Pharma's role is not to bankroll biotech

To the Editor:

The editorial in the February issue entitled 'The worst of times, the best of times'[1] is well meaning and timely but misunderstands the nature of big pharma's relationship with small biotechs.

Your hypothesis—"big pharma should be more proactively investing in cash-hungry biotech companies"—is supported by data showing large companies have cash reserves plus two impossible-to-prove assertions. First, that we underestimate the "promising products" from "undervalued" biotechs; second, that biotechs are our "drug discovery engine."

Let's start with the word "should" in your hypothesis. Those of us who manage R&D investments prefer the word "must." We must invest our shareholders' funds in areas of unmet medical need. We must consider the feasibility and/or practicality of the science and likelihood of success. We must have evidence that payers will value our experimental medicines.

All this acknowledges a simple truth of our industry—there is no shortage of good ideas. Instead, we are exhilarated by the enormous number of opportunities—from within our own laboratories and from outside. Success is picking and nurturing those few with real potential. At Pfizer (New York), our choices are guided by the criteria above plus a five-point strategy that includes the directive "pursue the best external science."

As president of global research and development at Pfizer, I oversee an extensive pipeline. The majority of projects in that pipeline have come from our own laboratories, but I gladly acknowledge those discovered elsewhere. Our drug discovery engine is, in fact, a broad federation of in-house and external science. We are doing everything possible to maintain that diversity. Together with our Biotherapeutics and Bioinnovation Center, we fund academic work, incubate startups, collaborate on early science and partner in development. Two examples illustrate how, sometimes, we take on all the risk.

Sutent (sunitinib malate) is Pfizer's oral multi-kinase inhibitor indicated for the treatment of advanced renal cell carcinoma and gastrointestinal stromal tumor (GIST). Other indications are under investigation. It was discovered by the biotech company Sugen (formerly of San Francisco, before acquisition by Pfizer in 2003) but was not that company's first choice for development. The medicine's success is a tribute to Sugen's chemistry, plus significant scientific, medical and other investments from Pharmacia (Kalamazoo, MI, USA), then Pfizer.

Acquired as part of Pfizer's 2006 purchase of Rinat (S. San Francisco, CA, USA), tanezumab is a humanized monoclonal antibody designed to have high specificity and affinity for nerve growth factor. Clinical efficacy was recently demonstrated in the treatment of osteoarthritis in phase 2 trials, and phase 3 clinical studies were initiated in November last year. Tanezumab is poised to be the first biologic agent approved specifically for the treatment of pain, and it may transform the way severe, unremitting chronic low back pain is treated. Pfizer essentially assumed all of the development risk with this compound.

These two anecdotes, plus the thousands of smaller partnering deals, point to our keen appreciation for benefit sharing and financial risks. Our knowledge of biotech is considerable, we listen carefully to our external advisors and our sensitivity is based on decades of partnering with smaller biotechs and technology companies.

On behalf of our shareholders, we are enthusiastic small biotech investors but we cannot, and should not, adopt all the risks now owned by the broader financial community.

COMPETING INTERESTS STATEMENT

The author declares competing financial interests: details accompany the full-text HTML version of the paper at http://www.nature.com/naturebiotechnology/.

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1. Anonymous. *Nat. Biotechnol.* **27**, 101 (2009).

Conflating MTAs and patents

To the Editor:

It is unfortunate that the paper by Zhen Lei, Rakhi Juneja and Brian D. Wright entitled "Patents versus patenting: implications of intellectual property protection for biological research" in your January issue[1] obscures an important result with the red herring of "patents are bad for research." Indeed, the piece records that a cohort of agricultural scientists from leading research schools have a subjective belief that patenting has a negative affect on research. Paradoxically, however, respondents reported that they routinely ignore the existence of patent protection for research tools. More than 90% of respondents report that they "have never checked whether a tool that they might need in planned research is patented." The reason, according to the scientists, is that most think they won't be sued.

Upon reading the article, it is clear that the scientists polled are woefully misinformed about the difference between patents and intellectual property (IP), and that most of their responses are self-serving and reflect the cultural differences between academics and industry, with university technology transfer professionals being caught in the middle. The issue is not patents, but rather material transfer agreements (MTAs), private contracts between research universities that govern the disposition of tangible research materials. There are many and significant differences between

patent protection and MTAs. For example, patents promote disclosure, whereas MTAs typically require continued confidentiality. MTAs are exactly that: agreements concerning the transfer of materials. This means they are limited to tangible items that can be transferred and exclude IP, such as know-how, trade secrets and methods (indeed, their tangibility makes them more akin to personal property than IP). Patent rights are exhausted by a sale, whereas with MTAs the granting institution typically retains ownership of the transferred materials and requires either their return or certification that they have been destroyed after the term of the agreement has expired. In addition, although patents are governed by federal statute, and are encumbered with protections against improper use, MTAs are private contracts between the parties, governed by state common law that typically permits any behavior not in direct contravention of criminal or other statutes (that is, contract law is much more permissive than patent law).

Thus, the actual conclusions of the paper are not related to the effects of patenting on academic research at all. Rather, the authors report that institutionally mandated MTAs delay research, and these MTAs put "sand in the wheels" of an otherwise "lively system of interdisciplinary exchanges" of research materials. I do not doubt the researcher respondents feel this way; however, the disparity between these results and the results of several other academic reports (which argue that IP protection has a negligible effect on academic research) should raise a few questions about the nature of the study and the elicited responses. Academic researchers are focused, ambitious (and some would say even egotistical) people used to having their own way; these traits are perhaps necessary for them to have the temerity to believe they can make sense of a complex world, and are certainly an expected consequence for individuals having the intelligence of most academic researchers. The law presents them with another, different set of rules and a logical structure that differs from science. Particularly in view of the power differential between tenured professors and the staff of most university technology transfer offices, the scientists frequently believe they can ignore the rules (see their disdain for potential patent infringement reported in the paper), or if 'forced' to comply believe that it must have a negative effect on the only thing they are interested in, getting their research done as timely as possible (because there are usually other researchers actively engaged in their area).

Indeed, rather than patenting or other IP protections, academic competition may be the greatest impediment to the 'free exchange' of research materials and information. As the study authors admit, "[l]ong before the proliferation of IP protection, scientists were often secretive and uncooperative in their interaction with competitors (Hagstrom, W.O., *Am. Sociol. Rev.* **39**, 1–18, 1974)," and "[Respondents] anticipate moderate degrees of difficulty ["3.2 on a 5-point scale"] in getting tools from rivals…."

But recognizing these nuances of the problem is not as 'sexy' as pitching the results as being "contrary" to the "developing consensus" that patents have not had a negative effect on university research. Although the authors believe that there is an advantage to obtaining "direct" results of the effects of "IP protection" from the researchers, an uncritical acceptance of the responses and a failure to appreciate the important distinctions between MTAs and patents (which promote disclosure and hence academic cooperation and the free flow of information) leads them to conclude that IP protection impedes academic freedom and stifles research. From the responses reported in this paper, nothing could be further from the truth, and failing to address or even simply report that does little to illuminate an important issue for US patent policy.

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1. Lei, Z., Juneja, R. & Wright, B.D. *Nat. Biotechnol.* **27**, 36–40 (2009).

Zhen Lei and Brian D. Wright reply:

To a reader unfamiliar with intellectual property (IP), Noonan's thesis might well be persuasive. Researchers have problems with material transfer agreements (MTAs), not patents. MTAs are different from patents, and more "akin to personal property than IP." Indeed, they are "limited to tangible items that can be transferred and exclude IP, such as know-how, trade secrets and methods." Noonan implies that MTAs are not used in the transfer of IP, so scientists surveyed in our paper[1] are "woefully misinformed" when they attribute problems with MTAs to the recent proliferation of patents and other IP.

Scientists who rely on the counsel of attorneys or Office of Technology Transfer personnel, or draw on their own experience of patenting tangible research tools, understand that patentable compositions of matter, including those that are research tools, are IP. They also understand that their Offices of Technology Transfer have, since the 1980 Bayh-Dole Act, taken a greater interest in patenting and other means of IP protection, and urged scientists to use MTAs in sending research tools to others or receiving materials from peers.

For example, the relevant University of California, Los Angeles website[2] advises: "The purpose of the MTA is to protect the intellectual and other property rights of the provider while permitting research with the material to proceed." Furthermore, "If the material is not yet patented (or, publicly disclosed) and of possible commercial value, a material transfer agreement with secrecy provisions may be required." For scientists on the research frontier, the tools they want to exchange, often unpatented at the time of transfer, may be protected by MTAs as part of a strategy for preserving rights to royalties, and other benefits from patents or other IP related to inventions arising from the materials transferred. Another aspect is that MTAs might restrict use of materials in ways that go beyond what a patent would protect.

Since 1980, patenting by academic institutions has greatly increased. MTAs on materials sent from academia and industry "are often associated with having patent rights to the material in question"[3]. Scientists surveyed in the United States and Japan by the American Association for the Advancement of Science (AAAS; Washington, DC, USA) report that ~30% of the patented technology they acquired was transferred via MTAs; a substantially smaller portion was acquired by licensing[4]. It is not surprising, then, that the scientists we surveyed perceive a connection between the surge in patenting and the proliferation of MTAs on transferred tools.

Indeed, the connection between patenting and MTAs is evident in the behavior of our own respondents. When the nonpatentees among them provided tools to academic peers, they used MTAs in only 12% of the cases, whereas formal contracts (predominantly MTAs) covered 34% of such transfers by patentees. (Noonan will surely concede that these patentees should be familiar with the distinctions among patents, MTAs and other types of IP. Nevertheless, patentees agree with their peers on the net effects of intellectual protection on research.)

Noonan conjectures that the greatest impediment to tool exchange might be academic