Risky business

Public-private partnerships can reinvigorate precompetitive scientific research and de-risk drug discovery programs to help them meet demand for better and safer therapies.

With the establishment of the National Center for Advanced Translational Sciences (NCATS) in December of 2011, the National Institutes of Health (NIH) and the US government made a commitment to directly invest in translational research. With NCATS, the NIH will invest tax payer dollars in the riskiest 'precompetitive' stages of drug discovery. NCATS has also articulated a commitment to bring together expertise from the public and private sectors to promote collaboration and transparency. A year after the formation of NCATS, it remains less than clear why public monies should be allocated to de-risk drug discovery; how precompetitive space will be defined, especially as it relates to intellectual property (IP); and how their investments will be leveraged to draw private sector involvement and to maximize efficiency in a manner that is distinct from approaches that have failed to keep pace with the needs of society.

Important aspects of the vision that shaped NCATS are shared with other emerging models for research. Public-private partnerships (PPP), which are funded and operated as collaborations between government (or governments) and one or more private companies or institutions, are one such model. In this issue, Knapp and colleagues (Commentary, p. 3) outline a progressive PPP, a kinase chemical probe partnership, where reagents, data and knowledge resulting from the partnership are made publically available and the scientific strengths of these disparate sectors are combined to maximize efficiency by eliminating duplication of effort.

Improving efficiency or getting more high-quality science per investment dollar is a tangible outcome that justifies the investment of public money in these types of programs, and this objective should be intrinsic to any program launched by NCATS. Despite technological advances and efforts to increase productivity over the past 60 years, the rate of new drug approvals has remained constant at the same time that research and development (R&D) costs have grown exponentially (*Nat. Rev. Drug. Discov.* **8**, 959–968, 2009). Thus, modern paradigms for R&D are functioning at maximum capacity. In these R&D models, scientists at different institutions often work on similar or even identical problems; the outcomes of these programs can remain hidden behind the walls of IP or can take years to reach the public domain. By mandating public dissemination of all major findings, costly and time-wasting redundancies can be eliminated.

Involvement of the public sector in PPPs is the best way to ensure that participants will make reagents and the data generated by the initiative openly accessible. Thus, a public partner is necessary to maintain open access to emerging scientific knowledge, and having this information in the public domain provides the type of end value beyond efficiency gains that merits public investment. Indeed, the competition that ensues once precompetitive data is released can be a powerful force driving innovation. Thus, public dissemination of emerging scientific knowledge should be another major objective for NCATS.

This open-access model, however, comes at a cost. Information in the public domain becomes more limiting as research progresses; it can restrict opportunities for IP, which is the engine that ultimately drives private sector involvement in research. Thus, defining precompetitive space and adopting a plan for IP is a major challenge for any drug-discovery initiative.

Defining precisely what constitutes precompetitive research and whether precompetitive research should be subject to patent protection are major questions that NCATS has yet to address. Precompetitive space can be defined by the state of biological understanding, where research is focused on discovery as opposed to optimization. Most agree that early-stage research with relatively high biological risk (pretarget validation), where cost-benefit models for sharing information are most advantageous, constitutes precompetitive space. Some argue that precompetitive space extends through Phase II clinical trials, where targets are ultimately validated in humans (*Nat. Chem. Biol.* **5**, 436–440, 2009). A challenge for the PPP model as projects are selected and research progresses will be finding consensus among partners as to where this space ends and where protected research should begin. This distinction will most likely need to be made on a case-by-case basis. Likewise, NCATS has delineated specific priority research areas (*Sci. Transl. Med.* **3**, 90cm17, 2011); the institute should provide scientists and potential collaborators with information about how precompetitive space has been or will be defined and how they will handle IP to encourage private sector investment without stifling efficiency or innovation.

The leadership at NCATS should look to existing initiatives to identify innovative ways to fund biomedical science. The Structural Genomics Consortium (SGC; http://www.thesgc.org/), a PPP with binational and multicorporate support, provides an interesting example. The SGC, which was started by the private sector with the directive to carry out basic science of relevance to drug discovery, has successfully provided open access to precompetitive data and explicitly never files patents. In particular, the government agencies behind the SGC can help NCATS address challenges implicit in collaborating with the private sector, investing in the best science while being restricted by their geographic jurisdiction (defined by national boundaries) and moving beyond traditional funding mechanisms that are based on a competitive process following a call for proposals. Because these traditional mechanisms are not suited to the type of objective-driven, collaborative and open-access research that are precisely the factors that distinguish these new models from those that have failed, we are eager to see NCATS discard tradition and find a new approach for funding high-priority science.

Risk-sharing partnerships that leverage the expertise and resources of the public and private sectors offer efficiency advantages that justify an optimistic outlook for the future of drug discovery. Given the immutable reality that drug development is an expensive and high-risk but necessary enterprise, public money should be invested in this space. The type of PPP described in the Commentary in this issue outlines a paradigm-shifting mechanism whereby public dollars can draw private sector funding toward the public good by providing an efficient, objective-driven and IP-free research plan. NCATS, which has articulated objectives in common with this PPP and the SGC, has an unparalleled opportunity to reformulate drug discovery models, but it must face the substantial challenges of defining the scope of precompetitive research, negotiating the complex IP landscape and creating new funding models that entice the private sector to co-invest in discovery science. ■