Chasing immune checkpoint inhibitors

Next-generation immuno-oncology targets continue to catalyze major deals, exemplified by the race to develop inhibitors of the immune checkpoint TIGIT.

Raveena Bhambra

In just a few years, PD1/PDL1 immune checkpoint inhibitors have transformed the treatment of multiple cancers, and the leading products from Merck & Co. and Bristol Myers Squibb have become mega-blockbusters. As the cancer immunotherapy field evolves, a key focus for biopharma companies is how other therapies could complement PD1/PDL1 inhibitors or reach patient populations that do not respond well to them. Indeed, according to Clarivate Analytics, >100 deals were signed involving checkpoint inhibitors this year alone.

Several of the largest deals (Table 1) have been driven by major companies seeking access to investigational drugs that target TIGIT, which is poised to be the next immune checkpoint target for which a drug reaches the market (*Nat. Biotech.* **38**, 1007–1009; 2020). While Genentech and Merck & Co. are at the front of the pack with their own candidates in clinical trials, GlaxoSmithKline, Bristol Myers Squibb and Gilead have all recently struck deals potentially worth more than $1 billion to get a foothold in the fast-moving field. Other emerging checkpoint inhibitor targets are also attracting interest, such as ILT2, which was the focus of a deal potentially worth more than $1 billion between Sanofi and Biond Biologics earlier this year.

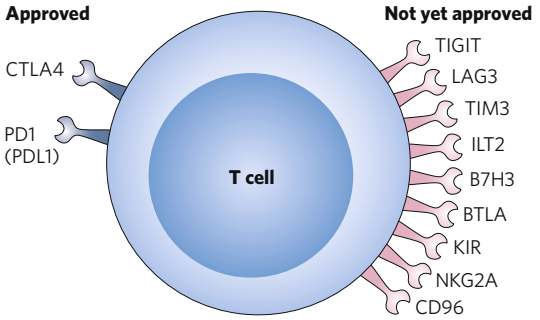

Fig. 1 | Immune checkpoint targets for cancer therapies. Since the approval of the first checkpoint inhibitor in 2011—ipilimumab, which targets CTLA4 expressed on T cells—several inhibitors that target the checkpoint protein PD1 or its binding partner PDL1 have been approved. These have transformed the treatment of multiple cancers for some subsets of patients, and intense efforts are ongoing to build on their success. Drug candidates that inhibit further checkpoint targets such as TIGIT are now being investigated in clinical trials for multiple cancers as single agents or in combination with PD1/PDL1 inhibitors and/or other anticancer drugs.

Table 1 | Selected recent deals involving immune checkpoint inhibitors

Companies	Date	Potential deal value ($ million)	Deal summary
GlaxoSmithKline, iTeos Therapeutics	June 2021	2,000	GlaxoSmithKline signs a potential $2 billion deal with iTeos Therapeutics, including $625 million upfront, to gain rights to its anti-TIGIT mAb EOS-448. The phase 1 drug is being developed for advanced solid tumors, and will be trialed in combination studies with GlaxoSmithKline's anti-PD-1 therapy Jemperli (dostarlimab) in 2022.
Bristol Myers Squibb, Agenus	May 2021	1,560	Bristol Myers Squibb purchases an exclusive license to Agenus' AGEN1777, a bispecific antibody that blocks TIGIT and a second undisclosed target, for $200 million upfront and up to $1.36 billion in development and commercial milestones. Bristol Myers Squibb will be responsible for development and marketing of the candidate.
Sanofi, Biond Biologics	January 2021	1,125	Sanofi acquires global rights to the anti-ILT2 mAb BND-22 from Biond Biologics, which is now in phase 1. The deal includes an upfront payment of $125 million and more than $1 billion in potential milestones.
Gilead, Arcus	May 2020	2,000	Gilead signs a co-development and co-commercialization agreement with Arcus, including its anti-TIGIT mAb domvanalimab, which is now in phase 3 trials for non-small-cell lung cancer. Gilead agrees to pay $175 million upfront along with a $200 million equity investment.

mAb, monoclonal antibody; TIGIT, T cell immunoreceptor with Ig and ITIM domains. Source: Clarivate Analytics, 2021.