Meletios Verras/Thinkstock/iStock

Trends in oncology dealmaking

Oncology is currently the leading area for dealmaking, driven by immuno-oncology, which accounted for 32 of the 35 multibillion-dollar oncology licensing deals of the last five years. In this feature, authors at Clarivate Analytics explore the recent trends in oncology deals.

Jamie Munro and Helen Dowden

Oncology continued to dominate the dealmaking landscape for therapeutics in 2017, as it did in 2016 (*BioPharma Dealmakers* B3–B5, June 2017). Of the top 21 companies most active in dealmaking in 2017, there were only 5—Astellas, Boehringer Ingelheim, Gilead, Novartis and Sanofi—for which oncology was not the area with the highest number of deals (**Fig. 1**). A key driver here is presumably the current dominance and expected growth in the oncology market. In 2017, EvaluatePharma forecasted that oncology will remain the highest grossing therapy area until 2022, expanding at a compound annual growth rate of more than 12% to reach a value of almost $220 billion.

A review of oncology dealmaking from 2013 to 2017 (**Box 1**) shows a steep rise in activity during the first three years of this period (**Fig. 2**). One important contributor to this increase could be the approval of the first two PD1–PDL1 checkpoint inhibitors—Merck & Co.'s Keytruda (pembrolizumab) and Bristol-Myers Squibb's Opdivo (nivolumab)—in the second half of 2014, which accelerated a wave of dealmaking, not only around other checkpoint inhibitors, but also for molecules and technologies that could offer synergistic benefits when used in combination with these drugs.

In 2017, the volume of oncology dealmaking was slightly decreased compared with the levels in 2015 (–6%) and 2016 (–4%). Possible factors that may have contributed include companies awaiting the impact of tax changes in the US and the potential plateau in the number of PD1 or PDL1 combination therapy options. Nevertheless, the total value of these deals has been maintained (**Fig. 2**). The July 2017 deal between AstraZeneca and Merck & Co., valued at $8.5 billion inclusive of contingent payments, is a key

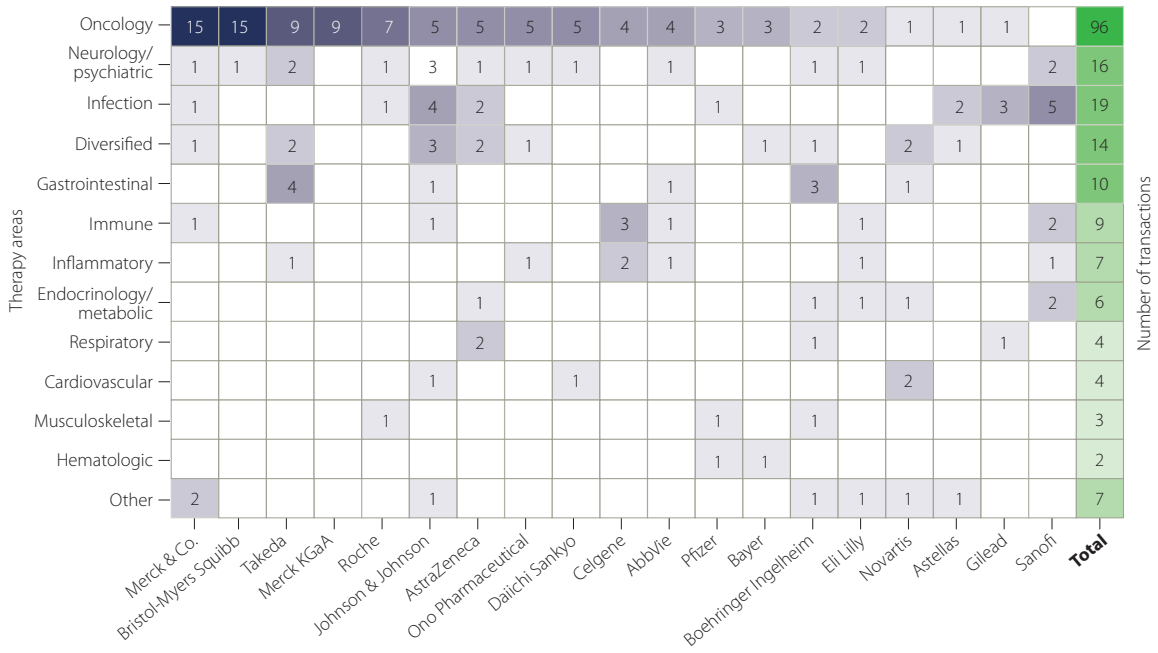

Fig. 1 | The top 50 pharmaceutical companies (ranked by 2016 revenues) with five or more buy-side transactions in the oncology area in 2017. The transactions assessed include all mergers and acquisitions, licensing deals, joint ventures and research-only deals with a therapeutic area focus initiated between January 2017 and December 2017. See **Box 1** for details of the data.

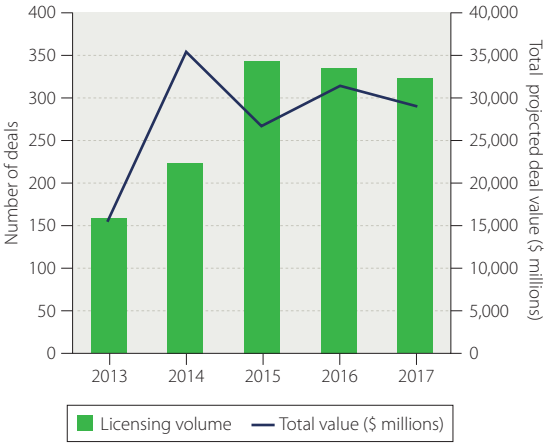

Fig. 2 | Licensing, joint venture and research-only oncology deals by volume and value from 2013 to 2017. Activity increased substantially from 2013 to 2015. See **Box 1** for details of the data.

contributor to this total. This deal—focused on the clinical evaluation of AstraZeneca's PARP inhibitor Lynparza (olaparib) and MEK1/2 kinase inhibitor selumetinib, used in combination with the companies' PD1-specific and PDL1-specific antibodies—demonstrates how a multibillion-dollar deal can skew the overall value of dealmaking in any given year. Without this deal, the overall total deal value for 2017 is approximately $20 billion, substantially below the $31 billion average of the previous three years but still much higher than the $15 billion for the deals signed in 2013.

The AstraZeneca–Merck & Co. deal is the largest recorded within the past five years, but there are an additional 34 deals in this time period with a total value in excess of $1 billion (**Table 1**). Of these 35 deals, 32 are focused on immuno-oncology, and many involve emerging platforms, such as chimeric antigen receptor (CAR) T cell therapies. In contrast, the drivers behind the 14 largest oncology merger and acquisition (M&A) transactions within the same time period are more diverse (**Table 2**). Aside from the immuno-oncology deals made by Bristol-Myers Squibb, Gilead and Astellas, there are three large deals focused on next-generation hormone-based cancer therapies (Pfizer–Medivation, Johnson & Johnson–Aragon and Genentech–Seragon) and four deals focused on small-molecule tyrosine kinase inhibitors (AbbVie–Pharmacyclics, Takeda–ARIAD, Amgen–Onyx and Roche–Ignyta). Additionally, approximately one-third of these large deals are strategic portfolio acquisitions aimed at near-term revenue generation, such as AbbVie's $20 billion purchase of Pharmacyclics to diversify from its Humira franchise, which faces pressure from biosimilars.

Multibillion-dollar M&A transactions are dominated by large pharmaceutical companies. However, smaller companies are just as active in terms of the volume of M&A activity. Juno Therapeutics was the most active acquirer from 2013 to 2017, acquiring four companies (ZetaRx, X-Body, AbVitro and Redox) for less than $400 million in total. This supported its development into a fully integrated cancer immunotherapy company, making it an attractive acquisition target itself.

In terms of the distribution of licensing deals by phase of development of the lead asset at the time of deal-signing, 58% of deals were

Table 1 | Oncology licensing, joint venture and research-only deals valued at more than $1 billion from 2013 to 2017

Licensee	Licensor	Year	Technology/mechanism of action	Phase of lead asset	I-O	Total ($ millions)	Upfront ($ millions)
Merck & Co.	AstraZeneca	2017	PD1/PDL1 small-molecule combinations	Launched	✓	8,500	1,600
BMS	CytomX	2014	Immunotherapies using Probody Platform	Discovery	✓	5,028	50
Merck & Co.	Ablynx	2014	Multispecific nanobodies against checkpoint proteins	Discovery	✓	4,563	27
Incyte	Merus	2016	Bispecific antibody platform	Discovery	✓	3,700	120
Celgene	OncoMed	2013	Anti-stem cell products, incl. bispecific antibody	Phase 2	✓	3,332	155
Pfizer	Cellectis	2014	CAR T cell therapies	Discovery	✓	2,855	80
Pfizer	Merck KGaA	2014	PD1/PDL1 development, and co-promotion of Xalkori	Phase 2*	✓	2,850	850
Celgene	Jounce	2016	I-O therapies	Discovery	✓	2,824	225
Sanofi	Regeneron	2015	Antibodies against LAG3, GITR and PDL1	Phase 1	✓	2,665	640
Novartis	Xencor	2016	Bispecific antibodies	Discovery	✓	2,560	150
J&J	Aduro BioTech	2014	Cancer vaccines using LADD immunotherapy platform	Discovery	✓	1,999	12
Servier	Pieris Pharmaceuticals	2017	Bispecific therapeutics using anticalin platform technology	Discovery	✓	1,831	31
Eli Lilly	CureVac	2017	Cancer vaccines using RNActive technology	Discovery	✓	1,803	50
Shire (Baxalta)	Symphogen	2016	Checkpoint inhibitors	Discovery	✓	1,775	175
Shire (Baxalta)	Precision BioSciences	2016	Allogeneic CAR T cell therapies using ARCUS genome-editing technology	Discovery	✓	1,705	105
Celgene	Acetylon	2013	HDAC inhibitors (incl. option to acquire Acetylon)	Phase 2		1,700	600
Sanofi	BioNTech	2015	mRNA-based immunotherapies	Discovery	✓	1,560	Undisclosed
Bayer	Loxo Oncology	2017	Next-generation selective tyrosine kinase inhibitors	Phase 2		1,550	400
Amgen	CytomX	2017	T cell-engaging bispecific antibodies	Discovery	✓	1,465	40
Eli Lilly	Innovent Biologics	2015	Bispecific antibodies (incl. anti-cMet and anti-CD20)	Phase 2	✓	1,456	56
Celgene	BeiGene	2017	Anti-PD1 antibody, and marketing of Celgene's products in China	Phase 1*	✓	1,393	263

Table 1 (cont.) | Oncology licensing, joint venture and research-only deals valued at more than $1 billion from 2013 to 2017

Licensee	Licensor	Year	Technology/mechanism of action	Phase of lead asset	I-O	Total ($ millions)	Upfront ($ millions)
GSK	Adaptimmune	2014	T cell therapy targeting the NY-ESO antigen	Phase 2	✓	1,253	42
Arrys Therapeutics	AskAt	2017	Prostaglandin EP4 receptor antagonists	Phase 2	✓	1,200	Undisclosed
Celgene	Sutro Biopharma	2014	Antibody–drug conjugates	Discovery	✓	1,185	Undisclosed
Novartis	Cerulean Pharma	2016	Nanoparticle–drug conjugates using Dynamic Tumor Targeting technology	Discovery		1,173	5
Roche	Molecular Partners	2013	DARPin–drug conjugates	Discovery	✓	1,160	60
Roche (Genentech)	NewLink Genetics	2014	TDO/IDO inhibitors	Phase 1	✓	1,150	50
Servier	Cellectis	2014	T cell therapeutics, incl. UCART-19	Discovery	✓	1,120	10
Amgen	Kite Pharma	2014	CAR T cell therapies using autologous cell therapy (eACT) platform	Phase 2	✓	1,110	60
Gilead	MacroGenics	2013	Dual-Affinity Re-Targeting (DART) products	Discovery	✓	1,085	30
Merck KGaA	F-Star Alpha	2017	Bispecific antibodies, incl. anti-PDL1 antibody	Discovery	✓	1,067	66
Amgen	Immatics Biotechnologies	2017	T cell-engaging bispecific immunotherapies	Discovery	✓	1,030	30
Roche	Blueprint Medicines	2016	Small molecules against immunokinases	Discovery	✓	1,010	45
Servier	Sorrento	2016	Anti-PD1 antibody	Discovery	✓	1,000	28
Pfizer	BioAlta	2015	Conditionally Active Biologic (CAB) antibody–drug conjugates	Discovery	✓	1,000	Undisclosed

See **Box 1** for details of the data. BMS, Bristol-Myers Squibb; CAR, chimeric antigen receptor; GITR, glucocorticoid-induced TNF-related protein; GSK, GlaxoSmithKline; HDAC, histone deacetylase; IDO, indoleamine 2,3-dioxygenase; I-O, immuno-oncology; J&J, Johnson & Johnson; LAG3, lymphocyte activation gene 3 protein; PD1, programmed cell death protein 1; PDL1, PD1 ligand 1; TDO, tryptophan 2,3-dioxygenase. *Phase applies to the development asset at the time of deal signing.

signed at the discovery stage. Nonetheless, they still had a significant total value (**Fig. 3**), with a median total value for discovery deals of $200 million over the five-year period analyzed (of which the median upfront payment was $17 million).

The ranking of the top oncology dealmakers by deal volume reveals not only that large pharmaceutical companies dominate the licensee list, but also that a handful of these major players figure prominently in the sell-side category (**Fig. 4**). The most notable example is AstraZeneca, ranked just below the major oncology research institutions, indicative of the company's publicly stated strategy to sell or share rights to its molecules to generate income to invest back into R&D and meet the company's return-to-growth target. Merck & Co., Johnson & Johnson, Bristol-Myers Squibb, Eli Lilly and Amgen have also executed a number of out-licensing deals around

Table 2 | Oncology M&A deals valued at more than $1 billion between 2013 and 2017

Sell side	Buy side	Date	Stage						Financials ($ millions)	Asset/ technology
			D	P1	P2	P3	PR/R	L		
Pharmacyclics	AbbVie	03/2015						✓	$20,800	Small molecule
Medivation	Pfizer	08/2016						✓	$14,300	Small molecule
Kite Pharma	Gilead	08/2017					✓		$11,900	Cell therapy
Stemcentrx	AbbVie	04/2016							$10,426	Conjugated Ab
Onyx	Amgen	06/2013						✓	$9,700	Small molecule
ARIAD	Takeda	01/2017						✓	$5,200	Small molecule
Engmab	Celgene	09/2016	✓						$3,100	Multivalent Ab
IFM Therapeutics	BMS	08/2017	✓						$2,320	Small molecule
Seragon Pharmaceuticals	Roche (Genentech)	07/2014		✓					$1,725	Small molecule
Ignyta	Roche	12/2017			✓				$1,700	Small molecule
Celator Pharmaceuticals	Jazz Pharmaceuticals	05/2016			✓				$1,500	Small molecule
Ganymed Pharmaceuticals	Astellas	10/2016			✓				$1,398	Chimeric Ab
Aragon	J&J	06/2013			✓				$1,350	Small molecule
Flexus Biosciences	BMS	02/2015			✓				$1,250	Small molecule

A total of 57 of the M&A deals in the time period disclosed financials. Only deals for therapeutics were considered. See **Box 1** for details. Ticks indicate the latest stage of the assets involved. Ab, antibody; BMS, Bristol-Myers Squibb; D, discovery; J&J, Johnson & Johnson; L, launched; P, phase; PR, pre-registration; R, registration.

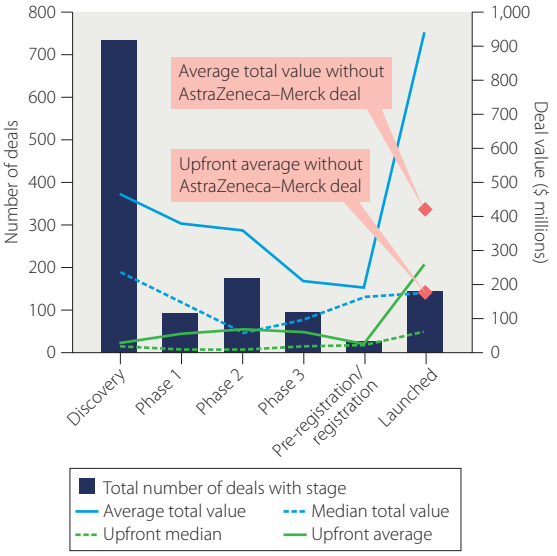

Fig. 3 | Licensing, joint venture and research-only oncology deals by phase at signing from 2013 to 2017. The $8.5 billion deal between AstraZeneca and Merck & Co. has had a substantial impact on the value of the deals for launched products, and thus an average of the deals excluding this deal is also shown. See **Box 1** for details of the data.

Box 1 | Data and methodology for oncology deals analysis

All oncology business transactions with a deal start date between 1 January 2013 and 31 December 2017 were extracted from the Cortellis database from Clarivate Analytics. The deal "transaction type" of acquisitions (100% or majority stake), mergers, reverse mergers, joint ventures, research-only and the "license" subtypes of "basic license," "codevelopment," "comarketing," "copromotion" and "collaboration" were selected for analysis.

The resulting datasets were filtered to exclude non-therapeutic-focused deals using the "technologies" categorization. Deals in which the primary focus was any of the following were excluded: assays, bioinformatics, biomarkers, diagnostic methods, drug formulation, drug screening, generics, genomics technologies, imaging, instruments, lab reagents, manufacturing, medical and other devices, radiolabeling, service agreements and software. All "pending" deals and "terminated" acquisition deals were also excluded. The final datasets were as follows: mergers and acquisitions (94 deals), and licensing and joint ventures (1,385 deals).

early-stage assets that these companies have presumably currently deprioritized for internal investment. Such deals may include return options that will allow companies to regain rights to the asset at a later phase.

With respect to the geographical location of the deals, US-based companies are involved in more than half (56%). A substantial proportion of the overall activity is within particular regions, again dominated by the US, with approximately 40% of dealmaking activities occurring between US-based organizations. Internal dealmaking activities within Europe are a distant second, constituting 13% of the total activity, followed by transatlantic partnerships in either direction (10% for those with US-based licensees and ~9% for those with Europe-based licensees). Activity between the west and east constituted only a small fraction of the deals.

In conclusion, oncology remained the most competitive area for dealmaking in 2017, with immuno-oncology therapeutics continuing to be the principal driver. The licensing landscape is dominated by early-stage discovery deals, which usually have very large upside valuations. It is difficult to predict the future, owing to global financial uncertainty and the possibility that the flurry of dealmaking that followed the first checkpoint-inhibitor approvals has plateaued. However, we anticipate another strong year for dealmaking in 2018, on the back of the US tax reforms and as clinical evidence emerges to support next-generation technologies such as CAR T cell therapies, antibody–drug conjugates and bispecific antibodies. Indeed, one of the largest deals of 2018 so far is Celgene's $9 billion acquisition of the CAR T cell company Juno Therapeutics. Additional factors that could help sustain a high level of activity include the apparent willingness of some large pharmaceutical companies to out-license pipeline assets in order to generate additional revenue and fully explore their potential, and the opportunity for more cross-regional partnering.

Jamie Munro and Helen Dowden work in Life Science Professional Services at Clarivate Analytics.

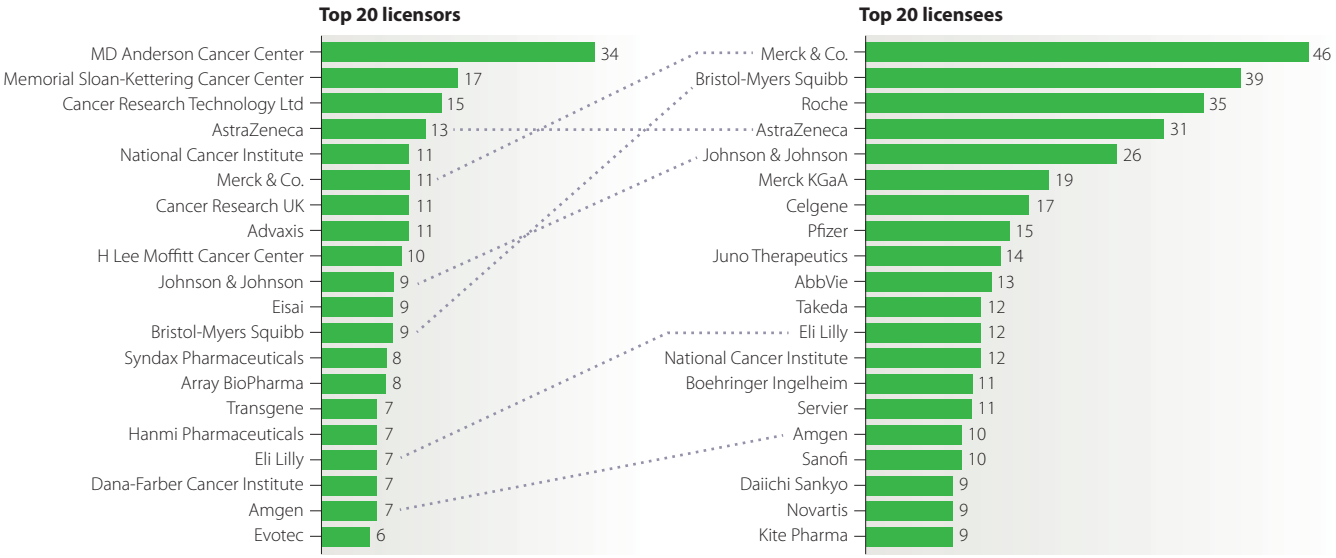

Fig. 4 | The top 20 oncology licensors and licensees from 2013 to 2017. See **Box 1** for details of the data.