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Oncology dealmaking in 2019

While dealmaking in oncology continued to feature immunotherapies—particularly multi-targeted agents—there was also diversification, with prominent deals for precision medicine and novel platform technologies.

Sarah Hardison

2019 was another big year for oncology dealmaking (*BioPharma Dealmakers* B2–B3, December 2019) with a total disclosed deal value of $171 billion. Drug licensing activity accounted for $47 billion, while merger and acquisition (M&A) activity contributed $119 billion, including the mega-deal by Bristol-Myers Squibb (BMS) to acquire Celgene for $74 billion.

Immuno-oncology (IO) was prominent once again in oncology licensing deals, with IO deals representing 65% of the total projected deal value and 44% of transactions. Interestingly though, while all of the top drug licensing deals in 2018 were in IO (*BioPharma Dealmakers* B3–B6, March 2019), four $1 billion-plus deals announced in 2019 were not related to immunotherapies, and instead focused on other areas, including protein degradation and RNA modulation (Table 1).

The top deal in Table 1, in which AstraZeneca made an upfront payment of $1.35 billion and committed up to $6.9 billion to partner with Daiichi Sankyo on the HER2-targeted antibody–drug conjugate (ADC) trastuzumab deruxtecan, has already been fruitful. In December, the US Food and Drug Administration (FDA) approved the ADC for breast cancer, and it is expected to quickly reach blockbuster status. Interestingly, the next three deals in the list—all potentially worth $4 billion or more—involve bispecific drugs, including Merck KGaA's bifunctional fusion protein bintrafusp alfa, Amgen's approved bispecific T cell engager blinatumomab and Abpro's bispecific platform (Table 1). After many years of interest in the wide variety of bispecific and multi-specific platforms (*Nat. Rev. Drug Discov.* **18**, 585–608; 2019), this indicates that their therapeutic potential is increasingly being validated in the clinic.

Table 1 | Billion-dollar oncology drug licensing deals in 2019

Licensee	Licensor	Total projected value ($ millions)	Upfront payment ($ millions)	Mechanism	Drugs	Status (deal start)	I/O
AstraZeneca	Daiichi Sankyo	6,900	1,350	HER2 antibody–drug conjugate	Trastuzumab deruxtecan	Phase 3	✓
GSK	Merck KGaA	4,221	342	PD-L1–TGFβR fusion protein	Bintrafusp alfa	Phase 2	✓
BeiGene	Amgen	4,030	Unspecified	Anti-RANK-L antibody, anti-CD19 antibody, proteasome inhibitor	Denosumab; blinatumomab; carfilzomib	Launched	✓
Nanjing CTT	Abpro	4,000	Unspecified	Bispecific T cell engagers	Drug discovery platform	Discovery	✓
Gilead	Nurix	2,345	45	Protein degradation (E3 ligase)	Drug discovery platform	Discovery	
Genentech	Skyhawk	2,000	Unspecified	RNA alternative splicing modulators	Drug discovery platform	Discovery	
Celgene	Immatics	1,590	75	TCR cell therapy	IMA-204	Discovery	✓
Amgen	Hummingbird	1,200	Unspecified	Antibody drug discovery	Drug discovery platform	Discovery	✓
Jazz	Codiak	1,076	56	Exosome therapeutics	Drug discovery platform	Discovery	
Takeda	Turnstone	1,020	Unspecified	Oncolytic virus expressing immunomodulators	RIVAL-01	Preclinical	✓
Cytovant HK	MediGene	1,010	10	TCR cell therapy, antigen-loaded DC	CVT-TCR-01	Phase 2	✓
Jazz	PharmaMar	1,000	200	RNA polymerase II inhibitor	Lurbinectedin	Pre-registration	

Drug licensing deals in 2019 with total projected deal value greater than or equal to $1 billion. 'Status' indicates the highest development stage of any asset included in the deal, at deal start date. 'I/O' indicates whether any asset in the deal involves immunotherapy. DC, dendritic cell; RANK, receptor activator of NF-κB; TCR, T cell receptor. Data from Cortellis Deals Intelligence from Clarivate Analytics.

Multi-targeted boom

Multi-target proteins achieved the second highest licensing deal values in 2019, accounting for 22% of the total accumulated disclosed deal value (Fig. 1). This is despite the fact that multi-target proteins account for only 10% of the transactions. In addition to the deals related to multi-target drugs noted above, Genentech paid $120 million upfront and up to $160 million in potential milestones to license Xencor's XmAb-24306 fusion protein, which comprises an IL-15/IL-15Ra heterodimer fused to an Fc domain. And AbbVie expanded an existing collaboration with Harpoon Therapeutics on trispecific T cell engagers (TriTACs), with a deal that included an upfront payment of $50 million and up to $50 million in milestone payments related to HPN-217, a BCMA-targeted TriTAC in preclinical development for multiple myeloma.

While bispecific and trispecific T cell engagers generally seek to bring a cancer cell into close proximity to a cytotoxic killer T cell, multi-target fusion proteins are interesting in that they often act like drug combinations within a single molecule. For example, Merck KGaA's bintrafusp alfa—which attracted GlaxoSmithKline to sign a deal including an upfront payment of $340 million and potential milestones of almost $4 billion—acts as a trap for the immunomodulatory cytokine TGFβ while also targeting the PD-1/PD-L1 immune checkpoint. The fusion protein is being compared with Merck & Co.'s leading PD-1 checkpoint inhibitor pembrolizumab as first-line therapy in non-small-cell lung cancer in a phase 2 trial, and is one to watch.

Platforms and precision medicines

In terms of development stage, the largest proportion of drug licensing deals in recent years has been at the discovery stage, and this continued in 2019 (Fig. 2). The highest average deal values and upfront payments were at later stages, with assets in phase 3 achieving the highest average upfront payments ($130 million) and deals involving launched drugs achieving the highest average total potential value ($937 million) (Fig. 2). However, of the top $1 billion-plus licensing transactions in 2019, five were for drug discovery platforms (Table 1), indicating the high value in developing novel technologies from an early stage. Indeed, discovery-stage transactions account for 39% of transactions by development stage (Fig. 2), and 56% of the discovery-stage deals are for drug discovery platforms (data not shown).

The majority of these drug discovery platforms are for small molecules and traditional antibodies, but multi-target protein platforms have a high total potential value. These include bispecific and multispecific antibody engineering platforms, such as the bispecific drug discovery platform Abpro licensed to Nanjing CTT with a total potential deal value of $4 billion (Table 1). Both Sanofi and Eisai licensed multi-target platforms from Biomunex and Numab, respectively (values undisclosed), which use modular, plug-and-play technology that allows engineering of antibody-like binders with multiple target specificities without having to develop individual antibodies first.

While the AstraZeneca phase 3 deal with Daiichi Sankyo for an ADC was the highest-value drug licensing transaction in 2019 (Table 1), 53% of the phase 3 licensing transactions were for small molecules (compared with 7% for multi-target proteins), the majority of which are targeted therapies against kinases. For example, Boehringer Ingelheim licensed Lupin's MEK inhibitor to combine with its KRAS inhibitor in a deal worth $20 million upfront and up to $720 million in total.

Precision medicine was also prominent among M&A deals, with three of the nine $1 billion-plus M&As in 2019 focused on targeted therapies underpinned by patient genetics (Table 2). Early on in the year, Eli Lilly announced its $8 billion acquisition of Loxo Oncology, which had recently gained FDA approval for larotrectinib (Vitrakvi). This drug was approved in November 2018 for metastatic tumors with an *NTRK* gene fusion regardless of tumor type, thereby becoming the first drug to be initially approved for a tumor-agnostic indication. Loxo had originally licensed

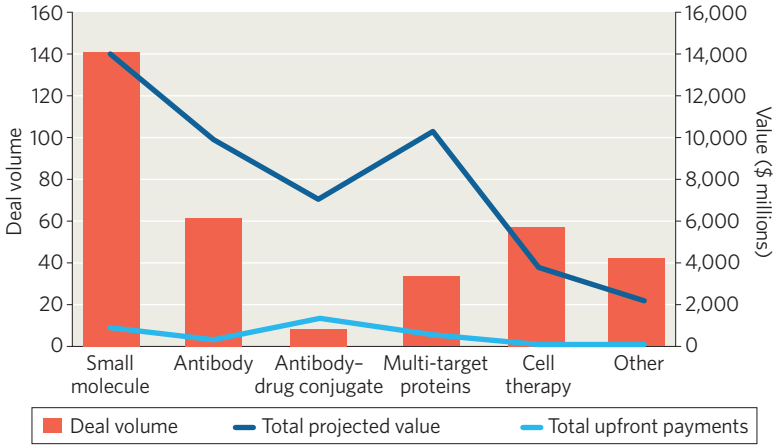

Fig. 1 | Drug technologies licensed in 2019 by value. Drugs were categorized using the 'Technologies' field of oncology deals extracted from Cortellis. Multi-target proteins capture the second highest accumulated deal value, where disclosed. Small-molecule deals as a class achieve the highest total deal value and account for 41% of drug licensing transactions by volume. Data from Cortellis Deals Intelligence from Clarivate Analytics.

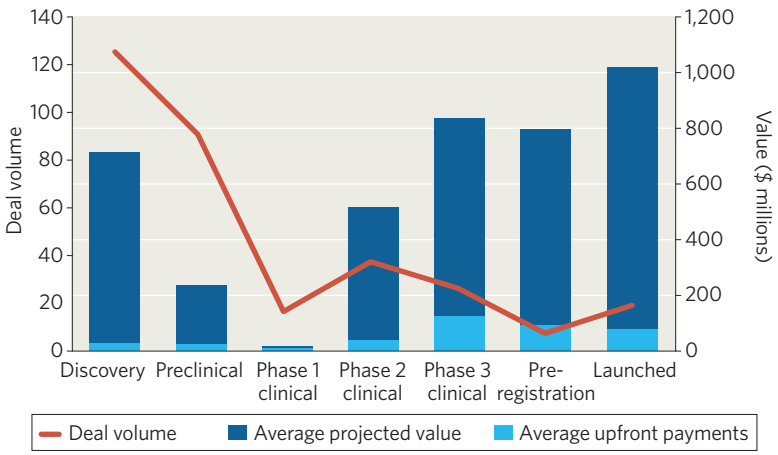

Fig. 2 | Oncology drug licensing in 2019 by development phase. Development phase refers to the highest status of any asset included in the deal at deal start. The greatest volume of transactions occur at discovery stage, and the majority of these are for drug discovery platforms. Highest average upfront payments are achieved by phase 3 assets, where disclosed. Data from Cortellis Deals Intelligence from Clarivate Analytics.

Box 1 | Data and analysis

The analysis is based on data extracted from Cortellis Deals Intelligence and Cortellis Competitive Intelligence from Clarivate Analytics (data extraction performed 6 January 2020). Deals with a start date between 1 January 2019 and 31 December 2019 with Therapy Area indexed as 'Cancer' or 'Diversified' with at least one cancer indication were included.

- The licensing category includes deals with agreement type 'drug' and deal transaction type 'license' of any kind. Financial values are representative of disclosed deal values. Out of 343 drug license transactions, 94 reported financials.
- The M&A category includes deals with agreement type 'company' and deal transaction type 'M&A' of any kind where financials are disclosed.

Table 2 | Billion-dollar oncology M&A deals in 2019

Buy side	Sell side	Total projected (US$millions)	Oncology technology	I/O
BMS	Celgene	$74,000	Cell therapy; small molecule (various)	✓
Pfizer	Array BioPharma	$11,400	Precision medicine (MAPK/BRAF)	
Eli Lilly	Loxo Oncology	$8,000	Precision medicine (NTRK)	
Ethicon	Auris Health	$5,750	Diagnostics (robotics)	
Sumitomo Dainippon	Roivant	$3,000	Small molecule (GnRH inhibitor)	
Exact Sciences	Genomic Health	$2,800	Diagnostics (genomics)	
Merck & Co.	ArQule	$2,700	Precision medicine (BTK/AKT/FGFR)	
Sanofi	Synthorx	$2,500	Synthetic biology (cytokines)	✓
Merck & Co.	Peloton Therapeutics	$2,200	Small molecule (HIF2a)	

M&A deals in 2019 with total projected deal value greater than or equal to $1 billion. 'I/O' indicates whether any asset in the deal involves immunotherapy. Data from Cortellis Deals Intelligence from Clarivate Analytics.

larotrectinib from Array BioPharma, which Pfizer acquired in 2019 for $11.4 billion—picking up the BRAF inhibitor encorafenib (Braftovi) and the MEK inhibitor binimetinib (Mektovi), which are approved in combination for patients with metastatic melanoma harboring BRAF mutations, as well as a pipeline of precision medicine candidates. Finally, also in the $1 billion-plus M&A deals of 2019 was Merck & Co.'s acquisition of ArQule, which has a pipeline that includes mutation-specific BTK, AKT and FGFR inhibitors.

In summary, 2019 was another big year for oncology dealmaking. There were also signs of a diversification beyond IO in both licensing activity, as noted earlier, and also M&As; seven of 2018's top M&As were for IO companies, but in 2019 only two were (Table 2). Are success rates and the numbers of patients available for trials affecting the value of IO medicines? Are the next-generation IO technologies so new they are not yet garnering high price tags? Such questions will be interesting to consider as dealmaking continues in 2020.

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