Response to RFI concerning the President's Blueprint for the Bioeconomy

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Responses to questions in order:

1. Grand Challenges: The greatest challenge in biomedical science today that will have a tremendous impact on healthcare and long term healthcare costs is in learning to manipulate the human immune system. The immune system is the key to curing cancer, autoimmune disease, responding to infectious diseases, asthma & allergy, even affecting long term remodeling processes. If you have to pick a single focus, it should be to first develop the tools to study the human immune system (animal models, in vitro platforms- reconstituted elements of the immune system, in silico response simulations and predicting immune phenotype based on genotype, and finally safe human testing methods). This is very hard to do and has not been done well so far. Other than vaccine technology, which despite decades of use and research, is still not an exact science, we know very little about how to manipulate the immune system to create a therapeutic benefit. I am developing an immunomodulatory drug and this is a very difficult and underfunded field.
2. High throughput approaches are not the be-all end-all solutions. At the present time there is a glut of information from the Human Genome Project that we are still sorting through to create diagnostic and therapeutic products. It will take decades to mine the information we already have. Funding should be made available for meritorious high impact individual projects through programs like the NIH Cures Acceleration Network.
3. X
4. Commercialization of recombinant human protein therapeutics and diagnostics made possible by the Genome project will require market exclusivity to justify investment. Since the project was completed in 2000 and all sequences disclosed publically or included in massive composition of matter patent filings that no one can develop in 20 years, there is an issue with lack of strong IP coverage for most of the potential products to be derived form that project. To address this issue will require a paradigm shift in the US – suggestions as follows: extend patent coverage for at least 7-10 years post FDA approval and enforce the 12 years of biologics market exclusivity in the Healthcare Reform act.
5. Funding is the main barrier to product development. Academic labs typically lack a fundamental understanding of the drug development process AND are not motivated to develop products as company personnel are motivated. (The academic product is the publication and the mission is not commercial.) The SBIR program and CAN should be receive greater level of funding through NIH. At the same time, NIH needs to maintain the clinical research infrastructure in academic and medical school settings to provide an environment in which to test new products.
6. Triple the NIH SBIR program immediately!

Clarassance, Inc. Aprile L. Pilon, Ph.D.

An Entrepreneurs Recommendations based on first-hand experience
November 2011

As a 17 year veteran of the biotech industry, having participated in 5 start up biotech companies, I make the following recommendations based on first-hand experience of the issues faced by companies developing biologic drug products that require protracted development and approval processeses.

I. **Increase funding for the FDA Orphan Products Grant Program**. These grants are for "shovel-ready" drug development projects for drugs that must have already received orphan drug designation (requiring in depth knowledge of the disease condition and market) and must have an active Investigational New Drug Application.

An enormous amount of credit for the development of the entire biotechnology industry should be given to the Orphan Drug Act and the Orphan Product Grant Program. Biotech drugs like erythropoietin (Amgen), human growth hormone (Genentech), and Ceredase (Genzyme) would, arguably, never have been developed if not for the act and the grant program. Patent protection was not possible for many of the first biologic drugs because their compositions and uses were in the public domain before it became possible to produce them recombinantly and thus feasible to produce sufficient drug product to serve their patient populations. These biologic drugs were too risky to invest private capital in and the orphan product grant program provided the critical funding for early clinical trials. Thus, the Orphan Drug Act and the Orphan Product Grant Program are responsible for generating thousands of high paying jobs, enabling the growth of several multi-billion dollar companies, building enormous value in the capital markets, in the biotechnology industry over the past 40 years, not to mention the millions of patient lives positively impacted by the products supported by the program.

The Orphan Product Grant Program budget has been nearly flat since 1995, when it was $12 million in the program budget, through the 2012 budget for which $14M has been allocated. The budget has remained at $14M for the past 5 years, while the number of grant applications has at least tripled from 30-40 in 2007 to well over 100 in 2010 and 2011. Only 10-15 new grants per year can be funded, a success rate well below that of NIH academic grants, during a time when more company and product development grants should be funded. For the relatively small grant investment (up to $400K/yr for up to 4 years, $1.6M total), a large increase in product value may be realized.

The FDA is the only government agency well-suited to administer this program because it is intimately familiar with the issues and challenges encountered during drug development. No other government agency can serve this function. The FDA Office of Orphan Product Development (OOPD) understands the urgent need to develop therapies for rare conditions and takes an active role in supporting and monitoring the clinical trials that are sponsored by the grant program, even advocating for these trials with other divisions within FDA. As a result of OOPD's involvement, the success rate for gaining approval is significantly higher than for drugs outside the program.

**For these, and many other reasons[A], we strongly recommend that the budget for the orphan product grant program be expanded immediately to $30M for 2012. We understand that this is up to the discretion of the Agency and urge that FDA does its part to stimulate the economy.**

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A. Rare Diseases and Orphan Products: Accelerating Research and Development. Marilyn J. Field and Thomas F. Boat, Eds.; Institute of Medicine of the National Academies. The National Academies Press (Washington, DC.) (2010).

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II. Determine whether FDA or Dept of Commerce is supposed to enforce the 12 year post-approval period of exclusivity for biologic products (**Healthcare Reform Act of 2010**; HR3590, Section 7001-7003, pp 1860-1906). **Accelerate release of guidelines for what the new law means and how it will be enforced.**

"We can't wait!"

A significant period of post-approval market exclusivity is required for these types of products in order to incentivize and obtain the investment required to develop them. The development of orphan drugs without patent protection has shown that a period of at least 7 years of market exclusivity is required before an investment will be made in drug development. In my own discussions with large pharmaceutical companies, they want at least 10 years of post-approval market exclusivity to incentivize the required investment in product development, 12 would be better. Note that most business development people at large pharma companies aren't even aware of this legislation. They will not pay any attention to it until FDA issues guidances on enforcement. Small biotechnology companies with outstanding biologic products that are short on patent life, like mine, can't wait months or years to get an answer from the FDA on how, or even whether, they will enforce the new law. It is unacceptable that promising products, some that have even advanced into the clinic and demonstrated efficacy in some instances, are abandoned, and don't receive the investment required to gain regulatory approval and make it into the marketplace. Conversely, inferior products with more recent patent claims may receive the resources to be developed. In the worst case, promising products with short patent life may be modified for the purpose of creating a new patentable composition and not necessarily to improve product performance, which could ultimately increase the likelihood of hypersensitivity reactions or otherwise compromising safety. It is a disservice to the American public to be denied the best therapies due to arbitrary patent deadlines which were never intended to have been applied to modern drug products requiring lengthy testing and approval processes. Failure to invest in partially development products represents a senseless loss of investment capital that discourages further private investment in the biotechnology industry. The clarification and subsequent enforcement of this exclusivity period for novel biologics will enable the investment required to advance promising products for which the limit of patent protection is insufficient.

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III. **Increase the period of market exclusivity for first to market (eg. first to approval) drugs and devices from the current 5 year period to a minimum of 10 years (like Europe)**. This applies to

all drugs, not just biologics. Chemically synthesized drugs are generally less expensive to produce and it is typically less expensive to develop synthetic processes for chemical drugs than for biologics, hence the shorter period of exclusivity. Due to the protracted timelines for development of regulated biomedical products, patent life is often insufficient to provide any period of market protection once the product has been approved for market by the FDA. This minimum period of market exclusivity enables corporations and investors time to recover their investment and return a profit on the enormous investment required for these types of products to reach the marketplace.

There is no published rationale for the number of years required to recoup investment made in product development and clear a reasonable profit. Product valuation models are unique to each company or investor and there are a tremendous number of variables that can drastically alter projections of product development costs and eventual profits from marketed products. However, there is no question that the number of years of exclusivity must increase from five in order to stimulate investment in new product development. Other jurisdictions, like Europe and Japan, allow 10 years of market exclusivity for first-to-market, first-in-class drugs. Given new requirements for post-approval safety monitoring programs now required by FDA (REMS), which are projected to cost up to 6% of the net sales to comply with, 10 years should be a minimum.

IV. Increase and strengthen the SBIR program at NIH to stimulate innovation in biotechnology and biomedical product development. I am a founder of the Small Biotech Business Coalition (www.smallbiotechcoalition.org) and I cannot emphasize how important this program.

V. Appropriate funding for the NIH's Cures Acceleration Network to provide funds to develop therapeutic products.
VI. Provide greater tax incentives not only for companies developing pediatric drugs but also to their investors, including new drug testing in children AND reformulation of existing drugs (approved in adults) for pediatric populations. The FDA has a carrot and a stick for companies developing drugs for children (Best Pharmaceuticals for Children Act, 2002), but it's not sufficient to incentivize the investment required for pediatric drug testing.
VII. Extend patent protection for 10 years AFTER regulatory approval is obtained for all drugs and biologics.

I would be happy to address any questions you may have about this response. Please feel free to contact me.

Sincerely,

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