Liquid refreshment

Christopher Scott

Compared with the long time horizons and diminished returns of traditional antibody startups, Ablexis gave investors a deal they couldn't refuse.

Monoclonal antibodies (mAbs) are the fastest growing therapeutic class. Global therapeutic mAb sales were \$45 billion in 2010 and expected to climb (ref. 1 and Fig. 1). In comparison to small-molecule R&D, mAb therapeutics boast higher clinical success rates, predictable toxicity and less risk of generic competition². Despite this rosy picture, executives at Ablexis (San Francisco) found themselves in a hard place in 2009. They needed new financing to further develop AlivaMab, their humanized mouse technology, and venture capital wasn't biting. Investors were no longer willing to stomach long development times and low returns on investment. But Ablexis management felt they had something special and didn't want to become a glorified contract research organization, living on licensing deals and developing mAbs against targets supplied by partners. These arrangements often tied mAb companies to pharma's fate: make a mouse, make an antibody, and, hopefully, one day make some money.

Ablexis previously raised \$12 million in an A round of funding and wanted to strike a deal to provide a nondiluting outcome for its investors. It also recognized venture capital's need for liquidity and it understood potential drug partners' wishes for a straightforward, ambitiously delivered platform that would tailor an end product specifically to them. But pharma's business development units look for a venture-backed balance sheet, and venture capitalists want to see pharma's skin in the game. And so ensued a delicate dance, with Ablexis counting tempo.

The only way forward, management figured, was something completely new. It crafted a deal featuring a consortium of pharmaceutical companies, capped at five. Each partner contributes a seven-figure upfront payment, which gives Ablexis working capital to build a mouse to an individual partner's specifications. Once the mouse is successfully delivered, each partner is obligated to an eight-figure license payment. Distributions of these license payments provide initial liquidity to VC investors and other LLC members. Future license payments from partners would be similarly distributed.

Christopher Scott is Contributing Editor at Nature Biotechnology.

All partners signed the same, standardized deal sheet: nonexclusive rights to the technology, no reach-through clauses and no restrictions on field of use. At delivery, partners get a first and final version of a mouse producing mAbs with natural fully human sequence binding domains and constant and intracellular domains comprising natural fully mouse sequence.

What the consortium does is guarantee a return for investors and LLC partners, while also eliminating deal risk and competitive risk. Importantly, it leaves Ablexis free to pursue traditional licensing deals outside the group; one such arrangement was signed last July. Pfizer (New York), the only pharma named under the arrangement, is both a venture capital investor and partner. Pfizer Ventures didn't want a long-term investment in an exclusive platform that competitors could copy; it also didn't want to lead the round. Enter Third Rock Ventures (Boston), which led the round and brokered the deal with all the parties.

In traditional models, when a pharmaceutical company signs a development deal with a mAb company for target discovery, the commitment requires foremost the scientific expertise of the biotech partner. But on the back end, if the platform produces a handful of candidates, the collaboration often ends up with the purchase of the biotech. A prime example is Medarex (Princeton, New Jersey), and its founder, Donald Drakeman, famous for his 'shots on goal' model of drug development, whose business philosophy was, do deals with anyone, and hope for royalty streams on the ones that succeed. Medarex's co-development deal with Bristol-Myers Squibb (New York) produced Yervoy (ipilimumab), a human mAb for melanoma approved in 2011. The pharma saw that approval coming and bought Medarex in 2009 for \$2.4 billion, acquiring the cancer and immune disorder mAb technology, the rights to seven experimental antibodies and stakes in three others, and complete control over Yervoy's future revenue stream. This ended Medarex's future as a fully integrated company.

Another example is Abgenix. Amgen bought the company in late 2005 for \$2.2 billion, picking up the XenoMouse mAb lead discovery model, a promising cancer drug in panitumumab and a pipeline of candidates.

Figure 1 Total and forecasted sales of the mAb market (2008–2015)¹.

In acquiring former partner Abgenix, Amgen (Thousand Oaks, CA, USA) escaped the additive royalties specified by their licensing deal, which it inherited when it bought Immunex (Seattle) in 2002. Abgenix, for its part, found it needed the buyout—it had bet the farm on panitumumab, and in June it had laid off 15% of its workforce, holding out for those royalties on the horizon.

As it happens, Ablexis CEO Larry Green was a co-founder of Abgenix, and he learned his lessons well—he'd seen how cutthroat competition and exclusivity fractured the mAb space. Deals were done on a target-by-target basis, many targets were occupied by the spectrum of mAb service providers, and companies carved out entire fields of use, such as cancer, leaving competitors the increasingly smaller markets. It was in that era that Medarex and Abgenix formed deals that brought in product revenue streams, but in turn made them valuable enough to be snapped up by the partner.

Shareholders approve of such buyouts and it's smart business, but when Green shunned the partnership-leads-to-royalties model as Ablexis' main goal, he may have leveled the playing field for mAb-derived drugs. The consortium gives Ablexis the financial flexibility to pursue its own blockbuster dreams, but still has venture backers smiling all the way to the bank.

1. Anonymous. *Monoclonal Antibodies: 2010* <http://www.datamonitor.com/store/Product/monoclonal_antibodies_2010?productid=HC00029-002> (Datamonitor, 2010).
2. DiMasi, J. et al. *Clin. Pharmacol. Ther.* **87**, 272–277 (2010).