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Rewiring the Memory of the Public Markets

By bioscentric | Biology

In *The Wide Lens* author Rod Adner explores a question that has dogged entrepreneurs and investors for decades: why do some innovations replace their predecessors rapidly while others only grow gradually? Adner argues that we must view each technology as part of a dynamic technological ecosystem and understand that competition takes place between emergent and old ecosystems, not individual technologies. Innovations fail to gain traction in the market when they arrive early and without a sufficiently developed ecosystem of services, standards, regulations, and complementary technologies to support their success. Inversely, incumbents are sometimes able to maintain dominance precisely because they are part of a more resilient and extensible ecosystem. (https://hbr.org/2016/11/right-tech-wrong-time)

How is this relevant to markets for applied biology? The “first-mover disadvantage” may sound all too familiar to those following the field of engineered biology. Despite raising hundreds of millions of dollars in the past decade, many pioneering industrial biotech

platforms failed to rapidly displace incumbent production methods. Numerous factors, some unique and some ecosystem based, played a role, but the consequences linger.

Looking closer, there are signs that "second wave" engineered biology firms of more recent vintage have learned critical lessons and are benefiting from ecosystem maturation and outlook. The entourage of technologies, interdependent services, adopted standards, markets and (semi) coherent regulations around industrial biology are co-evolving rapidly. This better positions new innovators for success, especially those able to absorb disparate aspects of the ecosystem under one roof, and mitigate their reliance on slow to evolve pieces. But will this shift be enough to make up for the magnitude of the financial losses from the field's first publicly traded companies and refresh appetite for development stage engineered biology platforms? What will it take to rewire the memory of the public markets?

A lingering hangover

The numbers aren't pretty. Amyris, Solazyme (now TerraVia), Gevo, Codexis, Metabolix, and other engineered biology innovators that sought to replace petrochemicals with renewable alternatives have had a rough existence as publicly traded companies. Each stumbled out of the IPO gate and has failed to regain its footing since. All of the stocks listed above have lost at least 95% of their value since debuting, save for Codexis, which is only down 69%. The stock has nearly tripled since 2014 after successfully pivoting from cellulosic fuels to biopharmaceutical manufacturing services.

The last two companies to IPO, BioAmber and Intrexon, have performed better since their debuts in 2013, losing 58% and 7%, respectively. Despite the losses, they have substantially higher revenue totals (Intrexon) and healthier balance sheets (Intrexon and BioAmber) than the pioneers. It has been argued that these stocks are suppressed by the lack of appreciation for the now stronger technology ecosystem around industrial biotech, and investor unfamiliarity with the breadth of applications and markets of biology derived molecules.

But contrast these valuations to biopharmaceuticals, a more familiar class of stock to investors with an ecosystem regarded as largely stable and mature. While gene editing represents new and uncharted territory, the ecosystem that nurture ideas for new therapies through development and to potential commercialization is well developed. So it should be no surprise that CRISPR stocks, which plug neatly into this array, have performed relatively well since their debuts, especially after the recent legal settlement in which the U.S.P.T.O. decided against invalidating any of the original intellectual property involved in the case.

Editas Medicine, holding onto patents from the Broad Institute, has risen nearly 30% since its IPO. CRISPR Therapeutics and Intellia Therapeutics, holding onto patents from the University of California, have risen over 25% and lost 40%, respectively, since their debuts. As it turns out, investors are much more comfortable with the uncertainty of clinical trials than the uncertainty of legal rulings.

This is an important observation. Investors continue to assess the risk of biopharmaceutical businesses (Codexis and CRISPR stocks) much differently than the risk associated with industrial biotech companies. Even though uncertainty exists in each basket of development stage companies, investors have success cases to point to when it comes to novel therapeutics, and a notional belief in the robust stability of the pharma ecosystem. The same is not yet abundantly true — or at least not perceived to be true by investors — in industrial applications of biology.

Moving forward

How do you convince investors that the industrial biotech ecosystem has undergone rapid changes in the last several years and is now capable of supporting not only stronger businesses, but more of them?

Before proposing solutions, it helps to assess the pain points that led to previous failures. One way to interpret the field up to this point is that a lack of market traction and sales growth was due largely to the excessive costs of product. The inability to reign in R&D and production costs stemmed from the challenges of (1) rapidly scaling organism engineering without adding headcount and (2) achieving consistent, reliable, large-scale manufacturing operations across a range of products. Those two gaps in the technology ecosystem represented costs and risks, depended on additional innovation, and ultimately bottlenecked the pace of products coming to market reliably and profitably.

How and where is there progress to show against these structural challenges? Demonstrating recent improvements in the technology ecosystem could persuade the public markets to regain belief. Ginkgo Bioworks provides one illustrative example. The organism engineering startup, Boston based, has invested heavily in automating the design of microbial factories, allowing more strains across more chassis organisms to be engineered and tested at much lower cost. Importantly, Ginkgo Bioworks has decided to consciously address the ecosystem challenge by cultivating strategic alliances with field leaders such as Amyris and Genomatica. [full disclosure: Bioscentric works closely with Ginkgo.]

A partnership with Amyris provides access to commercial scale facilities for piloting and production — without the need to spend hundreds of millions on a greenfield construction project. A collaboration with Genomatica will leverage that partner's process engineering and facility design expertise in commodity chemicals. These two alliances alone enable Ginkgo to access almost 20 company years and $1.2 billion worth of R&D and deployment expertise. Most recently, the acquisition of Gen9 means that in-house DNA synthesis is at hand for cheaper gene length sequences. Finally, close relations with hardware suppliers and vendors allows instrumentation and control systems built to spec.

Separate capabilities and pieces within the ecosystem are being consolidated by Ginkgo. Software, hardware, DNA sequencing, DNA synthesis, 'omics, scale down, scale up fermentation, and DSP process design are native capabilities that are nested within a milieu of vendors, service providers, and partner relationships orienting around Ginkgo. Ginkgo's foundry is the center of a hub and spoke model for bioengineered microbes that then ship to partners and clients where they are scaled, ranging in market size from fine to commodity. An ecosystem has taken shape around the firm, allowing former bottlenecking dependencies on slowly developing parts of the tech chain to open up. For a variety of reasons, some strategic and some structural, the ecosystem option wasn't executed on by pioneers of the field, but the emergence of the Ginkgo ecosystem bodes well for the new generation of industrial biotech firms. It permits great compounding effects for the firm and others that can track this model or embed into the same ecosystem. While it may be too early to determine the ultimate success of this approach, it marks an important step for moving forward — for both startups and the public markets–and may the step one towards rewiring the memory of the markets.