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Lessons From Hollywood: A New Approach To Funding R&D

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Could science-based industries benefit from a financing model similar to one used to make Hollywood movies?

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BY ANDREW W. LO AND GARY P. PISANO

SCIENCE-BASED INDUSTRIES such as biotechnology offer the potential of high growth, but they are fraught with risk. The payoffs, if they ever come, can take many years to materialize. Amid intensifying capital market pressures for short-term financial results, even large and successful companies are finding it increasingly challenging to justify longer-term risky research and development investments. The challenge is particularly acute in research-intensive fields including biotechnology, nanotechnology, and advanced materials, which involve massive R&D investments, extended gestation lags before investments bear fruit, and high risks of failure.

Many would argue that given these requirements, such industries don't lend themselves to corporate R&D and are more suited to early-stage venture capital (VC) investment. However, even though the traditional venture capital/entrepreneurial model has been shown to stimulate innovation in a wide range of technology settings (software, computers, Internet, electronics, etc.), it wasn't designed



THE LEADING QUESTION

Is there a more effective way to finance early-stage R&D in fields such as biotech?

FINDINGS

- ▶ The authors suggest creating project-focused organizations whose purpose is to conduct specific R&D projects.
- ▶ This model is similar to one used for movie projects.
- ▶ Project-focused organizations can minimize overhead and contract out for resources as necessary.

to deal with the costs, risks, and slow payout of science-based industries. In biotechnology, for example, the journey from basic scientific discovery to fully approved drug can span 10 to 20 years and require investments exceeding \$2 billion. Moreover, only a tiny percentage of drug R&D projects ever result in approved drugs; a recent study in *Nature Biotechnology* calculated a success rate for drug development from initial indication to approval by the U.S. Food and Drug Administration (FDA) of only 10%.¹ The success rate was only about 7% in important therapeutic categories such as oncology. In comparison, the Google search engine was operating on Stanford University computers about a year after Sergey Brin and Larry Page, cofounders of Google Inc., began collaborating on their research. Although venture capital continues to flow into industries like biotechnology, there has been a significant shift away from funding ventures at the earliest stages of the R&D cycle.²

The typical science-based business startup is not unlike a long-range multistage rocket mission: Each stage must fire perfectly for the next step of the mission to begin. If any stage fails to execute, the entire mission fails. Even investors with a high tolerance for risk are deterred by the uncertainty of the risk — the “unknown unknowns” associated with a lack of well-defined indicators of day-to-day performance. Why bother to invest in such uncertain prospects when you can select projects with clearer and less daunting payoffs?

As Ramana Nanda and Matthew Rhodes-Kropf of Harvard Business School have argued, there are even good theoretical reasons why the venture capital model fails for long-gestation, high-risk science-based businesses.³ A key concern is that lack of availability of future rounds of financing can shut off the flow of VC funding abruptly, even when there are no indications that current funding is in jeopardy.

In this article, we suggest an alternative structure for undertaking the long-term, high-risk, highly capital-intensive R&D programs that typify science-based settings. We refer to this structure as a *project-focused organization* (PFO). PFOs are entities that are created with the sole purpose of conducting a specific R&D project. When the project is completed, the PFO is disbanded, residual

returns (if there are any) are distributed to investors, and intellectual property and other assets are sold off. We think PFOs are an attractive alternative to both the traditional vertical integration model and the traditional venture capital/entrepreneurial startup model. We discuss how such PFOs could work in practice, using the example of biopharmaceutical R&D, although we argue that the structure has much broader applicability.

Revamping How We Innovate

Researchers innovating in a science-based context must overcome two specific challenges. First, they need to raise sufficient capital to fund a long-term, highly risky, and very expensive project. Second, they must have a governance mechanism for allocating capital (human and financial) and conducting projects. Financial engineering has provided a solution for the first challenge. As one of us (Andrew W. Lo) has shown, if you combine a large number of independent high-risk projects into a single megafund, the increased likelihood of at least one success and the reduced risk from diversification makes the investment considerably more attractive. To reduce the risk of failure to statistically small levels, a very large amount of capital may be needed — as in the case of biomedicine — which can overwhelm the VC industry. However, that can be accommodated by debt markets. Even small portfolios of projects can diminish risk enough to attract significantly more capital than today’s levels of investment.

But raising the capital for research may be the easy part. The process of commercializing scientific discoveries often follows the startup-company model: Startups must first vie for venture capital to advance their research, and only after reaching certain milestones will deep-pocketed corporate partners be willing to acquire them to shepherd products through the later stages of commercialization. We see this model operating all the time in the biomedical world: Startups raise capital from venture capitalists, conduct the translational research needed to move the scientific concept into clinical trials, and then sell the company or license the project to an established pharmaceutical company that distributes the product globally.

Traditionally, the dominant organizational model for technological innovation has been the

corporation. If an innovator has a new idea for a project, he or she creates a new enterprise to attract capital and talent to carry it out. If the project is successful, the innovator, the founding team, and the investors are typically rewarded by appreciation in the market value of the enterprise, through publicly traded shares, or the sale of the entire enterprise to an established company. Since the end of the financial crisis, Silicon Valley, Cambridge, San Diego, and other hot spots have been awash in startups.

However, even in places like Silicon Valley, innovation is a two-tiered system made up of corporate entities and projects. The innovation happens at the project level; enterprises take responsibility for allocating resources across projects and managing individual projects. It was economist Ronald Coase's insight that firms exist to reduce transaction costs.⁴ For example, a single budgeting process is usually cheaper and more efficient than writing many different contracts, one for each internal transaction. Then there are the important intangibles of management, to ensure that incentives are clearly aligned with goals. The notion that enterprises should organize innovation has existed for so long and feels so natural that it seems to be the only way to approach innovation. But is it?

Over the past four decades, the biotechnology industry has spawned more than 3,000 new businesses. Although there have been a number of notable success stories (Amgen, Celgene, Genentech, Genzyme, Gilead, etc.), the vast majority have not been profitable. Although failure is also common among startups in other industries, the cumulative profits of the winners generally exceed the cumulative losses of the losers. However, between 1984 and 2004, the cumulative losses in *publicly traded* biotech companies exceeded cumulative profits (and, of course, virtually all privately held biotech companies lose money, so the cumulative losses would be even greater if we consider them).⁵ Even for the most successful biotech companies, remaining independent has been challenging. In the past five years, two of the industry's most successful players, Genentech and Genzyme, have been acquired by major pharmaceutical companies.

The returns on innovation in the biotechnology industry — and in biopharma research, in particular — have been highly skewed. This reflects the basic nature of biomedical research. In other

industries, many important breakthroughs are well within the scientific frontier. They may qualify as engineering or conceptual triumphs, but they don't address unknown unknowns. By contrast, an innovation in biotechnology (for example, the development of a first-in-class drug) represents a new scientific advance, the nature of which is inherently unpredictable. What's more, the time period over which such risks must be borne can span a decade or more. As with a long-range rocket mission to a newly discovered planet, no one can forecast what the researchers will ultimately find. The incredibly long odds of successfully putting a drug on the market mean that very few biotech startup teams will ever launch a single drug; even more daunting, those that *do* have equally slim odds of doing it again.

Project-Focused Organizations

The combination of high failure rates and high potential rewards often means there's a misalignment of incentives between companies and projects. It's easy for startups to overcommit to projects, for reasons that are subtler than the sunk-cost fallacy, although corporations can fall prey to this as well. For example, a corporation might invest in multiple approaches to a new project because the potential payoff is so large and the false-negative rate (the chances that a truly high-value project will falsely appear to be a loser) is still unknown. In practice, this approach can result in a failure to cut losses on projects quickly enough. On the other hand, overemphasizing a *single* approach can lead to a loss of dynamic capability. The rapidly evolving frontier of knowledge means that corporations need to acquire new sets of capabilities over time. Large companies in science-based industries often achieve this by exploiting economies of scale: They acquire startups and pursue many projects at once. Smaller enterprises are often burdened with high overhead and don't have the resources to adapt as easily.

For these reasons, we propose that a form of governance centered on the project rather than the company may be a more efficient way to organize innovation in science-based industries. After all, a project is a natural unit for innovation. The trend of large pharmaceutical companies buying promising startups is an implicit acknowledgment of this.

How might you put this view into practice? To begin with, it's necessary to address the issue of

overhead. Instead of buying their own plants and equipment, individual projects can contract out for resources as necessary. Instead of hiring scientific and managerial talent for open-ended periods, they can hire people for a particular project or selected phases of the project. And instead of allowing companies to shift capital from one project to another, investors could choose the project they want to invest in, with the understanding that they will receive returns only if that project succeeds.

The Movie Industry Model

The model described already exists in the movie industry. The highly integrated Hollywood studios of yore have given way to individual movie projects as the central organizing unit. Movie projects are organized as independent entities typically incorporated as their own limited liability corporation or similar legal entity. The key resources for each film — financing and human talent — come from different sources and are committed specifically to that project. The project is not a permanent entity but acts as a contractual clearinghouse for its various obligations, which include returns to the initial investors and payments to the creative talent with residual claims. Once the movie has been distributed, the film entity essentially vanishes except as a legal mechanism to transfer payments during the film's lifetime — which, in today's information age, is essentially forever.

Movie projects are similar to biopharma projects in organizationally important ways. For one thing, they have a high failure rate (defined as earning less than the cost of production). Although many movies are formulaic, the tastes of audiences change in unpredictable ways,⁶ a state of affairs that is analogous to the unknown unknowns of the biopharma industry. Movies can also have a long development time, much like the drug-development process. For example, the intellectual property for *Spider-Man* was first optioned in 1985. When the film was finally released 17 years later, it became a box office hit, grossing more than \$400 million in the U.S. and more than \$800 million worldwide.

Movie projects can be financed independently, which is the basis for the independent film movement. However, most major U.S. movies are still produced by large movie studios such as Paramount Pictures, Twentieth Century Fox, and

Warner Bros. Traditionally, a movie studio provided projects with the soundstages and back lot for filming — hence the name, analogous to an artist's studio. It also provided office space for management, financing, distribution, and marketing, and theaters for viewing until the Supreme Court ruled in 1948 that studios could no longer own movie theaters (in *United States v. Paramount Pictures, Inc.*). From the projectcentric view, the movie studio is a specialized organizational structure that exists to aid movie production companies in bringing their projects to fruition.

The movie industry is not the only setting where PFOs have taken hold. As video game development costs have increased and the potential downsides of failed projects have escalated, the video game industry has explicitly organized itself along project lines. This was the case, too, in the pre-Internet music industry, where record companies treated albums as distinct projects as opposed to a continuous stream of music. A key development came in 1997, with the creation of a PFO to facilitate the issuance of an asset-backed security based on music royalty streams. Music royalties were bundled into catalogs that continue to make payments to the royalty owners (in other words, the artists or their estates) long after the initial recording of an album or, more often today, the recording of a digital single. Such royalty streams can form the basis of bond payments on an asset-backed security. One of the earliest PFOs was based on the royalties from rock musician David Bowie's first 25 albums; Bowie received \$55 million up front, and investors received payments for a period of 10 years. The Weinstein Co. and Miramax Film Corp. have also issued asset-backed securities tied to film revenues, thus suggesting how securitization of future pharmaceutical sales and royalties might finance a biopharma innovation megafund.

Adapting the Model to Biotech

What would a PFO look like in the biotech industry? Each project would have the equivalent of a movie producer — a researcher who believed in a new drug concept and was working to develop the concept into a therapy approved by regulators. But instead of bringing it to a venture capitalist or a pharmaceutical company, the researcher might pitch the idea to



Like biopharma projects, movies can have a long development process. The intellectual property for *Spider-Man* was first optioned in 1985 — but the film was released 17 years later.

an innovation studio, which could be a single investment fund or a consortium of co-investors, with its own state-of-the-art facilities. If the innovation studio gave the project the green light, the startup would set up shop in the studio's facilities. Much of the project's operation would be outsourced (for instance, evaluation and testing, toxicology studies, animal models, pharmacodynamics, and structure determination), in a way analogous to the use of a network of support businesses involved in movie production (for example, set design, costumes, lighting, special effects, shoot location, and catering). The idea is to have third parties doing as much as possible to maintain the project's "weightlessness."

Most participants in the startup project would be hired as contractors and consultants just for particular tasks and phases. The only full-time employees would likely be the project director and a small core team of critical talent, who would be in a privileged position for any future possible revenue. Star talent with proven track records should be able to direct resources efficiently for their project and, as in the movie industry, negotiate for bonuses, residuals, and percentage points.

Innovation studios, be they divisions of large pharmaceutical companies or groups of entrepreneurs, would provide the bulk of the financing to the startup project. Dreamworks SKG, the studio founded by director Steven Spielberg, former Disney executive Jeffrey Katzenberg, and record company executive David Geffen, is an example from the movie industry. Initially funded with \$500 million from Microsoft cofounder Paul Allen, Dreamworks later issued asset-backed securities based on its intellectual property and expected future income streams to fund its operations. The innovation studio would oversee the startup project. The financing deal between the studio and the project would set project milestones and specify exactly what rights the studio had regarding the project; one important right would be a right to withdraw financial and material support.

The major difference between this process and a simple buyout of a startup is that the startup keeps its intellectual property rights until the project is complete. If successful, the project sells its rights to the studio and receives a structured compensation, as specified in the contract. If unsuccessful, the

project team can try their luck at another studio. The studio, not the project, owns any innovations discovered at the studio and assumes responsibility for scaling up production, marketing, and distribution. Ultimately, the project team will disband, ready to move on to other projects.

Organizing innovation through PFOs has a number of benefits. For investors, it's the difference between having a portfolio of individual options and having an option on a portfolio. Investors can diversify across multiple projects, picking and choosing according to their own preferences. For companies, PFOs provide a way to keep overhead to a minimum, with only the core team in-house and other capabilities added as needed. The analogy to the entertainment industries suggests that star power can play an important role. Good researchers and research directors also need to be excellent entrepreneurs to be fully rewarded for their talents. In a star system, they can devote themselves to the important processes of innovation and know that they will be compensated accordingly.

Making PFOs Work

The biggest challenge in making PFOs work is the absence of two core elements of industry infrastructure: (1) a standardized platform for development, and (2) a well-functioning liquid market for proof-of-concept projects.

Lack of a Standardized Platform In the pharmaceutical industry, the term "platform" is widely used to describe a set of related technologies that companies can use to create drugs. However, in other settings, it has a different meaning. It refers to an organization that sits at the hub of a network of buyers, sellers, and users. Amazon.com Inc., for example, provides a host of value-creating capabilities and infrastructure that permit buyers and sellers to efficiently find each other and arrange transactions. For sellers, Amazon provides services for selling payment systems and order fulfillment, all designed to make it easier for sellers to operate and to find potential customers. The more sellers who join the Amazon ecosystem, the more attractive it becomes as a place to shop; the more customers who choose to shop in the Amazon ecosystem, the more attractive it becomes as a place for companies to sell. Amazon

creates value by making a set of large fixed-cost investments—such as server farms, Web infrastructure, warehouses, and logistic systems—that can serve a massive number of buyers and sellers, exploiting the economies of scale. Individual retailers—even large ones—would be hard-pressed to make comparable investments, but they can join the Amazon platform at a relatively low marginal cost.

Currently, outsourcing in pharmaceutical development is extremely cumbersome. There are dozens of companies offering services ranging from screening, toxicology studies, and preclinical development to clinical-trial design and execution, operations process development, and manufacturing. If a biotech company partners with an established pharmaceutical company, the pharma partner typically assumes a significant chunk of the development tasks. Yet every organization tends to follow a different approach, using different protocols, different assays, and different standards. What's missing is any semblance of a “plug-and-play” platform that would accelerate drug development and reduce its cost. Instead, when a piece of a biopharma project is outsourced, the project originator and the contractor or development partner must go through a learning curve together. Even worse, the incentives of the partners are often misaligned. The pharmaceutical company, for instance, may have internal programs that compete directly with its external partner. Nor do third-party contractors necessarily solve the problem, since some of them also have their own proprietary programs.

One reason the PFO model works so well in the movie industry is that, even though movie studios outsource many specific functions, they still control the platform: They provide overall project management and process integration. Of course, no two industry environments are identical—Hollywood's version of “plug and play” could be very different from how it might work in the biopharma industry.

One template for how deals might be structured can be found in a clinical trial led by the University of California, San Francisco.⁷ The clinical trial in question is a public-private partnership called I-SPY 2. It involves a host of oncologists, cancer biologists, and biostatisticians from the National Cancer Institute, the Food and Drug Administration, 20 cancer research centers in the U.S. and Canada, and a number

of biopharma companies, all focused on an effort to develop new breast-cancer therapies more efficiently. The collaboration is organized as a PFO—it will exist only for the duration of the trial, after which it will disband. It uses patient outcomes to inform treatments and has the ability to test new treatments in half the time and at a fraction of the cost of traditional trials. Although the trial is still ongoing, it has already identified biomarkers and efficacy for two drugs, with several more candidates in the pipeline.

I-SPY 2 provides a vision of what it may take to create a standardized set of development processes and services in the biopharma industry. To enable rapid “plug and play” integration, platform development providers need to make their development process as transparent as possible, a step that includes making critical building blocks (such as development protocols, databases, and development tools and methods) open and available. As a result, they need to adopt a different business model than traditional pharmaceutical companies. Rather than trying to generate revenue from a few big winners, platform providers would seek to capture small shares of value from a large number of projects. With the emergence of targeted therapies, precision medicine, and drugs for rare but serious diseases, such a business model is becoming more feasible and compelling.

Lack of a Liquid Market In addition to requiring a standardized platform, the PFO model is based on the assumption that value from a successful pharmaceutical proof of concept can be captured through the sale of the asset to an established pharmaceutical company. The buyer takes over large-scale Phase III trials, the regulatory approval process, and commercial marketing and distribution. This is not a trivial assumption. Today, while many biotech and pharma companies acquire projects at the proof-of-concept stage via various types of licensing and development agreements, the process typically is extremely cumbersome: Negotiations, due diligence, and internal approvals can drag on for many months; valuation is highly subjective; and information asymmetry between the project originator (the biotech company) and the buyer (the pharma company) makes it hard to reach compatible valuation decisions. Even after the fact, parties may disagree on whether

agreed-upon milestones were met. The process in no way resembles an efficient market.

Drug development, to be sure, is a complex undertaking. Although there are many drug projects under development, making comparisons is often difficult. While it may be possible to compare similar inhibitors for the same type of cancer, comparisons across classes (for example, an inhibitor for cancer vs. one for diabetes) are meaningless. Because there are often so few projects within the same class, the market for proofs of concepts is thin compared with the markets for stocks, bonds, commodities, and even real estate. In addition, the value of a drug program is determined by a relatively large number of parameters, some of which are known but difficult to assess *ex ante*, and some of which are unknown and unknowable *ex ante*.

Although creating an efficient market for proofs of concepts in drugs will be difficult, we think it may be possible to make the market work better, at least for certain kinds of programs. One step would be to standardize the definition of “proof of concept.” The term is widely used today in the industry, but rarely does anyone specify what is meant by “proof” and what is meant by “concept.” Pharmaceutical companies themselves could help standardize the definition by being transparent about their specific standards for a proof of concept in specific therapeutic classes. Companies don’t need to agree on the same standard; the market can sort out which standards are best. Nevertheless, the industry must get past the point where project originators are guessing about what proof-of-concept standard pharmaceutical companies will find acceptable. Depending on the therapeutic category, it may not always be possible to specify standards in advance (especially for new targets and new therapeutic approaches). However, for more established therapeutic areas and better-known targets, a public and transparent statement of requirements may be more realistic.

In other industries, third-party evaluators and auditors can lead to improved efficiency. In real estate, for example, banks use third-party appraisers to understand the value of a piece of property. For stock markets there are investment analysts, and for debt markets there are rating agencies. Unfortunately, as we learned during the financial crisis, there are risks of conflicts of interest. But that experience only

underscores the critical importance of objective and high-quality third-party evaluations.

In the pharmaceutical industry, third-party evaluations don’t exist until the final stages of a development program, when a government agency (in the United States, the FDA) evaluates all the data and makes a final judgment about a drug’s safety and efficacy. However, for the purposes of creating a market for proofs of concepts, the review comes too late. We are not suggesting that reviews of proofs of concepts need to be done by a government agency; in fact, we think it would be more efficient if objective, well-informed third parties in the private sector did them. Today, there are no such specialists. Companies do their own evaluations using their own standards and approaches, and typically the data are not public. A shift to third parties and transparent processes that use clearly stated standards and well-defined methods would create a more efficient market for proofs of concepts, and thus a more efficient drug R&D process. Although no entities perform this function today, we see no reason why such an absence should persist given the value such a function would generate.

In our view, PFOs would enhance the efficiency of the overall R&D process in the biopharma industry by enabling better diversification of risk, more dynamic resource allocation, and better alignment of incentives. However, one size doesn’t fit all when it comes to organizing innovation. Even within the same industry, there can be competing models. In the movie industry, for instance, the highly networked model of traditional studios is juxtaposed with the highly vertical structure used by Pixar (now part of Disney). Similarly, we don’t expect the PFO model to completely replace traditional venture-funded biotechs or traditional pharmaceutical companies. Where significant up-front investments are needed to develop new technological capabilities or create entirely new markets, it may be more efficient to establish a more permanent entity that can leverage investments over a series of future projects. However, in rapidly changing industries where a single scientific discovery can make a dominant technology obsolete overnight, the PFO offers significant advantages.

As noted, some additional institutional changes and structural developments in the industry will be required to alter the economics of pharmaceutical R&D.

But if the history of innovation over the past century has taught us anything, it is that institutional and structural innovations are critical enablers of technological innovation. If necessity is the mother of invention, we expect to see the biopharma industry develop several new business models in the near future.

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Commentary on Lo and Pisano's Proposal

Phillip A. Sharp



Phillip A. Sharp is Institute Professor at MIT and a researcher at MIT's Koch Institute for Integrative Cancer Research. He was a cofounder of Biogen and received the 1993 Nobel Prize in Physiology or Medicine.

The idea of developing a translational step between basic science and therapeutics that's funded and nurtured by a fund that monetizes the risk over tens, if not

hundreds, of initiatives could be a wonderful addition to the whole biomedical and pharmaceutical environment. I think it should be tried. You could share services such as management,

laboratories, intellectual property, toxicity — and that could reduce the costs of translating advances into pharmaceuticals.

I agree that there is inefficiency in the current system as it is constructed. For example, there is a subset of projects that get dropped that could be successful if they were carried further. Behind every successful new drug there is a story of a

champion who kept it alive when the company tried to kill the project, or someone who resurrected it on their own time after it was killed. But what does that tell you? One thing it tells you is that people frequently don't have enough data to decide if a project is valuable enough to continue investing in to take it to fruition. There are a lot of unknowns that make it hard to determine whether to keep funding something. However, just because people can conceive of something doesn't mean it's going to be valuable or useful in the marketplace, or that it will benefit people.

The authors correctly identify the challenge of establishing proof of concept. Yes, it could be helpful to have regulatory agencies define what proof of concept is and to have a scientific and systematic way to prove clinical results. But given the uncertainty in our knowledge of biological systems, the variation of clinical needs in the real marketplace where people are being treated, and in some cases the lack of good biomarkers that can show the nature of the pathology and the response to the treatment, that's a tall order. There's just a lot of uncertainty.

Every year, the U.S. government, pharma companies, and foundations and philanthropies invest somewhere close to \$100 billion in biopharma-related research. Although the initiative the authors envision is relatively modest, it could play an important role in shaping the direction of how we develop new pharmaceuticals and treatments or

preventions. It could provide double benefits: the benefit of the actual outcome and the benefit of being able to lessen the risk (and increase the efficiency) of the process. The second benefit might be the more important one.

Getting to the point where the funded projects generate revenues to sustain the cost of the bonds is likely to be a big challenge. Although the analogy to Hollywood may be helpful to people who understand how movies are made but don't understand what a gene is, I don't

think it's that useful. Ultimately, people are going to judge this idea based on whether the people who raise the money can do what they say they will do. Are they able to monitor the process? How do they monitor it? If you're asking investors to take greater risk because the investment provides societal benefit, what is that benefit? Will it result in increased efficiency and productivity for the whole drug development process (or the translation of science into better health care)?

Noubar Afeyan



Noubar Afeyan is senior managing partner and CEO of Flagship Ventures, an early-stage venture capital firm in Cambridge, Massachusetts, that he cofounded. He is also a senior lecturer at the MIT Sloan School of Management.

In the biotech industry, early-stage funding is a perpetual challenge, although it's been less of a problem in the past three years. Facing their own funding difficulties, we have seen during the last decade the increased popularity of "virtual drug-development companies," backed by certain venture capital firms. This approach involves an experienced research manager with a single drug asset developing it using outside contractors. Virtual drug-development companies have many similarities to what Lo and Pisano offer as the "project-focused organization," or PFO. "Virtual biotech companies" have also used several financing innovations, including option-based deals (where investors have rights to buy the company upon certain milestone achievements).

What's different about what Lo and Pisano propose is the idea of syndicating the risk — the value attribution and the financing — from day one (the way movies do) so you know what different components and different contributors stand to get if the project succeeds. That's not something the virtual biotech companies have done. (In the standard model, early-stage investors take the financial risk and *hope* pharma will reward them for it.) We've seen virtual developers, but we *haven't seen* risk syndication on the financial side.

Lo and Pisano describe PFOs, which they say will exist as long as a project is being advanced toward milestones. They propose that PFOs will be advanced through "innovation studios," which, unlike the PFOs, could be subsets of large companies or pharma companies or

bands of entrepreneurs working together. However, it's unclear to me how decision making will work. For example, who gets to decide when and whether to cut off funding — the innovation studio or the PFO? If the innovation studio, which is supposed to be enabling the PFO, has the ability to cut the funding of a PFO, I'm not sure what the PFO can actually decide on its own. The idea of an innovation studio is interesting and relatively novel — it strikes me as potentially as powerful as the PFO (which would be a legal entity as opposed to an organizational entity). But it's not entirely clear how the governance would actually work.

As innovative as the innovation studio model may seem, it's less “out there” than it sounds, which I think is a good thing. Currently, there are a number of entities (including some leading biotech companies such as Moderna, Alnylam, and Agios) that have set themselves up as platforms to develop multiple assets, some internal, some external. These companies are essentially innovation studios with specific project assets *they* (as opposed to the individual project managers) control. They are running each of them as individual projects within their studio — most of them internal but some from the outside.

In my view, one big unmet need in the biopharma industry is how to create a fair financial structure on day one that rewards all the elements of these new innovation supply chains. Because of all the ongoing experimentation in the industry, with virtual organizations and contract research and contract manufacturing organizations, we've seen deals featuring options instead of, or in addition to, equity deals, and partial acquisitions up front (built-to-buy models). The good news is we're seeing lots of experimentation. However, all of these models put a cap on the upside. The challenge is finding ways to attract the best talent and the best innovations without limiting the upside to talent if a drug is successful. At the end of the day, it's a free market. What you want is the *best* talent as opposed to talent that, for whatever reason, isn't getting funded.

Mark E. Davis



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I applaud Andrew Lo and Gary Pisano for stimulating people to think about new ways to finance groundbreaking endeavors. They are working on finding new ways to tackle some very difficult problems, and I think that it's great

that they challenge standard paradigms.

I like the idea of the project-focused organization (PFO). Organizations of this type that have in-house expertise to help inventors translate their discoveries into approved drugs would

be most helpful; I have thought quite a bit in recent years about how such organizations could be useful to those working on cancer therapeutics. Lo and Pisano describe interesting ways PFOs could be assembled and financed.

As I see it, though, there are some implementation differences between moviemaking and turning research and research discoveries into real drugs. Most researchers are more like writers than movie producers: They have a concept — possibly even a big scientific breakthrough — but they often don't have a clue about how to take it from there and turn it into a drug. That's where they need help, and focused PFOs could assist in meeting those needs.

A big issue in biotech, as Lo and Pisano point out, is the lack of a standardized platform. Particularly if you are doing high-risk research, you don't have standard puzzle pieces — you often have to invent things as you go. When you run into hiccups — and you *will* run into them — you need people who will dive in and solve the problem. It's not always possible (or even desirable) to contract for what you need to do in pieces. In my experience, the more you contract out, the more chances you have for failure: People do what they're contracted to do, and important things slip through the cracks. That's why I like the concept of a small biotech company developing high-risk types of therapeutics mainly in-house. When things go wrong, the people who are

committed to the idea are going to put their whole life into fixing it.

With any new concept, there are positives and negatives, and the approach Lo and Pisano

outline is no different. On the plus side, it is stimulating. A negative is that if a project runs into problems and you're not willing to shift capital, it may die. Therefore, success rates

may in fact decline rather than increase using this model of financing. Overall, I find the Lo and Pisano ideas intriguing, and I believe they will stimulate lots of positive discussion!

Josh Lerner



Josh Lerner is the Jacob H. Schiff Professor of Investment Banking and head of the entrepreneurial management unit at Harvard Business School. He is the author of *The Architecture of Innovation: The Economics of Creative Organizations*.

Lo and Pisano make an intriguing proposal: to create “project-focused organizations” to finance long-running, risky innovative projects. The article identifies a true problem and makes a creative suggestion as to how to address it. But the opaque nature of early-stage innovation and the opportunistic behavior that can rear its ugly head in these settings suggest that there are no easy answers here.

The authors correctly highlight the limitations of venture capital, the primary mechanism for financing high-risk early-stage projects. Venture capitalists, while they may style themselves as long-run investors, are at best providers of medium-term capital. The pressures to return capital to their limited partners and to go back on the fundraising trail drive venture investors to start thinking about exit investments after only a few years. Handing off these companies to the public market is frequently rocky and

hostage to the ebb and flow of market sentiment. Thus, it is no surprise that venture capitalists' returns from investments that require longer gestation periods (such as cleantech, advanced materials, and biotechnology) have lagged those of information technology and communications, which frequently reach maturity far sooner.

A key concern with this proposal, however, relates to the information problems that typically surround early-stage projects and the opportunistic behavior that often emerges in these settings (something economists call “agency problems”). Venture capitalists seek to limit such problems by intensely monitoring the new ventures in their portfolios, doling out funds in modest-sized bites and linking further financing to tangible progress, and writing preferred stock purchase agreements with draconian terms. They operate this way not out of mean-spiritedness but rather

because they fear that entrepreneurs will continue to pursue projects even if they encounter major setbacks. Venture investors realize that inherently optimistic entrepreneurs are unlikely to admit defeat and return money to their investors.

It is one thing to create an organization to provide financing for a set of already-issued music albums (as was done in the case of the “Bowie bonds”) where the product was well understood and the risks modest. More risky, but still plausible, is raising funds to finance a movie: The timeline of the production process and the budget tend to be well understood. But in early-stage entrepreneurial settings — particularly in the high-risk fields highlighted here — both timeline and the budget are full of questions. To provide a large sum to the entrepreneur up front is to ensure the funds will be spent but does not ensure the project will be a success. I urge the authors to explore ways to emulate some of the key aspects of venture capital governance — such as doling out funds in modest-sized bites and linking further financing to achieving agreed-upon goals.

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