

# Oncology dealmaking in 2021

Oncology-focused partnerships drove record-level licensing deals in 2021 as companies looked to gain access to novel therapeutic targets and platforms.

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In 2021, global biopharma licensing, collaborations and joint venture transactions hit record heights, although merger and acquisition (M&A) activity was lower than the previous two years. Similar to previous years, oncology-focused deals accounted for a large proportion of both activities.

The total headline value of the biopharma licensing, collaborations and joint ventures for which financial details were disclosed was \$213.5 billion, up from \$198 billion in 2020, with cancer-focused deals accounting for 29% of the 1,968 deals signed in 2021. Financial terms were only disclosed for 130 of the 574 cancer deals announced, with a headline figure of \$73.1 billion. Biopharma M&A activity was worth \$118.4 billion in 2021, down 32% compared with 2020, and cancer-focused M&As in 2021 were valued at \$19.7 billion.

## Licensing trends

Immuno-oncology (IO), which has featured strongly in previous years in oncology dealmaking, was only a component of 27% of transactions and accounted for 35% of headline deal values, although nine of the top 24 deals potentially worth \$1 billion or more had an IO component. In 2020, IO was a focus of 49% of biopharma oncology drug licensing deals, representing 66% of the total disclosed deal values. Interestingly, there was an increase in the number of deals that included multi-targeted approaches such as bispecific antibodies or antibody–drug conjugates (ADCs).

In terms of development stage, there was a sharp increase in the number of deals associated with late-stage clinical assets compared with previous years. Twenty-six deals involved phase 2 assets, which accounted for 20% of the total disclosed deal value. With biotech companies finding it easier to tap the capital markets to finance their company-building efforts, there was a clear uptick in the number of transactions in which the partners were willing to share development responsibilities in return for increased commercial upside.

Novartis was among the busiest pharma dealmakers in 2021. Bidding to bolster its IO ambitions, the Swiss pharma company signed two significant deals with Chinese biotech BeiGene. In the first agreement, signed in January 2021, Novartis gained rights to develop and commercialize tislelizumab in the US, Canada, Mexico, the European Union, the UK, Norway, Switzerland, Iceland, Liechtenstein, Russia and Japan, with BeiGene retaining the rights for China and other countries (Table 1). Tislelizumab, a monoclonal antibody with a higher affinity for PD-1 than the market-leading drugs Keytruda (pembrolizumab) and Opdivo (nivolumab), is being developed as a treatment for non-small-cell lung cancer (NSCLC), hepatocellular carcinoma (HCC),

esophageal squamous cell carcinoma (ESCC), gastric cancer and nasopharyngeal carcinoma outside of mainland China.

In a follow-up deal, signed in December 2021, Novartis paid BeiGene \$300 million upfront as part of an option, collaboration and license agreement for the late-stage TIGIT (T cell immunoreceptor with Ig and ITIM domains) inhibitor ociperlimab, with the promise of up to \$700 million if the option is exercised before late 2023. While Novartis gets development and marketing rights to ociperlimab in the US, Canada, Mexico, the European Union, UK, Norway, Iceland, Liechtenstein, Switzerland, Russia and Japan, BeiGene, which will provide 50% of the co-marketing efforts in the US following approval, will retain the rights to this cancer immunotherapy in China and all other countries. Ociperlimab is in phase 3 development for advanced NSCLC in combination with tislelizumab. As part of the deal, BeiGene was granted rights to market, promote and detail five approved Novartis oncology products across designated regions of China.

For BeiGene, the tie-ups with Novartis will help it build a commercial team across North America. With China's national drug reimbursement program restricting drug pricing, Chinese biotechs are currently looking—and will increasingly look—to broker deals with multinationals to access more lucrative international markets for homegrown medicines such as tislelizumab and ociperlimab.

In the past two years, TIGIT has emerged as a popular target for pharma companies to add to their IO arsenals. Indeed, GSK and iTeos Therapeutics agreed to share the costs for global development of the US biotech's anti-TIGIT monoclonal antibody EOS-448, which is currently in phase 1 for advanced solid tumors, with a randomized PD-1 combination study planned for 2022. The deals see the two companies co-commercializing in the US and evenly splitting the US profits, with GSK getting an exclusive commercialization license outside the US. GSK paid iTeos \$625 million upfront and committed to a potential \$1.45 billion in milestone payments. iTeos will also be entitled to tiered royalty payments.

Bristol Myers Squibb, an earlier leader in IO with Opdivo, was also very active in biopartnering during the year, with three deals in the billion-dollar-plus range. The US pharma giant signed a potential \$3.1 billion agreement with Japanese pharma Eisai to co-develop and co-commercialize the ADC MORAb-202 for advanced solid tumors. It also agreed a deal with Molecular Templates to use its engineered toxin body (ETB) platform to research multiple targets, with an option to obtain an exclusive worldwide license to develop and commercialize the ETBs for each target. Bristol Myers Squibb also secured a preclinical anti-TIGIT

Credit: Brain light / Alamy Stock Photo

bispecific antibody, agreeing to pay Agenus \$200 million upfront plus \$1.36 billion in potential milestones for development and commercial rights to the Fc-enhanced agent.

Beyond IO, Novartis, in a bid to enhance its radioligand programs—underpinned by the multibillion-dollar acquisitions of Advanced Accelerator Applications in 2017 and Endocyte in 2018—has agreed a three-year collaboration deal with UK biotech Artios Pharma to leverage its DNA damage response (DDR) discovery platform. Novartis agreed to pay \$20 million upfront in addition to near-term research funding to support the collaboration's efforts to identify DDR targets for use with Novartis' proprietary radioligand therapies. Artios is eligible to receive up to \$1.3 billion in discovery, development, regulatory and sales-based milestones, in addition to royalty payments.

### Platform technologies

As in previous years, big pharma's appetite for technology platforms such as gene and cell therapies, ADCs and bispecific antibodies remains strong. Indeed, while 48% of oncology transactions involved a small-molecule therapeutic component, 35% of deals involved antibody platforms, 27% had an IO focus, while cell and gene therapy and ADCs were associated with 11% and 8% of deals, respectively.

The year's largest oncology-focused biopartnering transaction, on paper, was the deal between Roche's Genentech unit and Adaptimmune Therapeutics to develop allogeneic cell therapies, underpinned by the UK T cell therapy company's induced pluripotent stem cell-derived allogeneic platform, for up to five shared cancer targets. In one arm of the collaboration, the partners will develop off-the-shelf alpha and beta T cell therapies directed to up to five collaboration targets. In a second, they will develop personalized T cell therapies isolated from patients.

Under the terms of the deal, Roche paid Adaptimmune \$150 million upfront, and will pay another \$150 million over the next five years. The UK biotech is also eligible for development, regulatory and commercial milestones payments from Roche exceeding \$3 billion, plus royalties. However, Adaptimmune secured a right to opt in to receive a profit share and to co-promote off-the-shelf T cell therapies that are part of the collaboration. If it exercises this option, this would make it eligible to share half the profits and losses from US sales and up to \$800 million in ex-US regulatory and sales-based milestone payments, as well as royalties on ex-US net sales.

The largest oncology-focused ADC partnership in 2021 saw US biotech Seagen license disitamab vedotin, a novel HER2-targeted ADC, from Chinese biotech RemeGen in an exclusive worldwide license and co-development agreement. Disitamab vedotin combines the drug-linker technology originally developed by Seagen with RemeGen's novel HER2 antibody.

Under the terms of the deal, Seagen made a \$200 million upfront payment for exclusive license rights to develop and commercialize disitamab vedotin outside of RemeGen's territory; the Chinese biotech retains development and commercialization rights for Asia, excluding Japan and Singapore. Seagen will pay RemeGen up to \$2.4 billion in potential total milestones based on development, regulatory and commercialization goals across multiple indications and products, while RemeGen will be entitled to royalties based on sales of disitamab vedotin in Seagen's territory.

Potentially the largest bispecific antibody platform deal in 2021 was secured by the Dutch biotech Merus. As part of a research collaboration and license agreement with Eli Lilly's Loxo Oncology arm, Merus received \$40 million upfront, and a \$20 million equity investment from Loxo to develop up to three CD3-directed bispecific T cell engager antibodies. Each

**Table 1 | Top ten licensing deals in oncology in 2021 with a projected deal value over \$1 billion**

Principal company	Partner company	Date	Total projected deal amount (\$ million)	Upfront payment (\$ million)	Deal summary
Adaptimmune Therapeutics	Genentech	September 2021	3,650	150	Adaptimmune partners with Genentech to research and develop allogeneic cell therapies indicated for multiple cancers.
BeiGene	Novartis	January 2021	3,200	950	Novartis signs a collaboration agreement to in-license PD-1 inhibitor tislelizumab from BeiGene.
Eisai Co	Bristol Myers Squibb	June 2021	3,100	Unspecified	Eisai and Bristol Myers Squibb sign an exclusive agreement to jointly develop and market Eisai's ADC, MORAb-202, for advanced solid tumors.
RemeGen	Seagen	August 2021	2,595	200	Seagen and RemeGen partner to develop and market a new HER2-targeted ADC, disitamab vedotin.
QED Therapeutics, an affiliate of BridgeBio Pharma	Helsinn Healthcare	March 2021	2,450	Unspecified	QED Therapeutics partners with the Helsinn Group to co-develop and commercialize infgratinib, an oral FGFR1-3 selective inhibitor for the treatment of cholangiocarcinoma (bile duct cancer).
Arvinas	Pfizer	July 2021	2,400	650	Arvinas and Pfizer enter an international partnership to jointly develop and market ARV-471, an investigational PROTAC therapy developed by Arvinas for breast cancer.
Shoreline Biosciences	Kite Pharma	June 2021	2,300	Unspecified	Kite Pharma signs a deal with Shoreline to develop novel allogeneic cell therapies targeted towards a variety of cancer targets.
iTeos Therapeutics	GlaxoSmithKline	June 2021	2,075	625	GSK and iTeos Therapeutics will jointly develop iTeos' anti-TIGIT monoclonal antibody EOS-448, currently in phase 1 for advanced solid tumors.
Kumquat Biosciences	Eli Lilly	July 2021	2,070	Unspecified	Loxo Oncology (part of Eli Lilly) and Kumquat Biosciences collaborate to discover small molecules that stimulate tumor-specific immune responses.
Artiva Biotherapeutics	Merck & Co.	January 2021	1,881	30	Merck signs deal with Artiva to license two off-the-shelf CAR-NK cell therapy programs for solid tumors.

ADC, antibody-drug conjugate; PROTAC, proteolysis-targeting chimera; TIGIT, T cell immunoreceptor with Ig and ITIM domains. Source: Clarivate; Cortellis Deals Intelligence; BioWorld 2022.

program, which will seek to marry Loxo's rational drug design and oncology expertise with Merus' Biclomics bispecific antibody platform, could generate \$540 million in development and commercialization milestones, taking the total potential value of the deal to \$1.68 billion.

Loxo Oncology was also involved in one of the year's largest discovery deals, with a huge upfront payment in a deal with Foghorn Therapeutics. Paying \$300 million upfront and investing \$80 million in Foghorn equity, Loxo signed a co-development and co-commercialization agreement that will access Foghorn's proprietary gene traffic control platform for modulating patients' chromatin regulatory system, to discover and develop therapeutic molecules directed to a BRM target, an additional undisclosed oncology target, plus three additional discovery programs.

Under the terms of the deal, for the BRM-selective program and the additional undisclosed target program, Foghorn will lead discovery and early research and Lilly will lead development and commercialization activities. Foghorn and Lilly will share 50/50 in the US economics, and Foghorn is eligible to receive royalties on ex-US sales based on revenue levels. For the additional discovery programs, Foghorn may receive up to a total of \$1.3 billion in potential development and commercialization milestones. Foghorn also has an option to participate in a percentage of the US economics and is eligible to receive tiered royalties on sales outside the US.

**Lackluster mergers and acquisitions**

While biopartnering deals in the oncology space were robust in 2021, it was a different story on the M&A front. Oncology-focused M&A deals that completed in 2021, for which financial details were disclosed, yielded just \$19.7 billion. Moreover, the lion's share of that total was down to Illumina's acquisition of its former blood-based diagnostics spinout GRAIL for \$8 billion (Table 2). Cancer diagnostics is still clearly a hot area in the oncology space, as Veracyte spent \$600 million cash acquiring Decipher Biosciences for its urologic cancer genomic diagnostics capabilities.

There were two major drivers underpinning the lackluster M&A performance in 2021. With the global biotech sector able to raise record sums from both venture capital sources (\$39.6 billion) and through initial public offerings (\$24.2 billion), the need to sell to big pharma was not as imperative as in previous years, as many biotech executives have enough capital to take their assets further into the clinic, and so retain and build value in their pipelines. Second, with uncertainty triggered by the COVID-19 pandemic, pharma companies were looking to conserve resources, with a preference for discreet bolt-on acquisitions. Consequently, there were no mega mergers or acquisitions in the oncology space, as in former years, with only eight \$500 million-plus M&A transactions completed in the year.

With a belief that the CD47 class of molecules has an important future in hematologic malignancies, Pfizer concluded the largest oncology biopharma M&A deal with its \$2.26 billion

**Table 2 | Top five mergers and acquisitions in oncology in 2021 by value**

Seller	Buyer	Total projected (\$ million)	Technology acquired
GRAIL	Illumina	8,000	Diagnostics (genomics)
Trillium Therapeutics	Pfizer	2,260	CD47-directed fusion protein drugs
Five Prime Therapeutics	Amgen	1,900	Monoclonal antibodies; bispecific antibodies
Constellation Pharmaceuticals	Morphosys	1,700	Small-molecule therapeutic
Amunix	Sanofi	1,000	Small-molecule therapeutic; bispecific T cell engager antibody

Source: Clarivate; Cortellis Deals Intelligence; BioWorld 2022.

acquisition of Trillium Therapeutics. The acquisition provides Pfizer with two lead clinical assets, TTI-622 and TTI-621, novel SIRPα-Fc fusion proteins that are currently in phase 1b/2 development across several indications, with a focus on hematological malignancies. While both molecules block the signal-regulatory protein α (SIRPα)-CD47 axis (which is emerging as a key immune checkpoint in hematological malignancies), they are also being tested in solid tumors.

The third largest oncology M&A deal that closed in 2021 was Amgen's \$1.9 billion acquisition of the IO-focused company Five Prime Therapeutics, which not only gives Amgen bemarituzumab, a potential first-in-class, phase 3-ready anti-FGFR2b antibody for gastric cancer, but also provides a potential royalty stream on future sales in China from a pre-existing co-development and commercialization agreement between Five Prime and Zai Lab.

Companies with T cell engager technology platforms were popular acquisition targets in 2021. Leading the way was Sanofi, which, in buying Amunix Pharmaceuticals for \$1 billion upfront and a potential \$225 million contingent on milestones, acquired a pipeline of T cell engagers and cytokine therapies, with lead candidate AMX-818 expected to enter the clinic in early 2022, and access to the XTEN, XPAT, and XPAC technology platforms, which the company believes are complementary to its existing research and development platforms. Similarly, Amgen paid \$900 million cash for Teneobio and its T cell engager platform, although it could be on the hook for another \$1.6 billion in potential contingency payments to Teneobio shareholders.

With big pharma companies sitting on large cash piles and many of them facing loss of patent exclusivity for key products in the coming years, it can be anticipated that biopartnering activity will remain robust and M&A, even if only bolt-on acquisitions, will recover.

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