Platform partnering sustains oncology dealmaking

While external factors have put a dampener on acquisitions of oncology companies in the past year, the search for next-generation therapeutics from innovative platforms has driven dealmaking.

Credit: Science Photo Library / Alamy Stock Photo

Mike Ward

When biotech funding flows began dropping off from the historic highs of 2020 and 2021, there had been an expectation that this would trigger a wave of biopharma mergers and acquisition (M&As) and partnering deals. And yet, while the main drivers for such activity—pharma companies needing to replenish their pipelines to make up for lost revenues from products going off-patent or getting access to cutting-edge technology platforms—are still in place, partnering and M&As have still not recovered to pre-pandemic volumes.

There are two main reasons for lacklustre M&A performance. First, the slump in biotech valuations means that shareholders are reluctant to sell at prices that are well down on historic highs. Second, pharma companies are waiting to gauge the effects of political headwinds such as the US Inflation Reduction Act of 2022 and the increased scrutiny of the impact that deals might have on competition.

Indeed, Pfizer's proposed $43 billion acquisition of the oncology-focused biotech Seagen, announced in March this year, is likely to be held up as both the US Federal Trade Commission (FTC) and the European Commission scrutinize the transaction. The deal, which would be the sector's largest since AbbVie acquired Allergan for $63 billion in 2019, would give Pfizer access to Seagen's antibody–drug conjugate (ADC) platform, bolstering the pharma's oncology franchise. If the deal passes anti-trust scrutiny, it is likely that it would be the year's largest transaction.

Other major M&A transactions with an oncology focus and completed since August 2022 include Bristol Myers Squibb's (BMS's) $4.1 billion acquisition of Turning Point Therapeutics and the $1.7 billion buyout of CTI Biopharma by Swedish Orphan Biovitrum (Sobi).

By acquiring Turning Point Therapeutics, BMS strengthened its precision oncology franchise, gaining a pipeline of investigational medicines designed to target mutations associated with oncogenesis in particular subgroups of patients. Turning Point's leading candidate is repotrectinib, a next-generation, potential best-in-class tyrosine kinase inhibitor targeting ROS1 and NTRK, which are oncogenic drivers in some patients with non-small cell lung cancer (NSCLC) and other advanced solid tumors. Repotrectinib could receive US Food and Drug Administration (FDA) approval later this year, as the Prescription Drug User Fee Act (PDUFA) goal date is 27 November.

Through its acquisition of CTI Biopharma, which is focused on blood-related cancers and rare diseases, Sobi expanded its position in rare hematological diseases—in particular, adding Vonjo (pacritinib) to its portfolio. This oral kinase inhibitor inhibits JAK2, IRAK1, and ACRV1, while sparing JAK1, providing a product differentiated from other JAK inhibitors for the treatment of myelofibrosis, specifically addressing patients with severe thrombocytopenia.

Oncology partnering leads the way

Biopharma partnering activity has been steadier than M&A activity, and although the volume of deals is below historical highs, valuations have remained robust. Oncology remains the most active therapeutic area for dealmaking, accounting for 33% of deals and 50% of deal value in the August 2022 to July 2023 period. Access to technology platforms that are expected to underpin the next generation of medicines were a popular focus for pharma licensing deals, although there was also an appetite for preclinical and clinical assets.

High-value deals focused on next-generation assets included Summit Therapeutics in-licensing ivonescimab from Akeso in a deal potentially worth up to $5 billion (Table 1). Ivonescimab is a potential first-in-class bispecific antibody combining the effects of immunotherapy via blockade of PD1 with the anti-angiogenesis effects associated with blocking VEGF and is in phase 3 trials for NSCLC. In addition, Kite Pharma, a Gilead company, signed a global strategic collaboration to co-develop and co-commercialize Arcellx's lead late-stage product candidate, CART-ddBCMA, for the treatment of patients with relapsed or refractory multiple myeloma. Currently in phase 2 clinical development, CART-ddBCMA is a cell therapy comprising autologous T cells that have been genetically modified to target BCMA, which is overexpressed on multiple myeloma cells.

In a bid to augment its oncology pipeline, Merck & Co. (known as MSD outside the US), was the most active dealmaker among the pharma giants, with four transactions in the top 10 highest-value oncology-focused partnering deals (Table 1), including the largest deal signed since the start of 2022. In this exclusive license and collaboration agreement, MSD paid $175 million upfront to China-based Kelun-Biotech to develop seven preclinical ADCs for the treatment of cancer, along with exclusive options to obtain additional licenses to ADC candidates. Kelun-Biotech is also eligible to receive future development, regulatory, and sales milestone payments totalling up to $9.3 billion. Like many deals involving Chinese companies, Kelun-Biotech retains the right to research, develop, manufacture, and commercialize certain ADCs for Mainland China, Hong Kong, and Macau.

The deal was an expansion of an existing relationship; earlier in 2022, MSD agreed to pay $47 million upfront to license rights to Kelun-Biotech's clinical-stage ADC SKB-264 outside Mainland China, Hong Kong, Macao, and Taiwan, although $17 million

Table 1 | Top 10 highest-value oncology-focused partnering deals (August 2022 to July 2023)

Principal company	Partner company	Date	Total projected deal amount ($ million)	Upfront payment ($ million)	Deal terms
Kelun-Biotech (a holding subsidiary of Sichuan Kelun Pharmaceutical)	Merck (known as MSD outside of the US and Canada)	December 2022	9,475	175	MSD to develop and commercialize Kelun-Biotech's antibody–drug conjugates with an option for cancer, worldwide excluding for mainland China, Hong Kong, and Macau.
Poseida Therapeutics	Roche Holding	August 2022	6,220	110	Poseida and Roche to develop allogeneic CAR-T therapies for hematologic malignancies worldwide.
Akeso Biopharma	Summit Therapeutics	December 2022	5,000	500	Summit to develop and commercialize Akeso's bispecific antibody ivonescimab against solid tumors in the US, Canada, Europe, and Japan.
Arcellx	Kite Pharma	December 2022	4,225	225	Kite and Arcellx to co-develop and co-commercialize late-stage clinical CART-ddBCMA in multiple myeloma.
Orna	MSD	August 2022	3,650	150	MSD and Orna to discover, develop and commercialize vaccines and therapeutics for infectious disease and oncology.
Immunome	AbbVie	January 2023	2,800	30	AbbVie and Immunome to discover oncology antibody targets worldwide.
Proxygen	MSD	April 2023	2,550	ND	MSD and Proxygen to jointly identify and develop molecular glue degraders against multiple therapeutic targets.
Synaffix	Macrogenics	March 2023	2,200	ND	Macrogenics expands its license agreement with Synaffix, adding up to four antibody–drug conjugate programs to the original three programs agreed in a deal in February 2022.
PeptiDream	MSD	December 2022	2,100	ND	Peptidream and MSD to develop peptide–drug conjugates using a peptide discovery platform system.
Belharra	Genentech	January 2023	2,080	80	Genentech to use Belharra's platform to discover and develop small molecule medicines in multiple therapeutic areas.

Source: BioWorld; Cortellis Deals Intelligence; Clarivate 2023. ND, non-disclosed.

had already been paid as part of an existing collaboration, with another $1.36 billion in potential milestone payments plus royalties on sales.

MacroGenics was another company that expanded an earlier license agreement on ADCs, increasing the total potential consideration of a 2022 deal with Synaffix by up to $2.2 billion, plus royalties on potential net sales of any resulting products. MacroGenics now has the option to pursue up to seven ADC programs under the expanded deal, which includes three programs from the original collaboration.

Beyond ADCs, MSD's platform-related deals included one to expand its RNA technology capabilities, by agreeing to pay Orna Therapeutics $150 million upfront and up to $3.5 billion in milestones linked to multiple vaccine and therapeutic programs in infectious diseases and oncology, as well as royalties on any resulting approved products. MSD also invested $100 million of equity in Orna's recently completed series B financing round. The focus of the deal is Orna's oRNA technology, which creates highly stable circular RNAs (oRNAs) from linear RNAs by self-circularization, potentially enabling the production of larger amounts of therapeutic proteins than from established mRNA platforms.

To get access to molecular glue degraders, MSD inked a research collaboration and license agreement with Proxygen, focusing on multiple therapeutic targets. Proxygen received an undisclosed upfront payment from MSD and will be eligible for future payments of up to $2.55 billion based on the achievement of milestones across all programs, as well as sales royalties. And in their fourth deal, MSD entered a collaboration with PeptiDream focused on peptide–drug conjugates for the treatment of cancer and other diseases, involving an undisclosed upfront payment and potential milestone payments of up to $2.1 billion.

Roche was also active in platform-related dealmaking to support its oncology franchise. In its most expensive deal, with a potential value of $6.22 billion, Roche secured from Poseida Therapeutics either exclusive rights or options to develop and commercialize several allogeneic CAR-T candidates in Poseida's portfolio that are directed to hematologic malignancies. These candidates include P-BCMA-ALLO1, an allogeneic CAR-T therapy for the treatment of multiple myeloma and for which a phase 1 study is underway, and P-CD19CD20-ALLO1, an allogeneic dual CAR-T therapy for the treatment of B cell malignancies, for which an investigational new drug (IND) application is expected to be filed in 2023. The partners will also collaborate in a research program to create and develop next-generation features and improvements for allogeneic CAR-T therapies, from which they would jointly develop additional allogeneic CAR-T product candidates.

Roche's Genentech linked up with Belharra Therapeutics, a privately held company with a novel photoaffinity-based, non-covalent chemoproteomics platform, in a collaboration to discover and develop small-molecule drugs in multiple therapeutic areas including oncology, immuno-oncology, autoimmune, and neurodegenerative diseases. Belharra's platform enables identification of any binding site, on any protein, in any conformational state, in any cell type. Belharra received an upfront payment of $80 million

and is eligible to receive milestones that could exceed $2 billion, as well as royalties on resultant products. Belharra has an option to co-develop the programs' compounds through phase 1 and to co-fund their remaining development.

AbbVie and Immunome also announced a discovery-stage collaboration, with AbbVie agreeing to pay $30 million upfront and up to $2.8 billion in milestones for the discovery and development of antibodies for up to 10 novel antibody–target pairs identified from three specified tumor types using Immunome's human memory B cell platform.

Deals on the winding road to bestsellers

A quick glance at the histories of some of the top-selling cancer drugs for big pharma companies demonstrates the key role dealmaking has had in the sector.

BMS's two highest-selling cancer drugs were both discovered outside the company. Revlimid (lenalidomide), for which revenues have declined from $12.82 billion in 2021 to $9.98 billion in 2022 following increased competition from generics, was developed by Celgene, which was acquired by BMS in 2019 for $74 billion. Meanwhile, BMS's anti-PD1 therapy Opdivo (nivolumab), which posted sales of $8.25 billion in 2022, was created by Japan's Ono Pharmaceutical and Medarex, a US antibody technology company. Medarex was purchased by BMS in 2009 for $2.4 billion to gain its immuno-oncology pipeline, which also included the first immune checkpoint inhibitor to be approved, Yervoy (ipilimumab). Opdivo's key patent expiry date is 2028.

Keytruda (pembrolizumab), MSD's bestselling competitor to Opdivo, was also discovered outside the company, although its potential was not realized at the time the deals involved were made. The anti-PD1 therapy was created by scientists at the Dutch company Organon in collaboration with the UK Medical Research Council in 2006. Organon was acquired by Schering-Plough in 2007, which in turn was acquired by MSD in 2009. Pembrolizumab was then reportedly on a list for out-licensing, but promising results in 2010 for Yervoy ignited interest in the field. MSD invested heavily in a huge clinical trial program for pembrolizumab across multiple cancers, and following its first approval in 2014, Keytruda's revenues reached a mammoth $20.94 billion in 2022. Its key patent expiry date is also 2028.

Treading the dealmaking tightrope

It is not surprising that with patent cliffs looming and biotech financing scarcer than in recent years, the stakes for pharma companies and biotechs alike are very high, and it is important that business development executives do not misstep. Indeed, panellists participating in a discussion (https://www.bio.org/events/bio-international-convention/sessions/2393212) entitled 'How to strike a deal in oncology: Innovative partnering approaches across biotech and pharma,' that I moderated at the BIO International Convention 2023, noted that while pharma is inundated with partnering pitches, it is essential that biotechs are offering innovative opportunities and that both parties have a mutual understanding of how a partnership might create value for both sides.

"ASCO was all about ADCs and there's a lot of deals in ADCs right now. How many KRAS treatments are in the clinic? It's the PD1 story all over again. There are niches you can find, but the commercial ramifications of not being first-in-class are prohibitive. It has to be a transformational change to dislodge a first-in-class treatment," noted Sasha Huhalov, Search and Evaluation Lead for Takeda.

Having a sense of a dealmaking partner's red lines is essential, according to Thaminda Ramanayake, Chief Business Officer at Affini-T Therapeutics. "If you want to keep deal momentum, you have to identify the deal-breakers quickly," he said, citing any potential stock-moving events, such as biotech bankruptcies, as a potential deal-breaker for pharmas.

And yet the structure of the deal can also be a deal-breaker. "Maybe they want you to move things forward, but they don't want you to be their partner forever, or you go in and say, 'This is my lead program—I can't give up rights,' but the pharma doesn't have the resources to do commercial co-development. Product potential can be a deal-breaker if you don't have the same view," added Rachel Zolot Schwartz, Chief Business Officer at Volastra Therapeutics.

Success starts with identifying the strategic priorities for each company, understanding what each is trying to advance, and using that as a vehicle. Each deal has a different thought process and a useful place to start in the biopartnering process is to determine what kind of value each side is trying to create for their companies.

Mike Ward is Global Head of Life Sciences & Healthcare Thought Leadership at Clarivate.