Evaluate Vantage

July 16, 2013

Early-stage asset risk no deterent to partnering deals

Jonathan Gardner

Lack of clinical evidence does not necessarily mean lack of value, as Genmab and MorphoSys can tell you. In the last couple of months both managed to extract huge amounts of money from partners for compounds that had been tested in only a handful of patients – the latest in a long line of substantial early clinical-stage licensing deals.

Of course, paying top dollar for a phase I asset does not guarantee success. A large proportion end up bust, according to the analysis below detailing some of the biggest deals struck over projects that in some cases had yet to generate any clinical data. It is also clear that once a drug class has seen one big early-stage deal others will follow; as well as the anti-CCR4 antibodies that returned so well for Genmab and MorphoSys, this was also seen with the glucokinase activators and the anti-NGF antibodies a couple of years ago. It seems that, to keep up with the Joneses, big pharma is willing to make risky and expensive bets (see table).

Hot assets

The remarkable €71m ($92m) that Celgene handed over for rights to MorphoSys's anti-CD38 antibody MOR202 represents one of the biggest sums paid up front for a phase I asset. The deal, announced last month, came less than a year after Johnson & Johnson handed over an only slightly less impressive €55m for Genmab's daratumumab, a similarly acting project at the same development stage (*MorphoSys squares up to Genmab in multiple myeloma, June 27, 2013*).

At the time the MorphoSys-Celgene deal was struck MOR202 had not generated any clinical results, although Genmab had presented data on daratumumab from 23 patients at a medical conference before it snared J&J – at the time of the deal the project had only been in 35 patients, the Danish company said at the time.

Despite the lack of clinical evidence both partners clearly felt the target was sufficiently validated to justify such sums; time will tell whether they were correct. According to *EvaluatePharma* the agents are two of three anti-CD38 antibodies in clinical testing – the other SAR650984 is owned by Sanofi, so MOR202 had scarcity value once daratumumab had been cornered.

For some assets in the table below, similar forces of market defence and scarcity value, no doubt fuelled by a competitive bidding process, were at play to push valuations through the roof. In others cases it looks more like a pipeline-hungry partner with the cash to place a high-risk/high-reward bet. The analysis includes all phase I deals with an up-front value of $50m or more that were struck in the absence of substantial clinical data. None has progressed further than phase II to date, and more than half have been abandoned.

Of course, all of the candidates in the list that remain active could go on to fail, given that success in phase I is hardly a guarantee of later glory. The analysis certainly suggests that paying sums normally associated with much later stages of development is not worth it.

When, or if, one of these deals pays off *EP Vantage* will let you know. But history tells us that the chance of Celgene and Johnson & Johnson breaking this pattern with their new assets is low.

Biggest early-stage licensing deals								
	Company	**Product**	**Pharma class**	**Partner**	**Current status**	**Up-front fee ($m)**	**Deal value ($m)**	**Deal date**
1	Abbott Laboratories	ABT-110	Anti-nerve growth factor (NGF) MAb	PanGenetics	Unclear	170	190	2009
2	Amgen	AMG 761	Anti-CCR4 MAb	Kyowa Hakko Kogyo	Assumed abandoned	100	520	2008
3	Celgene	MOR202	Anti-CD38 MAb	MorphoSys	Phase I/II	92	818	2013
4	Astellas Pharma	CTS-21166	Beta secretase inhibitor	CoMentis	Assumed abandoned	80	760	2008
5	Roche	TB-403	Anti-placental growth factor (PlGF) MAb	ThromboGenics	Assumed abandoned	66	662	2008
6	Sanofi	SAR256212/ MM-121	Anti-HER3 (ErbB-3) MAb	Merrimack Pharmaceuticals	Phase II	60	530	2009
7	Roche	PLX5568 (RG7376)	c-Raf kinase inhibitor	Plexxikon	Assumed abandoned	60	335	2009
8	Amgen	AMG 151/ ARRY-403	glucokinase activator	Array BioPharma	Phase II	60	726	2009
9	Johnson & Johnson	HuMax-CD38	Anti-CD38 MAb	Genmab	Phase II	55	1,055	2012
10	Forest Laboratories	TTP399	glucokinase activator	TransTech Pharma	Assumed abandoned	50	1,155	2010
11	Johnson & Johnson	AMG 403	Anti-nerve growth factor (NGF) MAb	Amgen	Unclear	50	435	2008
12	Human Genome Sciences	FP-1039/ HGS1036	Fibroblast growth factor (FGF) antagonist	FivePrime Therapeutics	Phase I	50	495	2011
13	Sanofi	SAR339658/ GBR500	Anti-VLA-2 MAb	Glenmark Pharmaceuticals	Phase II	50	663	2011

Anti-NGF antibodies was another class that saw huge early-stage deals. They were at one point viewed as promising new pain therapies – no drug with a novel mechanism of action to treat pain has reached the market in about 20 years.

This promise prompted J&J to pay $50m for an Amgen antibody, fulranumab, in 2008 – it is not clear what data were available at the time although it was only listed as being in phase I – followed by the outright acquisition of PanGenetics' ABT-110 for $170m by Abbott the following year. PanGenetics had only started a 56-patient phase I trial in patients with osteoarthritis knee pain a few months before the deal was announced, so very little if any data can have been available for Abbott to assess (*PanGenetics cashes in on Abbott's early stage bet, November 13, 2009*).

At that point, however, Pfizer's anti-NGF tanezumab was in several phase III studies, so at least these partners had a more clinically validated mechanism to point to when writing their respective cheques. Still, they could have both saved themselves a lot of money if they had waited – just months after Abbott pulled the trigger reports of rapid joint destruction in the tanezumab programme prompted the FDA to halt work on the entire class.

Last year, an advisory committee agreed that work could restart, but companies involved have been slow to resume and the future of the class is clouded (*Therapeutic focus - Return of anti-NGF class gets FDA panel's backing, March 13, 2012*).

Big bucks

Amgen was also responsible for the biggest straight licensing deal in this analysis, paying a huge $100m to Kyowa Hakko Kogyo for its anti-CCR4 antibody in 2008. This had completed Phase I studies in healthy volunteers and allergic rhinitis patients and was in a phase I lymphoma trial at the time of signing; the deal only included an option over oncology rights.

While Kyowa pushed on with development – it has won approval in Japan for lymphoma and started phase III trials in the US – Amgen rarely spoke about the asset. It no longer lists the compound and it has to be assumed to have walked away, with no hope of a return on that $100m.

For a company so successful at cancer innovation, it is surprising to see Roche feature in the list for an oncology compound, although the Swiss pharma giant was the logical partner for ThromboGenics and BioInvent International's anti PIGF antibody.

It was hoped that this could be used in combination with an anti-VEGF therapy like Avastin, producing greater efficacy at lower doses with a subsequent reduction of toxicity. Roche paid $66m on the basis of phase I results in 16 healthy subjects, but the project did not even make it into phase II. The rights were handed back in 2012 – pipeline prioritisation was blamed.

Not all these phase I bets have failed.

Three large phase II studies are currently on going with MM-121, and ErbB3 receptor blocker, in ovarian and breast cancers. Merrimack Pharmaceuticals had started a phase I safety trial with the project 10 months before the deal was signed with Sanofi, but had not publically revealed any data. This early-stage bet could still pay off.

And FivePrime Therapeutics' FGF/FGFR antagonist FP-1039 could still prove itself, albeit for its new owner GlaxoSmithKline, which inherited the project when it bought Human Genome Sciences. HGS snapped up rights for $50m on the back of phase I data from a trial that had recruited 39 patients. Work elsewhere in the class does not make for encouraging reading and progress with FP-1039 has been slow, so the jury is still out.

To contact the writer of this story email Amy Brown in London at amyb@epvantage.com or follow @AmyEPVantage on Twitter