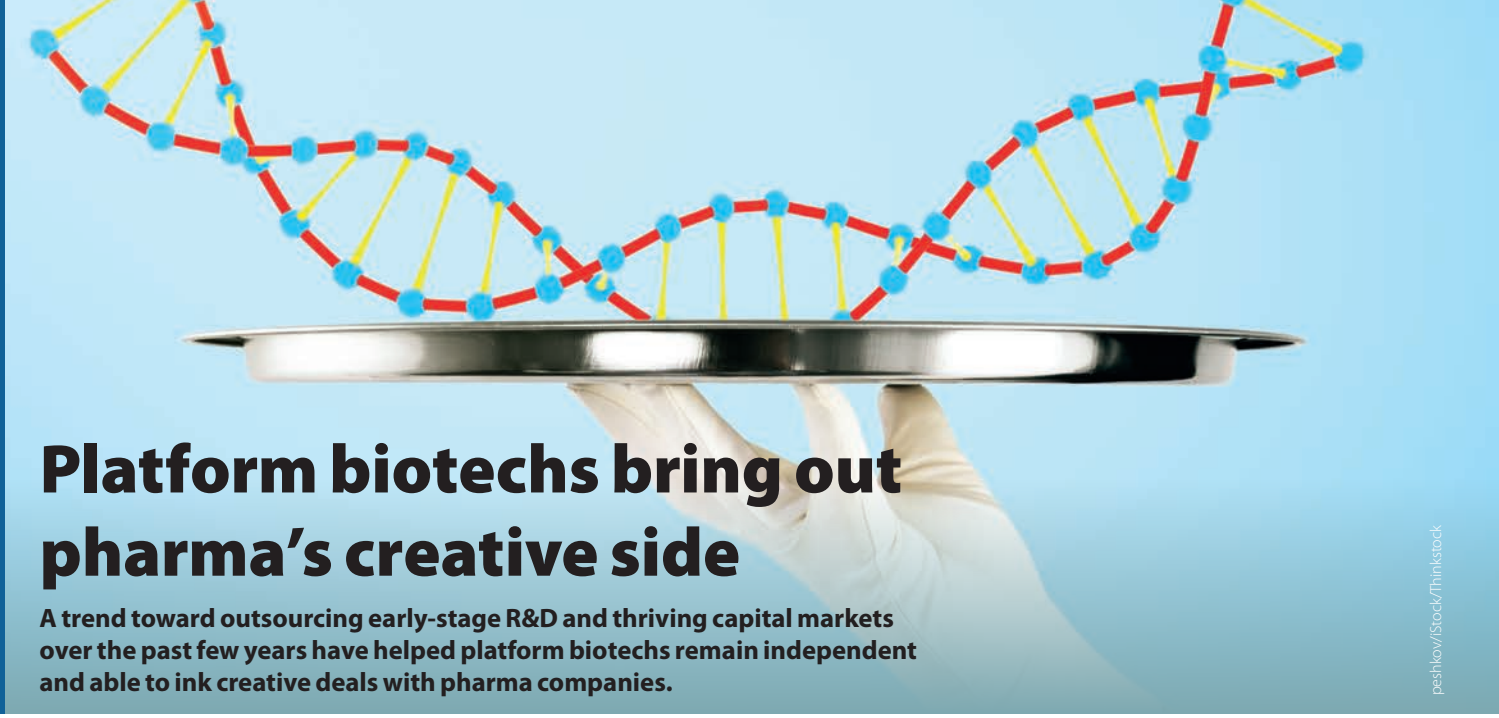

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Platform biotechs bring out pharma's creative side

A trend toward outsourcing early-stage R&D and thriving capital markets over the past few years have helped platform biotechs remain independent and able to ink creative deals with pharma companies.

Chris Morrison

Pharma companies were once voracious acquirers of technologies. But in recent years, platform biotechs have enjoyed easier access to capital as independent entities, obviating the need to sell out. At the same time, large and small biopharma companies alike have realized that they're often better off buying the fruits of those technologies than crushing them with an institutional embrace or reinventing them in house.

As a result, platform biotechs and their backers have wound up with more skin in the game—at potentially much higher valuations—while finding innovative ways to grant pharma companies access to potentially game-changing platforms. Companies pursuing groundbreaking technologies such as chimeric antigen receptor (CAR)-modified T cells (CAR-Ts) and mRNA therapeutics are among a vanguard of biotechs striking lucrative and creative platform deals.

Externalizing R&D

"The tendency right now is to externalize as much of R&D as possible, and much of that is through dealmaking or outsourcing models where you can access the stuff you need from others without having to own it. And it has made our industry much more efficient," said Tillman Gerngross, cofounder and CEO of the antibody discovery company Adimab. "Airlines don't build their own airplanes, and there's a good reason for that. They focus on the particular thing they're good at and leave other parts to others. And I think our industry is maturing in a similar way."

Arguments about airline quality aside, Gerngross would know. Before launching Adimab he built GlycoFi, a company manufacturing yeast-based antibodies, which was sold to Merck & Co. for $400 million in 2006. Adimab is still private and independent, is valued at more than $1 billion and has dozens of partnerships with major biotech and pharma companies, amounting to about 130 active antibody programs. Ten years ago, instead of signing a nonexclusive deal to access its technology, some pharma companies would probably have tried to buy Adimab. Indeed, brisk markets existed for antibody technologies, alternative antibody-like scaffold companies and even RNA interference (RNAi) companies as recently as 5 or 6 years ago.

Conventional wisdom holds that as biotech valuations drift back to earth, pharma buyers, with their growth imperatives and pipeline gaps, will become more eager to buy biotech products and companies. Although some acquisitions continue to be driven by platform access and coveted intellectual property, fundamental obstacles to mergers and acquisitions for platform biotechs have emerged in recent years.

One big hurdle is that previous—and often expensive—acquisitions of platform biotechs didn't work out for the pharma buyers, and those companies' institutional memories have led them to avoid similar scenarios. For example, Merck bought the RNAi company Sirna Therapeutics for $1.1 billion in 2006, the same year it bought GlycoFi. The impact of both acquisitions appears to have been much smaller than hoped: the company closed down the original GlycoFi research headquarters earlier this year and got out of RNAi altogether by selling what remained of Sirna to Alnylam for just $175 million plus milestones in 2014. Pharma's embrace of new technology too often smothers its potential. "It really does take people who are believers in these technologies with enough energy and clout and capital to drive [novel technologies] all the way through" to successful products, said Helen Kim, EVP of business development at the T cell therapeutics company Kite Pharma, which has a pipeline of CAR-T candidates as well as T cell receptor (TCR) candidates. In larger companies with competing priorities and products, that belief can get bogged down in committees and processes, "and people just get wary of sticking their necks out to champion technologies or products," she said.

"Big pharma companies are just that: they're very big and getting bigger," agreed Malcolm Weir, CEO of Heptares Therapeutics, a division of Sosei, adding that acquired technology can get lost inside huge organizational structures. Sosei, a small biopharma, bought Heptares and its structure-based drug design platform for G-protein-coupled receptors in 2015, for $180 million plus $220 million in potential milestone payments. Heptares is one of the rare platform companies left largely to its own devices after acquisition. In fact, Heptares has signed discovery partnerships with a handful of biotech and pharma companies since its acquisition. Most notably, Allergan paid $125 million up front (with potential milestones exceeding $3 billion) in April 2016 to access the biotech's portfolio of muscarinic receptor agonists for neurological diseases.

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> Malcolm Weir, CEO Heptares Therapeutics

Sosei made an ideal fit for Heptares, said Weir, because the latter was being acquired specifically as a drug discovery engine—which the relatively small Sosei did not have. One of the problems for acquired platform companies is technological or asset overlap with the acquirer's existing portfolio. "Unless you are from Mars and don't fit into any category at the pharma," said Weir, "when you get acquired you tend to get acquired for one or two leading assets, and once they're internalized the rest of the company is of limited use in the eyes of the pharma partner."

Valuation dilemmas

At a large company, the long-term commitment to any decision is always in question, said Weir. Whether a platform technology succeeds inside a large organization isn't only about technological attrition, either because the technology fails or because something better comes along; it is also about "failure, but from portfolio decisions that can effectively scupper your program," he said. Loss of control of an asset's future development happens with individual product candidates as well, but for platforms, a greater percentage of a deal's possible value can be tied up in earn-outs.

Valuing platform companies is more art than science, and agreeing on terms (especially in such volatile markets) is notoriously tricky. Biotechs with 'next big thing' platforms ascribe value to the technology, but pharmas typically see value only in products. As a result, platform buyouts are most likely to occur only when technologies have matured to the point of spawning late-stage drug candidates whose potential overshadows the myriad unpursued opportunities a platform represents.

Platform purveyors have learned to structure their companies accordingly. The mRNA therapeutics pioneer Moderna has created multiple internal portfolio companies to pursue different applications of its core technology. Several companies with platform technologies have created LLC umbrella structures under which individual drug candidates are nested as individual companies. When Gilead Sciences acquired Nimbus Therapeutics' acetyl-CoA carboxylase inhibitors, including a phase-2-ready candidate for nonalcoholic steatohepatitis, the $400 million upfront deal was structured as an acquisition of a wholly owned subsidiary (Nimbus Apollo). Nimbus, which discovers drug candidates with a computational chemistry platform, and other asset-centric developers have successfully monetized their 'golden geese' through corporate structures that allow value to be ascribed to individual products or disease areas rather than the platform itself, without interrupting the platform's development progress.

Getting creative

As pharma companies have grown comfortable keeping promising technology platforms at arm's length, deals around CAR-T platforms for cancer immunotherapy underscore big companies' efforts to participate in the promise of a broad technology platform while enabling their own work in product development.

> **"It used to be that biotechs needed validation of their platforms by creating a strategic partnership with a pharma**
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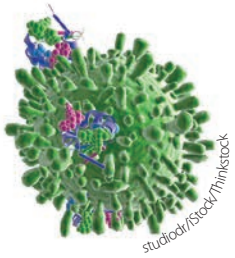
> Helen Kim, EVP of business development, Kite Pharma

"It used to be that biotechs needed validation of their platforms by creating a strategic partnership with a pharma, partly to access later-stage development and commercial capabilities but also to access nondilutive financing," said Helen Kim. Plenty of those deals still happen, she said, but some promising companies, such as Kite and competitor Juno Therapeutics, that happened to emerge during the recent biotech market boom have been able to bargain from strong positions. "Ultimately, if a company's vision and strategy is to create maximum value," those 'validation deals' can be counterproductive, she said. "If you encumber your lead programs or the tech platforms, it caps the potential value of your company."

Kite's strategic alliance with Amgen, inked in January 2015, gives the big biotech access to Kite's platform without ownership over any of its programs, and Kite similarly gets access to Amgen's oncology pathway and target expertise. "The collaboration was structured so that Kite has a certain number of targets from Amgen that we are developing as our own products," said Kite's Kim. Meanwhile, the deal grants Amgen a license to Kite's CAR-T technology platform, which Kite will take through investigational new drug (IND) filing before handing it off to Amgen. Milestones—up to $525 million—flow each way, and Kite received a $60 million upfront payment and will be reimbursed for early-stage R&D costs. "We get access to targets, they get access to CAR-Ts, but the license is only for the targets they're developing," said Helen Kim.

Juno's flagship deal with Celgene in June 2015 may tie the companies closely together, but it also, paradoxically, ensures Juno's independence for the foreseeable future. The companies' 10-year collaboration appears to be based on the successful Roche/Genentech model, as Celgene gains rights to develop Juno's CAR and TCR candidates outside North America, and both sides receive other co-development and co-promotion options on each other's pipelines. Celgene's upfront payment of $1 billion included an $850 million equity stake in Juno (10% of the company), which was bought at a ~100% premium to the company's share price at the time of the deal. By the end of the deal's 10-year term, Celgene's stake could be as high as 30%, but the company has agreed to limits on selling its stake or trying to take over the company.



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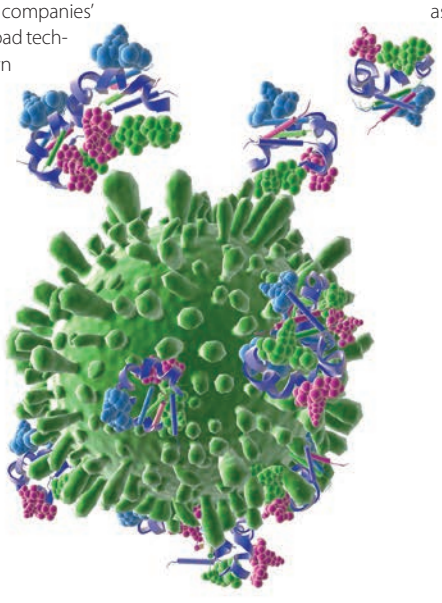

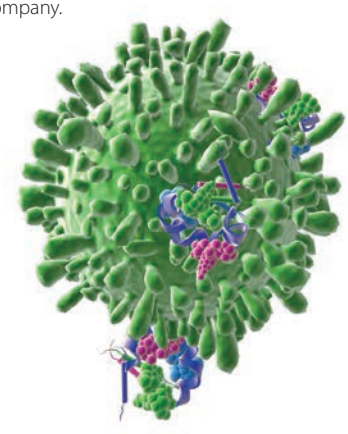

Table 1: Selected Moderna Therapeutics deals 2013–2016*

Date	Partnering company	Summary
July 2016	Vertex Pharmaceuticals	Vertex Pharmaceuticals partnered with Moderna in a deal potentially worth $315 million to discover and develop mRNA therapeutics for cystic fibrosis.
June 2016	Merck & Co. (known as MSD outside the United States and Canada)	Moderna signed a $200 million collaboration and license agreement with Merck to develop mRNA-based personalized vaccines based on Moderna's mRNA vaccine technology and evaluate them in combination with Merck's checkpoint inhibitor drug Keytruda (pembrolizumab).
January 2016	AstraZeneca	MedImmune, the biologics arm of AstraZeneca, partnered with Moderna to develop and commercialize mRNA therapeutic candidates for various cancers.
January 2016	Merck & Co. (known as MSD outside the United States and Canada)	Moderna licensed a new vaccine program against an undisclosed target and a set of vaccine candidates to Merck, in addition to the ongoing research collaboration to develop vaccines against virus targets established in January 2015.
February 2015	Institut Pasteur	Institut Pasteur signed a research collaboration partnership with Moderna to discover and develop drugs and vaccines for infectious diseases using Moderna's mRNA platform.
January 2015	Merck & Co. (known as MSD outside the United States and Canada)	Moderna's infectious-disease-focused venture Valera and Merck signed a license and collaboration agreement to develop five mRNA-based therapies and vaccines against undisclosed virus targets.
October 2014	Karolinska Institutet and Karolinksa Hospital	The Karolinska Institutet and the Karolinska Hospital partnered with Moderna to develop new drugs using Moderna's mRNA platform.
January 2014	Alexion Pharmaceuticals	Alexion Pharmaceuticals signed a $125 million deal with Moderna for the discovery and development of mRNA therapeutics to treat rare diseases. Alexion will have exclusive options to license rights for ten products.
March 2013	AstraZeneca	AstraZeneca signed a deal potentially worth $420 million with Moderna to develop mRNA therapeutics for cancer and for cardiovascular, metabolic and renal diseases. AstraZeneca will pay Moderna $240 million up front for exclusive access to any of the cardiometabolic targets and some of the oncology targets.

*Deals included up to the end of July 2016.

Moderna has been an active partner across a broad swath of therapeutic spaces **(Table 1)**. Large pharma and biotech players have staked hundreds of millions of dollars to access the company's mRNA therapeutics platform in areas including immuno-oncology, viral vaccines and rare diseases. Merck has inked three deals with Moderna, and AstraZeneca has made two. Lorence Kim, CFO at Moderna Therapeutics, pointed out that both companies' willingness to get creative in partnership negotiations reflects a shared commitment to turning new technologies into drugs for patients. "We present our partners with this ability to tap into our technologies to enable products in creative ways," he said. "We've shown that we're willing to structure the right deal for ourselves and for our partners to get the right commercial rights and economics in place." If both sides are getting what they need out of a partnership, a discussion of whether partners need to own technology is moot, he said.

Moderna's most recent deal, with the cystic fibrosis specialist Vertex Pharmaceuticals, is also its most narrow, covering only a single therapy, which coaxes cells in the lung to produce functioning copies of the cystic fibrosis transmembrane conductance regulator protein. "We will keep doing single-product opportunities" like the Vertex deal, said Moderna's Kim, where the company strikes a partnership with a collaborator that is incredibly deep in a specific disease area. "But we will also tailor future deals to the partner in question and what opportunities are in front of us."

Those opportunities are driven by pharmas' attempts to "look around the corner and anticipate what new potentially disruptive technologies will be out there," said Lorence Kim. "How do they keep their fingers on that pulse? That's what we've been witnessing and taking advantage of."

Not just pharma

Catering to pharma's appetite appears to be the template for a host of platform companies with focuses ranging from traditional modalities such as small molecules and biologics to newer technologies such as cell therapy and gene therapy. And the willingness of companies to access technologies through creative dealmaking isn't limited to large pharma organizations. Even venture-backed startups are re-evaluating the need to incorporate drug discovery technologies into their models.

"At the end of the day, venture-backed companies are in the biology testing business," said Adimab's Gerngross. Companies are often built around an idea about a new disease pathway or a set of new targets, and they need molecules to modulate that biology. "In the past, that required small companies to build an antibody discovery group," which can be expensive and time consuming and requires several full-time employees and a lot of equipment, he said.

Gerngross pointed out that several forward-thinking venture firms are telling their portfolio companies to outsource discovery efforts, and that Adimab has even offered some venture capitalists a template agreement. "If one of your portfolio companies wants something, just come to us. That's where we've seen the most dramatic change in behavior" around accessing technology platforms, he said.

Chris Morrison is a freelance writer for the pharmaceutical and biotech industry.