharmaceutical companies having exited research and development in infectious diseases, most recently Novartis ceasing antibiotic and antiviral R&D, it is perhaps not surprising that deals with significant financial terms in the infectious disease field were few and far between in H1 2018. Indeed, most deal activity in this therapy area in the first 6 months of 2018 involved universities/ research institutes or small to mid-sized companies. Less than 2 weeks after filing for an IPO, in June Translate Bio secured a high-profile, US$45 M upfront R&D partnership with Sanofi Pasteur, the vaccines unit of Sanofi, to develop next-generation mRNA vaccines for up to five undisclosed infectious disease

Figure 7: Number of deals by therapeutic area, H1 2017 vs. H1 2018.



Source: IQVIA™ Pharma Deals

pathogens (Deal no. 85914). Formerly known as RaNA Therapeutics, Translate Bio acquired its mRNA therapy platform from Shire in 2016 (Deal no. 75960). For Sanofi, the deal follows a number of setbacks in the vaccine field and continues the company's investment in mRNA technology after deals with CureVac (Deal no. 44076) and BioNTech (Deal no. 67639). Sanofi also agreed to integrate its infectious disease unit into Evotec as part of a transaction that will see Sanofi license more than 10 infectious disease assets to the German company (Deal no. 84170). In June, Gilead partnered with Hookipa Biotech to advance Hookipa's TheraT® and Vaxwave® arenavirus vector-based immunisation technologies for two major chronic infectious disease indications, hepatitis B virus (HBV) and HIV (Deal no. 85818).

The volume of product deals concerning CNS diseases increased 10% from 2016 to 2017, but the available data for the first 6 months of this year suggest that this upward trend is unlikely to continue in 2018. Interestingly, three therapy areas actually saw an increase in deal activity from H1 2017 to H1 2018: endocrine, nutritional and metabolic diseases; diseases of the musculoskeletal system; and diseases of the genitourinary system. Roivant Sciences signed two noteworthy licensing deals for Phase II diabetes drug candidates in H1 2018, licensing US and European rights to Poxel's oral antidiabetic agent imeglimin (Deal no. 83755) and gaining global rights to Ligand Pharmaceuticals' glucagon receptor agonist programme for US$20 M upfront (Deal no. 84158). High-profile deals in the genitourinary therapy area in H1 2018 include the US$1.3 B merger of Akebia Therapeutics and Keryx Biopharmaceuticals (Deal no. 86246) and Boston Scientific's US$406 M acquisition of NxThera and its minimally invasive treatment option for patients with benign prostatic hyperplasia (Deal no. 84684).

OUTLOOK FOR H2 2018

The life sciences M&A market was subdued in 2017 in terms of both deal volume and deal value amid uncertainty surrounding drug pricing, the Affordable Care Act and pending taxation reform in the US, as well as the impact of Brexit in Europe. In December 2017, the US government passed a sweeping overhaul of the US tax code, including a huge cut in the overall tax rate, a move that was expected to drive the repatriation of cash held overseas. While some industry observers expected these tax savings to fuel increased M&A activity, others speculated that US companies would instead channel repatriated cash towards share buybacks or dividends. The evidence presented in this White Paper suggests that biopharmaceutical M&A has yet to pick up in 2018 after a somewhat deceptive start to the year which suggested the contrary. While prohibitively high valuations will continue to deter some companies from engaging in M&A, a steady flow of M&A deals is likely in H2 2018 facilitated by those companies with strong balance sheets but sparse pipelines, lacklustre sales and/or dwindling growth forecasts. A general preference for smaller, pipeline-boosting acquisitions is expected.

Increased access to capital for early-stage companies should continue to slow partnering activity in the life sciences sector in H2 2018, with the lure of the public markets being particularly strong at present.

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A steady stream of biotech companies have been seeking a public listing and June 2018 saw the most active day for biotech IPOs in the history of the sector, with five pricings in one day. The funds raised by these companies will help fuel their R&D activities, negating the need for them to pursue partnerships as a source of funding. External sources of innovation in core therapeutic areas remain important for pharmaceutical companies with pipeline deficiencies but these companies are now very particular in the types of asset they wish to internalise after having streamlined their businesses in recent years and prioritised resources across an increasingly narrow number of R&D areas. Early-stage deals will continue to find favour, particularly those offering access to novel technology platforms and next-generation biologics. Because of this shift to early-stage dealmaking, clinical-stage licensing deals are likely to decline in popularity amongst large pharmaceutical companies. With two of the top 5 M&A deals of H1 2018 relating to gene therapy, the future looks bright for this technology area and increased deal activity and big pharma involvement can be expected, pending promising clinical results. Immunotherapy is also expected to be a significant driver of alliances and acquisitions, and not just in the cancer field. The upturn in CNS dealmaking seen in 2017 has thus far failed to continue in 2018, although certain companies remain willing to commit significant sums to deals in this therapy area. Finally, US and European biotech companies will increasingly look to out-license regional rights to their pipeline programmes to companies in China and other Asian markets.

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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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Taskin has been working in the field of market research and healthcare business intelligence for over 10 years, previously at Intelligentsia and Thomson Reuters. During this time, he was responsible for research, analysis and development of biopharma industry focused reports, journals and databases. He has evolved his expertise in the pharmaceutical licensing deals and alliances area developing business relationships with pharmaceutical companies globally. Taskin holds an MBA from the University of Surrey Business School.

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