

# IMS PharmaDeals Half-Year Review 2014

M&A returns to the top of the deal-making agenda

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After ostensibly refraining from acquisitions in 2013, big pharma appetite for M&A increased significantly in the first half of 2014 despite an overall downturn in deal activity in the life sciences sector. Creativity in M&A emerged, as evidenced by the asset swapping between GlaxoSmithKline and Novartis, and speciality pharma consolidation continued apace. Licensing upfront payments and deal values increased markedly as compared to H1 2013 and Celgene and Merck & Co. signed deals with record-breaking upfront payments. AstraZeneca retained its title as the most prolific dealmaker in H1 2014, although a number of its contemporaries significantly ramped up their partnering activity. Oncology continued to dominate the deal-making landscape and early-stage collaborations for the discovery and development of cancer immunotherapeutics comprised one of the major deal-making themes of the period.

## M&A gains momentum

Deal making in the life sciences sector in the first half of 2014 was dominated by M&A (defined here as mergers, business acquisitions and divestments). While a series of big pharma asset swaps suggested a paradigm shift might be on the cards, unsolicited takeover bids from Pfizer, AbbVie and Valeant indicated that the mega-merger model might not yet be obsolete. Despite an overall downturn in deal-making activity compared to the previous year (Figure 1), M&A activity in H1 2014 remained at the same level as H1 2013 (Figure 2). At US\$168 B, the aggregate total value of all M&A deals signed in the first half of 2014 was approximately three times that of the same period the previous year (Table 1). Furthermore, the mean total deal value for such deals more than doubled from US\$652 M in H1 2013 to US\$1528 M in H1 2014.

FIGURE 1: NUMBER OF ALL DEALS, H1 2013 VS. H1 2014.

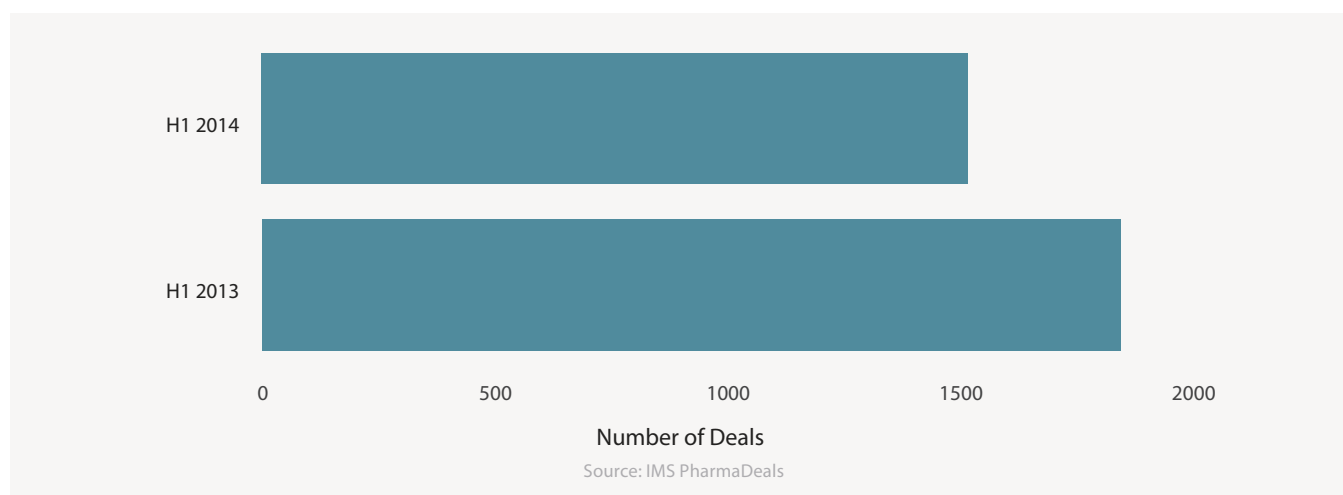


TABLE 1: AGGREGATE, MEAN AND MEDIAN VALUES OF M&A DEALS, H1 2013 VS. H1 2014.

	H1 2013	H1 2014	CHANGE
Aggregate value of all M&A deals	US\$56,095 M	US\$168,060 M	+200%
Mean deal value	US\$652 M	US\$1528 M	+134%
Median deal value	US\$170 M	US\$161 M	-6%

Source: IMS PharmaDeals

FIGURE 2: NUMBER OF M&amp;A DEALS, H1 2013 VS. H1 2014.

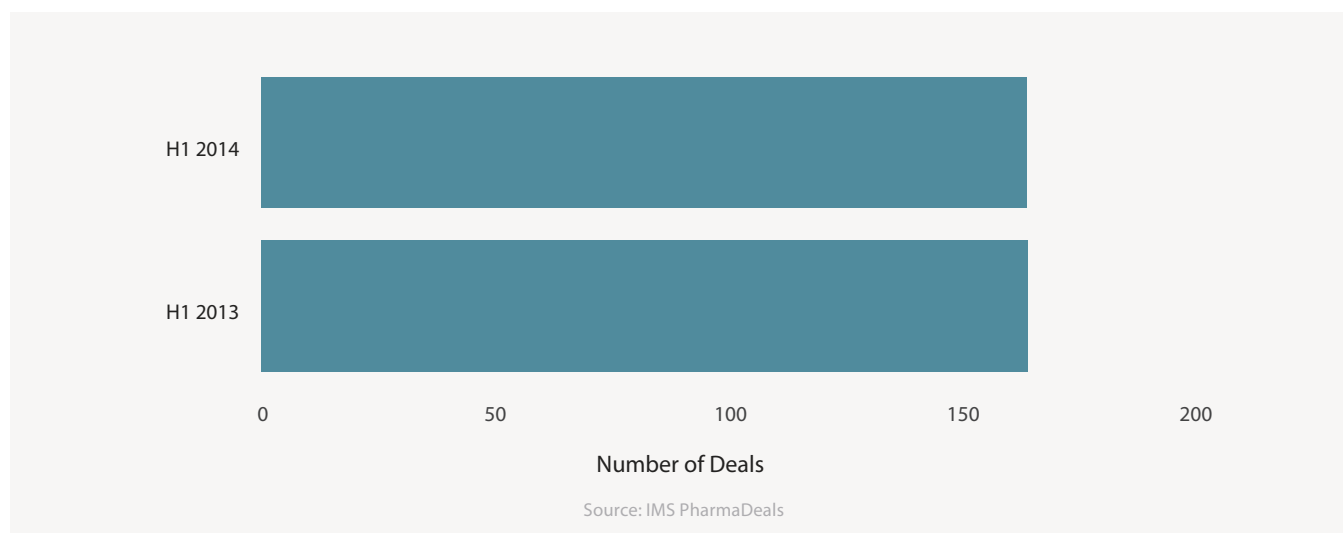


TABLE 2: TOP M&amp;A DEALS OF H1 2014 RANKED BY TOTAL DEAL VALUE.

TOTAL DEAL VALUE	COMPANIES	DEAL DRIVER
US\$42.9 B	Medtronic, Covidien	Medical devices/supplies
US\$25 B	Actavis, Forest Laboratories	Marketed products, speciality
US\$16 B	Novartis, GlaxoSmithKline	Marketed oncology portfolio (asset swap)
US\$14.2 B	Bayer, Merck & Co.	Consumer care business (asset swap)
US\$13.35 B	Zimmer Holdings, Biomet	Orthopaedic products
US\$7.1 B	GlaxoSmithKline, Novartis	Vaccines business (asset swap)
US\$5.6 B	Mallinckrodt, Questcor Pharmaceuticals	H.P. Acthar® Gel (repository corticotropin injection), which is approved by the US FDA for 19 diverse indications that have an inflammatory component
US\$4 B	The Carlyle Group, Ortho-Clinical Diagnostics	In vitro diagnostics
US\$4 B	Sun Pharmaceutical Industries, Ranbaxy Laboratories	Speciality and generic products
US\$3.85 B	Merck & Co., Idenix Pharmaceuticals	Clinical-stage hepatitis C drug candidates

Source: IMS PharmaDeals

Table 2 presents the top 10 M&A deals of H1 2014 ranked by total potential deal value. Combined, these deals were worth a total of US\$136 B, equivalent to 81% of the aggregate value of all M&A deals signed (but not necessarily completed) in this time period. In contrast, the top 10 M&A deals of H1 2013 had a combined value of just US\$40.4 B.

Medtronic's US\$42.9 B acquisition of medical device manufacturer Covidien (Deal no. 59426) was the largest deal to be announced in H1 2014 and somewhat dwarfs Thermo Fisher Scientific's US\$13.6 B purchase of Life Technologies (Deal no. 51973), the biggest M&A deal of 2013. The acquisition is the largest ever in the medical device sector and will give Medtronic the necessary size and scale to compete with the leading player Johnson & Johnson (J&J). It also continues a trend of US companies reincorporating abroad in order to make use of cash held overseas and benefit from tax advantages of being domiciled in countries with a lower tax rate than the US.

The trend of consolidation in the speciality pharma sector continued in the first half of 2014, led by acquisitive Actavis' US\$25 B purchase of Forest Laboratories (Deal no. 57051). Interestingly, Forest itself announced two bolt-on acquisitions in 2014, the US\$2.9 B purchase of Aptalis (Deal no. 56273) and a deal to acquire Furiex Pharmaceuticals for up to US\$1.46 B (Deal no. 58651), both intended to bolster its gastrointestinal portfolio. Another significant deal in the sector was Dublin-based Mallinckrodt's US\$5.6 B takeover of Questcor Pharmaceuticals and its key revenue generator H.P. Acthar® Gel (repository corticotropin injection), a naturally derived formulation of adrenocorticotrophic hormone extracted from porcine pituitary glands that is approved by the US FDA for 19 diverse indications that have an inflammatory component and which has been aggressively priced (Deal no. 58089). For Mallinckrodt, which was spun out of Covidien in July 2013 (Deal no. 53289), the deal represents another attempt by the company to expand its presence in the global speciality pharmaceutical market, coming less than a month after it completed its US\$1.4 B acquisition of Cadence Pharmaceuticals and thereby gained the fast-growing intravenous analgesic Ofirmev® (acetaminophen) (Deal no. 56902).

While speciality pharma has been looking to diversify its revenue base, many large pharmaceutical companies have been doing the opposite and the offloading of underperforming business units was a key deal-making theme in H1 2014. In a series of deals that will significantly reshape the companies' businesses, in April Novartis and GlaxoSmithKline (GSK) agreed to swap certain assets and combine their consumer healthcare units (Deal no. 58332) in order to focus on those business areas in which they are most competitive. While Novartis has agreed to acquire GSK's portfolio of marketed cancer drugs for up to US\$16 B (Deal no. 58341), GSK is to buy Novartis' struggling vaccines business, excluding its influenza vaccines, for up to US\$7.1 B plus royalties (Deal no. 58333). The transaction, which is expected to close by the first half of 2015, is an acknowledgement that big pharma is no longer willing to participate in markets where it is not in the top three. Continuing the trend of big pharma streamlining, the following month Bayer HealthCare succeeded in its pursuit of Merck & Co's consumer healthcare unit with a US\$14.2 B bid, somewhat higher than analyst valuations for the unit (Deal no. 58588). Merck has also divested nine ophthalmology products in Japan and key markets in Europe and Asia Pacific to ophthalmology specialist Santen Pharmaceutical (Deal no. 58781), while J&J has sold its Ortho-Clinical Diagnostics unit to private equity firm, The Carlyle Group, for approximately US\$4 B (Deal no. 56467) and Bayer is to sell its interventional device business to Boston Scientific for US\$415 M (Deal no. 58788).

Of the top 10 M&A deals of H1 2014 by total deal value, only one involves a development-stage biotech, namely Merck's US\$3.25 B acquisition of hepatitis C drug developer Idenix Pharmaceuticals (Deal no. 59245). The deal is notable for its 229% premium, the high valuation in part being driven by a competitive bidding process and in part by the commercial performance to date of Gilead Sciences' oral antiviral Sovaldi® (sofosbuvir), sales of which amounted to US\$5.8 B in first half of 2014.

## Breaking licensing precedents

M&A aside, the first half of 2014 also saw some unprecedented licensing activity. In April, prolific dealmaker Celgene paid a record-breaking US\$710 M upfront to license Nogra Pharma's GED-0301, an oral antisense DNA oligonucleotide targeting Smad7 mRNA that has completed a Phase II trial in patients with active Crohn's disease (Deal no. 58425). The drug candidate has been remarkably low profile to date and Phase II data are keenly awaited by industry analysts. The upfront payment is the largest recorded in the IMS PharmaDeals Agreements database for a clinical-stage licensing deal and for a time ranked as the largest upfront payment ever recorded for a licensing deal. It was soon usurped, however, by the US\$1000 M that Merck paid Bayer as part of a global collaboration between the parties to develop and market Bayer's portfolio of soluble guanylate cyclase modulators for cardiovascular diseases, including Adempas (riociguat), which was approved by the US FDA in October 2013 and by the EC in March 2014 for the treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension (Deal no. 58596).

The level of licensing activity in the life sciences sector in H1 2014 was down 19% on the same period the previous year (Figure 3), although significantly the mean upfront payment for all licensing deals more than tripled from US\$23.8 M in H1 2013 to US\$81.5 M in H1 2014, driven by the sizeable licence fees mentioned above (Table 3). The top 10 partnering deals by upfront payment in H1 2014, excluding settlements and product acquisitions, are shown in Table 4.

After being party to some of the highest value partnering deals of H1 2013, Moderna Therapeutics and Forma Therapeutics returned to the top deals list in H1 2014. In April, Celgene paid US\$225 M upfront to expand its relationship with Forma with a multistage drug discovery collaboration covering a broad range of protein target families and therapeutic areas that could ultimately see it acquire the US drug discovery company (Deal no. 57989). The new deal has an initial term of 3.5 years and could last for more than 7 years if Celgene elects to exercise options to enter into two additional collaborations. In January, Alexion Pharmaceuticals paid US\$100 M to purchase 10 product options to develop and commercialise treatments for rare diseases using Moderna's mRNA Therapeutics platform (Deal no. 56393).

FIGURE 3: NUMBER OF LICENSING DEALS, H1 2013 VS. H1 2014.

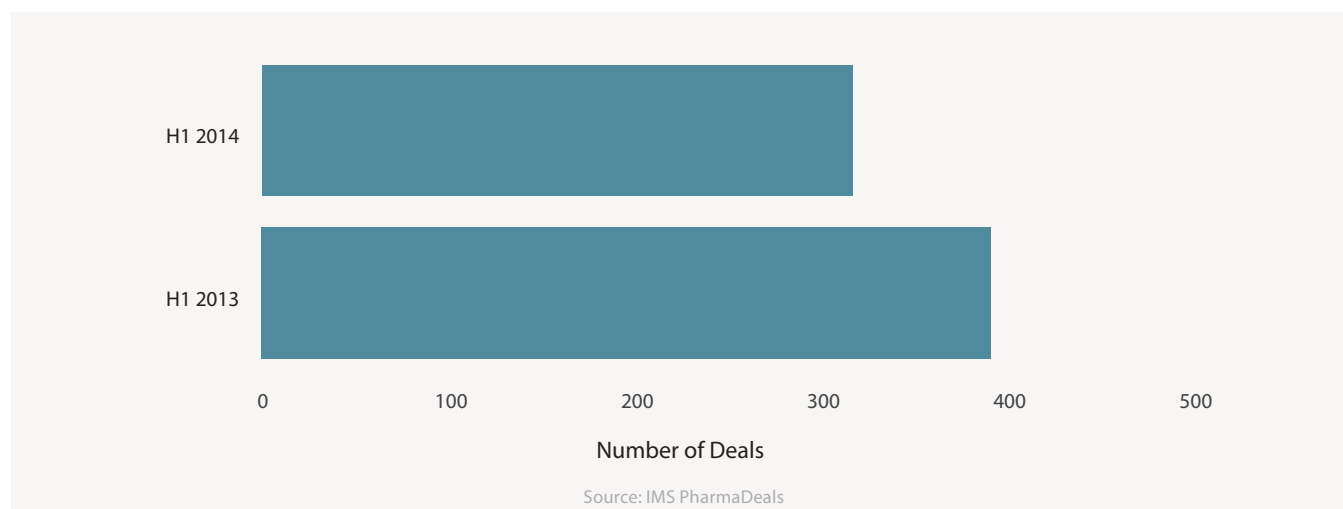


TABLE 3: AGGREGATE, MEAN AND MEDIAN VALUES OF LICENSING DEALS, H1 2013 VS. H1 2014.

	H1 2013	H1 2014	CHANGE
Aggregate value of all licensing deals	US\$9894 M	US\$22,842 M	+131%
Mean total deal value	US\$241.3 M	US\$617.3 M	+156%
Median total deal value	US\$116 M	US\$208 M	+79%
Mean upfront payment	US\$23.8 M	US\$81.5 M	+243%
Median upfront payment	US\$13 M	US\$20 M	+54%

Source: IMS PharmaDeals

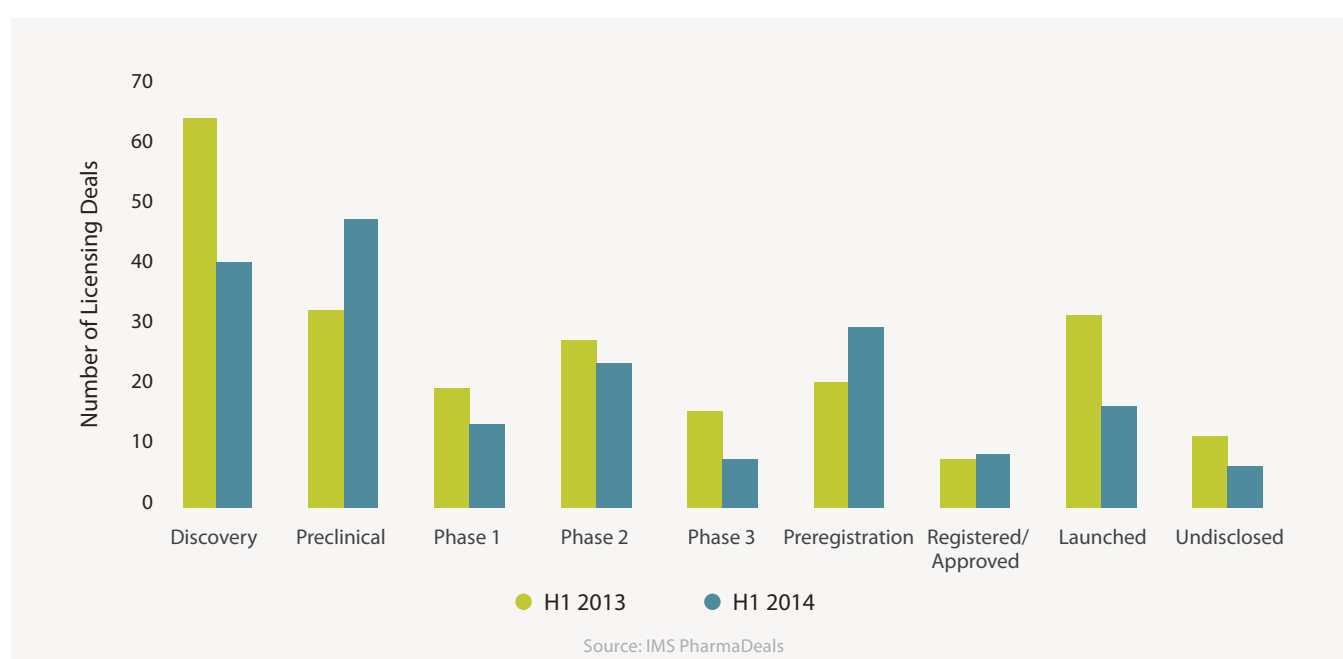
TABLE 4: TOP PARTNERING DEALS (EXCLUDING SETTLEMENTS AND PRODUCT ACQUISITIONS) BY UPFRONT PAYMENT, H1 2014.

TOTAL DEAL VALUE	UPFRONT PAYMENT	COMPANIES	INTEREST AREA	DEVELOPMENT PHASE
US\$2100 M	US\$1000 M	Bayer, Merck & Co.	Soluble guanylate cyclase modulators for cardiovascular diseases, including Adempas® (riociguat) and vericiguat	Launched, Phase II
US\$2750 M	US\$710 M	Nogra Pharma, Celgene	GED-0301, an oral antisense DNA oligonucleotide targeting Smad7 mRNA for active Crohn's disease	Phase II
US\$600 M	US\$225 M	Forma Therapeutics, Celgene	Multistage drug discovery collaboration covering a broad range of protein target families and therapeutic areas	Discovery
US\$1030 M	US\$200 M	Ophthotech, Novartis	Fovista® (anti-PDGF aptamer)	Phase III
Undisclosed	US\$100 M	Moderna Therapeutics, Alexion Pharmaceuticals	messenger RNA Therapeutics™ to treat rare diseases	Discovery
US\$2855 M	US\$80 M	Collectis, Pfizer	Chimeric antigen receptor T-cell (CAR-T) immunotherapies in oncology	Discovery
Undisclosed	€50 M (US\$68 M)	Orion, Bayer	ODM-201, an oral androgen receptor inhibitor for the treatment of patients with prostate cancer	Phase II
US\$1242 M	US\$50 M	CytomX Therapeutics, BMS	Novel therapies against multiple immuno-oncology targets using CytomX's Probody™ antibody masking technology	Discovery
Undisclosed	US\$30 M	Vertex Pharmaceuticals, Janssen Pharmaceuticals	VX-787 for influenza	Phase II
€1730.7 M (US\$2335 M)	€20 M (US\$27 M)	Ablynx, Merck & Co.	Nanobody candidates (including bi- and tri-specifics) directed toward immune checkpoint modulators	Discovery

Source: IMS PharmaDeals

Despite the overall decline in licensing activity from H1 2013 to H1 2014, deal making at the preclinical and preregistration stages has increased notably. Noteworthy deals for preclinical-stage assets include Merck's US\$526 M licence agreement for Australian Bionomics' BNC375, a research programme with an undisclosed mechanism of action that targets cognitive dysfunction associated with Alzheimer's disease and other CNS conditions (Deal no. 59466), and a worldwide collaboration and licence agreement between Biogen Idec and Sangamo BioSciences for the development of therapeutics for haemoglobinopathies (Deal no. 56289). Deals at the preregistration stage principally relate to ANDA settlement agreements and single territory or regional commercialisation deals, typically outside of major markets.

FIGURE 4: LICENSING DEALS BY DEVELOPMENT STAGE, H1 2014 VS H1 2013.



## Big Pharma targets early-stage collaborations

AstraZeneca was the most prolific dealmaker in the first 6 months of 2014 with 34 publicly disclosed deals, a slight increase on the same period the previous year (Figure 5). The company's deal making was predominantly at the discovery stage; its largest deal being an oncology research collaboration and licence agreement with Immunocore to research and develop therapies against selected cancer targets using the company's ImmTAC (immune mobilising monoclonal T-cell receptor against cancer) technology, which aims to redirect T-cells to destroy cancerous cells (Deal no. 56232). The deal is worth up to US\$320 M in upfront and milestone payments per target programme plus tiered royalties. Pfizer, Roche, Novartis and Merck all ramped up their deal making in H1 2014 compared to the same period the previous year. Roche's deals mostly spanned oncology research and molecular diagnostics, although its collaborations with Discuva (Deal no. 57359) and Spero Therapeutics (Deal no. 58147) demonstrate its renewed commitment to the field of antibiotics R&D.



Given the propensity of big pharma to sign early-stage drug discovery collaborations, it is unsurprising that collaborative R&D deal making remained robust in H1 2014 (Figure 6). The aggregate, mean and median total deal values, excluding royalties, for collaborative R&D deals all rose significantly in H1 2014 relative to H1 2013 (Table 5). These increases have principally been driven by three exceptionally large biodollar deals, the full values of which are unlikely to be realised. In January, Dainippon Sumitomo Pharma significantly broadened its relationship with Edison Pharmaceuticals with a collaboration for the discovery and development of drugs targeting cellular energy metabolism that could be worth as much as US\$4.3 B to the US-based company (Deal no. 56726). The majority of this deal value comes in the form of commercial milestone payments, however, the upfront payment is only US\$10 M. Ablynx (Deal no. 56736) and Collectis (Deal no. 59365) both secured back-ended deals potentially worth in excess of US\$2 B with big pharma partners (Merck and Pfizer, respectively), in each case providing access to their discovery platforms for multiple targets.

FIGURE 5: MOST PROLIFIC DEALMAKERS, H1 2013 VS. H1 2014.

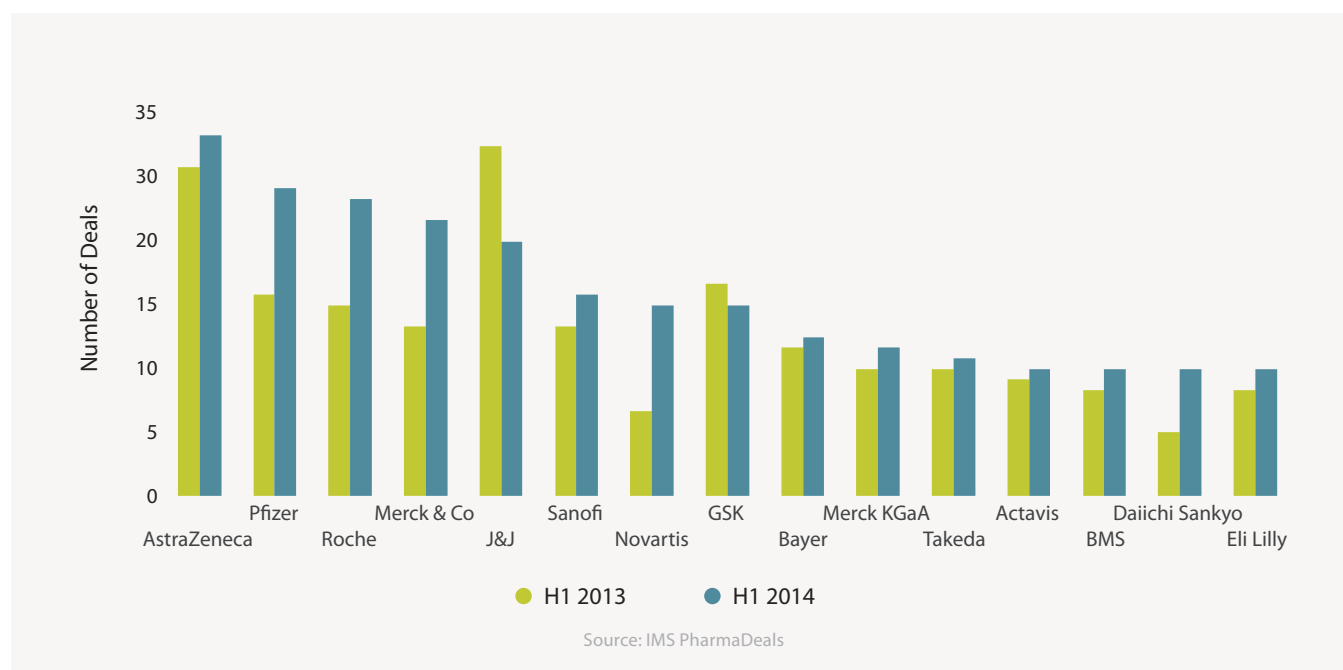


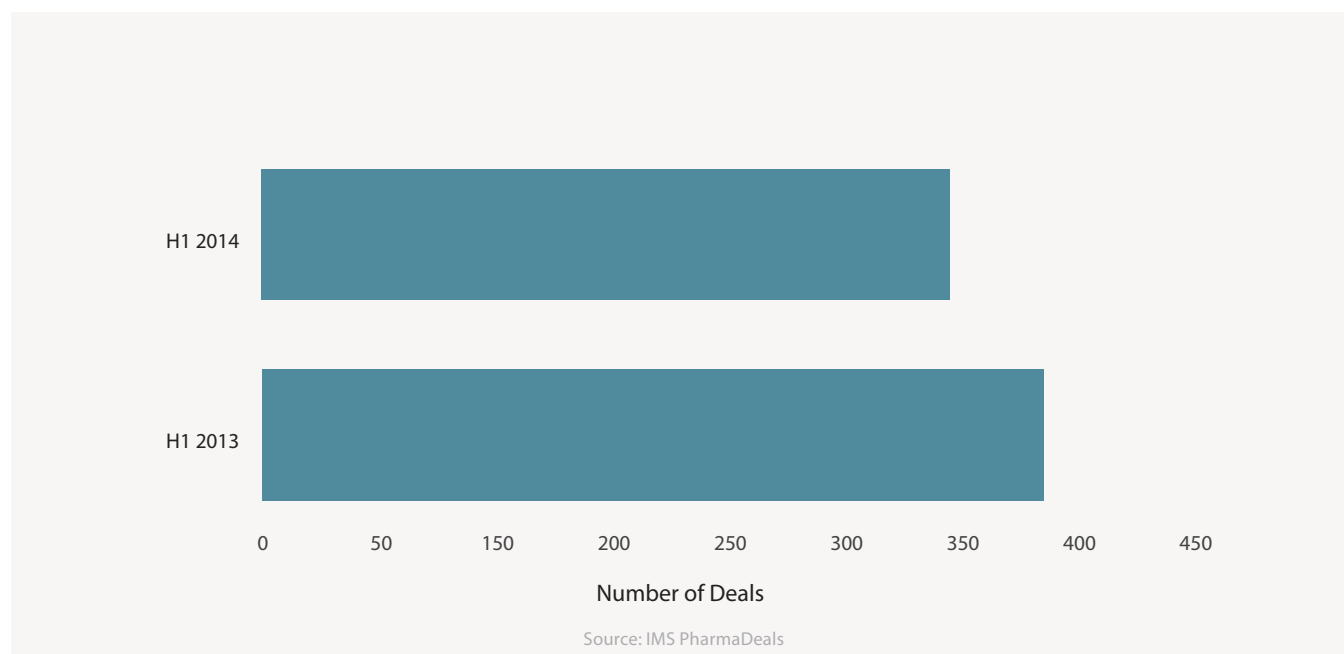
TABLE 5: AGGREGATE, MEAN AND MEDIAN VALUES OF COLLABORATIVE R&D DEALS, H1 2013 VS. H1 2014.

	H1 2013	H1 2014	CHANGE
Aggregate value of all collaborative R&D deals	US\$6348 M	US\$15,974 M	+152%
Mean total deal value	US\$353 M	US\$726 M	+106%
Median total deal value	US\$255 M	US\$331 M	+30%

Source: IMS PharmaDeals



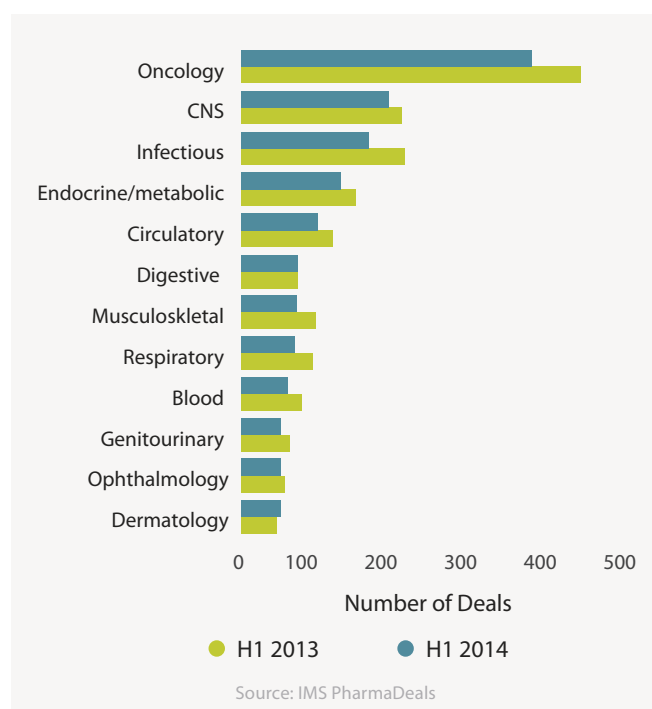
FIGURE 6: NUMBER OF COLLABORATIVE R&amp;D DEALS, H1 2013 VS. H1 2014.



## Oncology deals continue to dominate

Oncology continues to dominate the deal-making landscape, with twice as many deals being signed in this therapy area in H1 2014 than CNS, which was the second most popular therapy area for deal making in H1 2014 (Figure 7). Significantly, of the deals signed in H1 2014 that were ascribed an indication, approximately one third involved oncology. Infectious diseases, 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 2014, respectively. Deal-making activity in all therapy areas was down on H1 2013, however.

FIGURE 7: NUMBER OF DEALS BY THERAPEUTIC AREA, H1 2013 VS. H1 2014.



Despite the comparatively low level of deal activity in ophthalmology, there were some significant deals in this field in H1 2014. Just two weeks after it raised US\$55 M in an oversubscribed Series B financing round, California-based Avalanche Biotechnologies partnered with Regeneron Pharmaceuticals in May to discover, develop and commercialise next-generation gene therapies for ophthalmologic diseases using its adeno-associated virus (AAV)-based Ocular BioFactory™ platform (Deal no. 58592). For Regeneron, the deal is a long-term move by the company to find a successor to its blockbuster VEGF (vascular endothelial growth factor) inhibitor Eylea® (aflibercept). In the same month, Novartis paid Ophthotech US\$200 M upfront in order to gain rights to market Fovista®, an anti-PDGF (platelet-derived growth factor) aptamer that is in Phase III development for wet age-related macular degeneration (Deal no. 58853). The deal, one of the largest ex-US licensing agreements ever signed, also provides for development, regulatory and approval milestones of up to US\$830 M.

Within oncology, the hotly contested field of cancer immunotherapy field saw a number of high-profile partnerships in H1 2014, with six of the top ten pharmaceutical companies signing notable deals, the majority of which were at the discovery stage (Table 6). As several different immune checkpoint pathways are thought to be involved in subverting antitumour immune responses, H1 2014 also saw a plethora of clinical trial collaborations, with key players keen to test multiple combinations of assets. Merck alone signed deals to test its anti-PD-1 (programmed cell death-1) immunotherapy MK-3475 (pembrolizumab) in combination with cancer therapies in development with Incyte (Deal no. 56773), Pfizer (Deal no. 56776) and Amgen (Deal no. 56768).

TABLE 6: SELECTED CANCER IMMUNOTHERAPY DEALS, H1 2014.

TOTAL DEAL VALUE	UPFRONT PAYMENT	COMPANIES	INTEREST AREA	DEVELOPMENT PHASE
US\$2855 M	US\$80 M	Cellctis, Pfizer	Chimeric antigen receptor T-cell (CAR-T) immunotherapies in the field of oncology directed at select targets	Discovery
US\$1242 M	US\$50 M	CytomX Therapeutics, Bristol-Myers Squibb (BMS)	Novel therapies against multiple immuno-oncology targets using CytomX's Probody™ antibody masking technology	Discovery
€1730.7 M (US\$2335 M)	€20 M (US\$27 M)	Ablynx, Merck & Co.	Nanobody® candidates directed towards immune checkpoint modulator proteins	Discovery
US\$350.5 M	US\$20 M	Five Prime Therapeutics, BMS	Immuno-oncology therapies directed toward targets identified in two undisclosed immune checkpoint pathways	Discovery
US\$320 M	US\$20 M	Immunocore, MedImmune	Novel cancer therapies generated using Immunocore's immune mobilising monoclonal T-cell receptor against cancer (ImmTAC) technology	Discovery
US\$365 M	Undisclosed	Aduro BioTech, Janssen Biotech	Product candidates engineered for the treatment of prostate cancer based on Aduro's live, attenuated, double-deleted listeria monocytogenes (LADD) immunotherapy platform	Preclinical
US\$350 M	Undisclosed	Adaptimmune, GSK	T-cell receptor deployed to target the cancer testis antigen NY-ESO-1	Phase II
Undisclosed	Undisclosed	CoStim Pharmaceuticals, Novartis	Late discovery-stage immunotherapy programmes directed to several targets, including PD-1	Discovery

## Outlook for H2 2014

Unsolicited takeover bids hit the headlines in H1 2014 and the second half of the year has already seen AbbVie clinch Shire for US\$54.8 B with a sweetened deal that followed an intense series of negotiations between the parties and which will see the US-based company relocate its tax base to the United Kingdom (Deal no. 59882). At the time of writing, the outcome of Valeant's hostile US\$53 B approach for Allergan remains to be seen, however. Highly acquisitive Valeant aspires to become one of the world's top 5 largest pharmaceutical companies by the end of 2016 and to do so needs to increase its market capitalisation by more than US\$100 B. Rumours also abound that Pfizer could approach AstraZeneca with a revised offer at the end of the year. M&A is thus firmly back on the agenda of many major pharmaceutical companies, who have accumulated cash after paying down debt but which face stalling growth in the coming years, and we expect the momentum to continue in the second half of 2014, particularly with regard to tax-driven transactions. Although the level of deal making in 2014 may not reach that achieved in 2013, alliances and acquisitions in targeted areas remain of strategic importance to many companies in the life sciences sector and we are likely to see deal values rise further and deal-making precedents broken once again.

### About the authors

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