Recommendations for Building a 21st Century BioEconomy

From the Small Biotechnology Business Coalition

December 6, 2011

INTRODUCTION

This set of recommendations is in response to the October 11, 2011 Request for Information (RFI) from the White House Office of Science and Technology Policy (OSTP) titled *Building a 21st Century Bioeconomy*. The stated purpose of the RFI is "to solicit input from all interested parties regarding recommendations for harnessing biological research innovations to meet national challenges in health, food, energy, and the environment while creating high-wage, high-skill jobs."

The Small Biotechnology Business Coalition (SBBC) is the leading advocacy voice for the over 2,000 independently owned, U.S. based small biotechnology and medical device firms.[1] All SBBC members were provided with drafts of this document and 10 to 15 company representatives elected to contribute ideas or input.

Cognizant of the fiscal constraints facing the U.S. government at this time, **none of the following recommendations require new government spending.** At most they would require small shifts in funding from programs that are generally delivering less economic value. Furthermore, we believe that **most of these recommendations can be immediately implemented without the need for new legislation**. To the extent that any of these ideas require some legislation these would not require an appropriation and would likely garner bipartisan support.

RESPONSES TO SELECT REQUESTS FOR INFORMATION

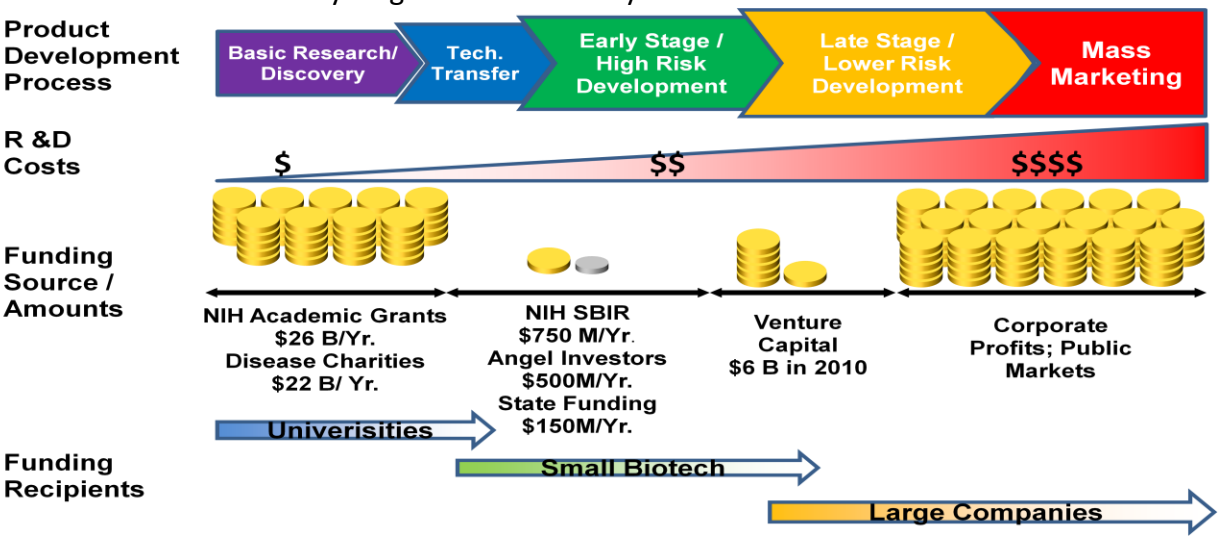
What are the barriers preventing biological research discoveries from moving from the lab to commercial markets? What specific steps can Federal agencies take to address these shortcomings? Please specify whether these changes apply to academic labs, government labs, or both. (Q5)

The single greatest barrier to moving biological research discoveries from the lab to commercial markets is lack of necessary funding. In the current funding environment in which investors and large corporations are reluctant to fund anything new, small biotechs are mostly reliant on the NIH SBIR program to commercialize promising

[1] www.SmallBiotechCoalition.org; Tel. 301-917-6538

technologies developed by academic researchers. However, nearly all of the ~$30 billion received by the NIH each year goes to hypothesis driven basic research by academics. While this research sometimes serves as a foundation for future clinical and commercial applications, NIH funding almost always ends long before private investors and corporations will commit to funding their commercialization. Furthermore, as the following diagram illustrates, the amount of funding available for basic research dramatically outweighs that available for the translation of early stage research into clinically useful products.

It is very difficult for small companies to find investors willing to absorb the substantial risks associated with early stage research. Policy makers need to be aware that the



amount of available private risk capital pales in comparison to the amount of public money invested in life science research.

More than 90% of small biotech companies in the U.S. today fund their R&D through a combination SBIR grants, state grants, and individual "Angel" investors. (Institutional venture capital is invested in well under 10% of companies, and these firms are disproportionately based in the San Francisco or Boston regions.) **Thus, basic / discovery life science research by universities receives about $50 billion per year in grants (NIH and philanthropy) while only about $1.5 billion is available to the 2,000 U.S. small biotech companies to translate this research into commercial products.**

The SBBC recommends the following specific initiatives to remedy the significant funding imbalance between basic and applied research as illustrated above. Importantly, each of these recommendations could be implemented by the Executive branch without new legislation or appropriation.

A. Allocate funds for a new NIH "Translational Research /Technology Transfer" award mechanism

Outside of the SBIR allocation, the NIH provides almost no funding directed at reproducing, validating, or expanding the research results of academic investigators so as to reduce the risk, costs and timelines associated with translating basic research into clinically useful and marketable products.

This urgent problem was described in a front page report in the *Wall Street Journal* only last week. According to the report, the vast majority of NIH funded research that is published in academic journals cannot be repeated or reproduced thereby leading pharmaceutical companies to waste large sums of money in clinical studies that fail. Smaller companies, in particular, especially suffer when we are required to invest considerable time and money attempting to develop products and technologies based on academic research which was either inherently flawed or insufficiently developed before being transferred to our companies.

The commercialization success rate small biotech would significantly improve and accelerate if the technologies that they are developing could be further advanced before they deploy significant private capital. To that end **SBBC recommends that no less than 15% of the NIH's extramural budget should be allocated to a new Translational Research / Technology Transfer (TRTT) contract or grant program**. Applicants for TRTT contracts would mainly be academic institutions seeking to replicate, expand, or validate their or their peers' RO1 grants results. Small businesses that have partnerships or licenses from universities could also compete for TRTT awards. Priority would be given to applicants with licenses or option agreements with companies that agree to take over funding after certain technical milestones are achieved. The size of award would range from $500,000 to $1 million per year over three years.

A related program could be implemented for the NIH's Intramural research program. Such an incentive is particularly needed since enthusiasm for CRADAs and other industrial collaborations by the intramural community has been dampened in recent years due to increased scrutiny of such relationships by NIH ethics authorities.

B. Create a new pilot "expert review" system for TRTT and SBIR awards

Peer review is a cornerstone of the NIH grants system and is ideal for hypothesis driven research, scientific publications and honors and prizes. However, it is less than ideal for advancing technologies towards commercialization. For these reasons agencies like the Defense Department and NASA use expert review rather than peer review in evaluating proposals for external for funding. Topics of interest to academic scientists often differ from the needs and priorities of patients, physicians or the commercial marketplace.

Under an expert review system, NIH program managers with relevant experience or training, aided by outside experts (physicians, patient advocates,) would play a key role in funding determinations. Continued funding would depend on the achievement of

technical milestones. Importantly, awardees could get feedback from the program officers before submitting an application and could negotiate technical milestones as the R&D progresses. Within a given topic area funds could be redirected from awardees who are not achieving their milestones towards groups having more success.

The NIH should experiment with an expert review system for its SBIR program and other applied and translational grants and contracts. Feedback from all stakeholders should be solicited before the pilot is made permanent.

What specific changes to Federal Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) programs would help accelerate commercialization of federally funded bioeconomy related research? (Q6)

A. Adopt a more commercial (rather than academic) review process for the NIH SBIR program

NIH's extramural funding is directed largely towards basic academic research, and the Center for Scientific Review draws heavily from their research grant recipients in the academic research community for reviewers. Review panels thus tend to reflect the basic research focus of much of NIH's extramural research. SBBC member companies often find that reviewers of their NIH SBIR proposals undervalue product innovation, rejecting proposals with high probabilities of commercial successes merely because they find the basic research underpinning the technology is insufficiently innovative. Since NIH's standard procedure is to have only one or at most two reviewers thoroughly examine each proposal, who then present their findings to the full group of reviewers, the product innovation element that is so critical for commercial success can be substantially undervalued.

- The NIH should explore the aforementioned "expert review" process for its SBIR program. This would bring the NIH SBIR program in line with the SBIR program at the National Science Foundation (NSF) wherein Program Officers actively group the triaged grant applications by technical subject matter, select appropriate technical and business subject matter experts as reviewers, and then join the review committee to guide the review process. Permitting Program Officers to participate in the review process would add speed and predictability to the review process and permit more useful interaction between the applicant and the SBIR program staff. For example, companies could ascertain their likelihood of success before investing the time of preparing a full grant application. The NIH model of providing a "Chinese wall" between the reviewers and program staff is useful only in an academic context.

- The aforementioned review system should first be implemented on a pilot basis and should provide safeguards to prevent domination of the review process by Program Managers.
- The NIH should follow the lead of the NCI SBIR program in hiring SBIR Program Manager with industry experience.
- The NIH should accelerate its efforts to recruit grant and contract reviewers with a combination of technical and business backgrounds, including representatives from small and large companies and venture capital firms. (The National Cancer Institute (NCI) SBIR program has recently been successful in this regard, particularly for their Phase II Bridge Award program.)
- In order to help recruit qualified reviewers from small business, consideration should be given to compensating companies that make available their personnel for this purpose. This could be structured, for example, as a small supplement to existing SBIR grants.
- Make clear to the reviewers that "innovation" for purposes of SBIR can refer to the product or technology being developed, not necessarily the research per se. Frequently research plans directed to routine but essential tasks (e.g. optimization, validation, toxicology testing, animal trials, etc.) are deemed "not innovative" even thought the product being developed is highly novel and unique. This results from reviewers improperly applying academic criteria when reviewing SBIR grants.

B. Shorten review and award cycle timelines

Currently, the NIH review/award process takes 8-9 months from proposal submission for work to commence. It is recommended that NIH condense the time frame for its SBIR reviews. We would suggest the use of the DoD SBIR process as a model as it has a shorter time frame, 4 months—half of NIH.

C. Create and expand programs to transition NIH SBIR funded technologies to the marketplace

SBBC members believe that the NIH lags behind other agencies such as DOD and DOE with respect to programs which help transition SBIR funded technologies into the marketplace. The following programs would help SBIR grantees transition to product launch or otherwise attract private investments and corporate partnerships.

1. Expand the NCI SBIR Phase II Bridge Award program

In 2009 the National Cancer Institute (NCI) began a pilot program called the SBIR Phase II Bridge Award program. Modeled after NSF's "Phase IIB Option," this is a three year, milestone driven grant (up to $1 million per year for three years) that requires matching

funding from private investors (Angels or VCs) or larger companies. Importantly, the reviewers for the Bridge Program came primarily from large pharmaceutical companies, venture capital firms, and successful small companies.

To help facilitate investments and partnerships for the Bridge Program the NCI SBIR staff hold an annual investor forum and are planning other initiatives in this regard.

SBBC members are enthusiastic about this pilot program and recommend that it be made permanent and be adopted by other Institutes at the NIH. However, if Congress amends the SBIR statute to permit companies majority owned by venture capital firms, it is important that the NIH provide safeguards to ensure the Bridge Program does not become dominated by the VC community. It is important that companies with smaller investments from Angels not be displaced. Also it is important that significant flexibility be according to investments from a variety of sources and input from small companies be given weight in structuring the rules for investment eligibility.

2. Create and implement a new NIH Phase III acquisition program

SBIR Phase III generally refers to the commercialization of SBIR funded research or technology using funds other than the SBIR Program. This can include federal funding (outside of the SBIR set aside) or private sector funding. The Departments of Defense and Energy have highly successful SBIR Phase III programs.

The NIH has historically avoided a formal Phase III program based on the premise that unlike DOD and DOE the NIH does not represent the end user or customer. This premise should be reconsidered. Public and private sector end users (large companies, research institutes, etc.) could be brought into the SBIR contract program in Phase I with the goal of eventually acquiring the product or intellectual property after successful Phase II development.

The SBBC recommends that NIH should develop a Phase III program along lines herein outlined.

i. *NIH Acquisitions*

Under a public sector Phase III program, the NIH Intramural Program could specify particular technologies or products that they need and participate in Phase I and Phase II SBIR contract reviews. The expectation is that following successful Phase II development those entities would purchase products from the company, who would also be free to sell the products to others. This program would likely work best for research tools, medical devices, and other products that do not require expensive clinical trials before they can be commercialized, but could also include supply of clinical trial materials.

EXAMPLES:

- The National Institute of Neurological Disorders and Stroke (NINDS) Intramural Program seeking the development novel animal models for Parkinson's disease research and drug testing.
- The NIH Clinical Center seeking innovative imaging software for analysis of tissue sections by their anatomic pathology lab.

ii. ***Private Sector Acquisitions***

A private sector Phase III program would involve large companies seeking innovative technologies that (i) meet a compelling unmet public health need and (ii) would be too risky for them to develop independently. These companies would assist in crafting SBIR contract RFPs and would have their R&D managers serve on review committees. The expectation is that following successful Phase II development those entities would enter co-development or license agreements with the SBIR firms (who would also be free to negotiate with others). This program would likely work best for novel therapeutics and diagnostics that require expensive clinical trials before they can be commercialized. In one implementation of this recommendation, the NIH would serve in a brokering capacity bringing together the SBIR entity with the private sector entity looking for a particular product/device/etc. Universities have these types of units to bring together faculty and companies or faculty companies with outside companies to partner on projects.

EXAMPLES:

- Pfizer seeking the development of new drugs for treating various autoimmune diseases.
- Roche Diagnostics seeking validated biomarkers for predicting lung tumor response to targeted therapies.

D. Increase the NIH SBIR/STTR allocation over three years

In light of the economic downturn, the SBBC strongly recommends a three-year increase in the percentage of NIH grants allocated under SBIR/STTR from the current 2.8% to at least 5.0%. This is justified since companies that successfully bring new products and technologies to market create new jobs that can be sustained without continued government funding. Furthermore, private equity capital has become significantly curtailed, especially for higher risk endeavors like biomedical R&D.

The SBIR statute provides that agencies allocate no less than 2.8% of their external funding to small businesses. This creates a floor, not a ceiling, which can be increased by the Executive branch without legislation.

2010 NIH SBIR applications increased by 40% from the prior year while the number of applications that received funding plummeted to 17.0% from 24.5% in 2009. At the National Cancer Institute 2010 SBIR applications rose by 68% from the previous year. This is likely due to the difficulty in accessing private sources of capital for early stage ventures. Competition is expected to increase substantially with the anticipated participation of companies owned by venture capital firms as a result of pending SBIR legislation.

It also is noteworthy that the European Union's biomedical research authority awards about 15% of their funds to small businesses.

After FY'14 an outside expert review committee could be convened to recommend whether the three year increase should be maintained or the allocation returned to current levels.

E. Create SBIR Advisory Boards

It is urged that each NIH Institute create an SBIR Advisory Board to provide ongoing input on operations and topic priorities. The SBIR Advisory Boards would comprise representatives of successful small and large businesses, disease advocacy organizations, as well as the investment community.

F. Appoint a Deputy Director for Small Business Innovation at the NIH

A new Deputy Director position should be created at the NIH with specific oversight over the SBIR program. While each Institute should maintain independent funding authority, the Deputy Director would seek to implement best practices across institutes and would serve as a primary liaison with various stakeholders including the business community and members of Congress.

What are the challenges associated with existing private-sector models (e.g. venture funding) for financing entrepreneurial bioeconomy firms and what specific steps can agencies take to address those challenges? (Q. 8)

The economic downturn has significantly transformed the funding environment for small companies engaged in high risk, high impact R&D. Institutional venture capital has generally moved away from early stage investments leaving individual "Angel" investors to fill this important void. In light of these trends the following initiatives could be implemented by the Obama Administration to create billions of dollars in new investments without any increase in the deficit.

A. Encourage Crowd Funding

As of this writing, legislation to make it easier for companies to promote themselves for small investments (under $10,000) from individual "Angel" investors is advancing through Congress. If enacted the Administration could help encourage "crowdfunding" by maintaining and promoting an SBA database of SBIR grantees who are seeking equity investments to advance their SBIR funded technologies. This website InvestAmerica.gov would be organized by technical fields and disease areas so that prospective investors interested in advancing cures to particular diseases can identify relevant companies.

B. Redirect Pharmaceutical Settlements to Small Biotech Companies

Merck & Co. recently agreed to pay $950 million to resolve government allegations that they illegally promoted Vioxx and deceived the FDA about the drug's safety. GlaxoSmitKline recently agreed to pay $3 billion to settle U.S. allegations of improper drug marketing. Pfizer, Eli Lilly and AstraZeneca have also entered expensive settlements with the federal government in recent years.

The Administration might permit these companies to reduce at least part of their settlement obligations if they invest an equal or greater amount in NIH SBIR grantees seeking corporate matching funds as part of their Bridge Program. Helping us bring our products to market faster gives the taxpayers a return on SBIR investments already made thereby creating far more economic activity that blanket payments into the U.S. Treasury.

Alternatively these settlement funds could be pooled into a common fund to supplement SBIR grants. The drug companies could offer advisors to the fund in more arms length manner.

What specific improvements in the regulatory process for drugs, diagnostics, medical devices, and agriculture biotechnology should federal agencies implement? What challenges do new or emerging technologies pose to the existing regulatory structure and what can agencies do to address those challenges? (Q. 15)

A. Implement progressive, staged approval for drugs, devices, and diagnostics developed by small companies

The burdens of regulation fall disproportionately hard on small companies which are responsible for the bulk of innovative products. The FDA should initiate an array of provisional approval processes to permit the marketing of products proven safe but for which efficacy data is promising but not yet conclusively proven. Post market surveillance data could be incorporated into subsequent assessments of the risks vs.

benefit of continued marketing of the product. This model is generally analogous the CMS' Coverage with Evidence Development initiative (below).

The SBBC formed a Diagnostics Working Group that met with the FDA Office of In-Vitro Diagnostics in September 2010 in connection with their anticipated regulations of Laboratory Developed Tests (LDTs). We submitted a formal proposal to the FDA (available on www.regulations.gov or the SBBC website www.smallbiotech.org) in August 2010 that seeks a limited "provisional PMA" for small companies to permit them to "test the waters" by selling their tests to up to a limited number of patients per year. Patient protections are included in the proposal.

B. Expand Medicare Coverage with Evidence Development (CED)

Timely reimbursement is essential for innovative small biotech companies and our investors but we face steep hurdles and long timelines before receiving national or even local coverage determination from Medicare. CMS's "Coverage with Evidence Development (CED)" program provides an ideal way to permit innovative small companies to launch their products and earn revenues while collecting additional data supporting the clinical value of our products. CED is particularly useful for medical device and diagnostics products which can often be launched by small companies before obtaining venture capital or large company partnerships. Since our companies typically lack resources for a national sales force and marketing campaign, local CED reimbursement from Medicare contractors should permit our companies to test market our products in a few states before a national roll out. Accordingly we urge the Administration to promote CED among its Medicare contractors for innovative products developed by small companies.

C. Accelerate the FDA Orphan Products Grant Program with Vouchers.

Small biotech companies often lead the development efforts for treatments of rare diseases as larger companies typically shy away from smaller market opportunities. The FDAs Orphan Product Grant Program is therefore very important to the companies that SBBC represents. Unfortunately the budget for this program (~$14M) has been nearly flat since 1995 even though the number of grant applications has at least tripled from 30-40 in 2007 to well over 100 in 2010 and 2011.

In 2010 the *Creating Hope Act* was introduced in the Senate to offer "priority review vouchers" to large pharmaceutical companies seeking expedited review for large market drugs if they agree to invest in cures for rare diseases. The Administration should consider implementing a similar program by Executive Order wherein pharmaceutical companies that invest in small companies addressing orphan diseases would be awarded priority review vouchers from the FDA.

D. Promptly promulgate regulations implementing the biologics data exclusivity provisions in the Healthcare Reform Act of 2010.

The Patient Protection and Affordable Care Act contained important provisions giving at least 12 years of post approval exclusivity for biologic products, in order to enable the required investment in product development from a large pharmaceutical company or private investor. Small biotechnology companies believe that the Administration needs to quickly publish regulations on the implementation of this provision in order to help us attract investment.