## nature biotechnology

## Expanding the innovation pool

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nvestment in biomedical innovation is not what it once was. Millions of dollars have fled the life sciences risk capital pool. The number of early venture deals in biotech is smaller than ever. Public markets are all but closed, biotech-pharma deals increasingly back-loaded with contingent, rather than upfront, payments. Paths to market are more winding and stonier. Government cuts are closing laboratories and culling blue-sky research. Never has there been a more pressing need to look beyond the existing pools of funding and talent to galvanize biomedical innovation.

This issue highlights several new ways of thinking about funding life sciences innovation in academia. It explores the increasing prominence of corporate venture funding—and the potential of university-based venture funding.

One popular idea is to find mechanisms of spreading risk, exemplified by the limited liability holding-company model currently adopted by certain traditional venture capital groups (e.g., Atlas Venture Development Corporation), nonprofit organizations (e.g., Fast Forward) and even state governments (e.g., the Israeli Life Sciences Funds). In this arrangement, several assets (in essence, R&D projects that can be owned) are simultaneously developed, each within its own business unit under an umbrella holding company. The model not only allows many 'shots on goal' and reduces risk, but also gives shareholders the prospect of returns that are both earlier and potentially more frequent than those from traditional companies.

A related means of spreading risk and funding cutting-edge discoveries is seen in arrangements like BioPontis Alliance in the United States or the UK's IP Group, which through formal arrangements use experienced advisors to fish in academic intellectual property pools for assets that can be developed in a capital-efficient manner using contract research organizations.

All the above approaches aim to use the existing pool of funding more efficiently. But a new proposal—suggested by Andrew Lo and colleagues (p. 964)—intends to expand that pool. Their 'megafund' model creates a capital structure that will attract investors across a spectrum of risk tolerance to fund development within a portfolio of assets that is so large it can produce a dependable flow of successes, despite high product attrition rates. Indeed, the scale of the fund would be unprecedented—on the order of \$5–\$30 billion—some destined for buying equity and the rest provided as debt secured against 'research-based obligations'.

The model is exciting because the spectrum of risk and return would likely attract pension funds, insurance companies and other large institutional investors, which have mostly eschewed biotech investment. The big question, of course, is whether an industry-savvy team would be able to effectively manage the assets in such a large financing mechanism.

Another opportunity for expanding the biomedical innovation funding pool is the internet. Just as charities gather donations online, citizens' fundraising could trawl the deeper ocean of net worth teeming with small fish. This has already worked for innovative firms in France where the tax-free scheme Fonds Commun de Placement dans l'Innovation raised over €6 (\$7.7) billion from hundreds of thousands of people investing €20,000 (\$25,800) or less. The UK Bioindustry Association now wants a similar scheme in Britain.

Megafunds and citizens' fundraising, if realized, would democratize life sciences and expand the funding pool. But what about expanding the talent pool?

Today, R&D is globalizing and the research world is flattening. Many outstanding researchers are in, or returning to, emerging economies where funding and resources are becoming ever more plentiful. The problem is that these regions still lack commercial ecosystems like those in the United States that draw together investors, management and research talent. In the short term, US investors and companies can partner with investigators in emerging economies to translate their discoveries (see p. 903). In the longer term, other commercialization solutions will be needed.

One way in which industry and investors will be able to interact with academic researchers in far-flung places will be through traditional academic-industry precompetitive consortia (e.g., the Structural Genomics Consortium, which already is seeking partnerships with academics in emerging countries through its open research environment). Another way is online social networking via such services as Knode, which is launching this month (p. 901). The site features profiles of investigators, including publicly available information on their specialties, patents, grants and publications. US and European investors and/or company scouts will likely initially use the service to consolidate their own knowledge of local faculty. But going forward, one can envisage that such tools could facilitate networks with researchers further afield, such as those in Latin America, Asia or Africa.

There is no doubt that the current biomedical commercialization ecosystem needs rejuvenation. Much of what risk capital and industry are now doing is simply shifting existing resources around to more efficiently capitalize nondisruptive innovation. As startups no longer expect to find funding on public stock markets, the only 'exit' for biotech assets is through trade sales to a shrinking number of larger firms. What's more, multinationals increasingly bypass biotech altogether, working instead directly with researchers at public institutions—but on a scale that is too small, supporting too few ideas.

All this means that a dwindling number of big pharma and device corporations now monopolize the funding environment for biomedical innovation. They dictate the innovation agenda at its outset and at its culmination. They dominate decisions on which innovations receive development resources. And they control the value calculus.

For all these reasons, 'out of the box' mechanisms that expand the talent available and capture more disruptive innovation have never been more important.