ONYX PHARMACEUTICALS

Request for Information: Building a 21st Century Bioeconomy
Office of Science & Technology Policy, The White House
Comments Submitted Electronically to bioeconomy@ostp.gov

Onyx Pharmaceuticals, Inc.
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Thank you for publishing a request for information to solicit input 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. As a manufacturer of innovative therapeutics for cancer, Onyx Pharmaceuticals, Inc. ("Onyx") witnesses first hand the challenges and necessary steps to successfully bring a new, effective product to market. We are excited about the future, and believe that biotechnology companies like Onyx will continue to play a crucial role in researching and developing the kinds of products that extend lives and improve patients' quality of life. Additionally, as one of the highest growth companies in the life sciences, we expect to expand our workforce by 50 to 60% in 2012, creating approximately 250 new jobs. As a result, we understand the importance of stimulating innovation as one of the key growth drivers of the emerging "new" economy. Based on these experiences, Onyx respectfully submits these comments for your consideration as you develop the *National Bioeconomy Blueprint.*

Public-Private Partnerships & Research Funding:

Today, the industry is at a crossroads. The old blockbuster model is waning, and we are moving toward an era of personalized medicine characterized by targeting treatments consistent with an individual's genotype and medical history. This is extremely positive for patients and good for agile companies like Onyx, but this rapidly advancing know-how is changing the entire structure of the industry and the nature of our partnerships and collaborations with public and private organizations. This is not unlike major shifts we have observed in a number of other areas, including defense and national security where we now approach both, with smaller, more targeted, and smarter approaches.

In some ways, the entire innovation paradigm is evolving. Historically, innovators have worked sequentially: basic science labs advance a discovery, and then transfer it to clinical experts who often, in the case of academic laboratories, license the promising technology to an organization with the money and resources to bring the treatment to patients. These handoffs are inefficient, and can slow or break down any time a member of this "innovation chain" bumps into the limit of their experience or expertise. As a result, Onyx believes the next great era of life science partnership will focus on greater integration throughout the discovery and development cycle, so that scientists and academicians performing early research can collaborate earlier and more directly with the organizations whose clear mission it is to make new therapies widely available to patients around the globe.

This kind of collaboration is especially important in an era of declining federal resources, which is requiring all of us to become more efficient and collaborative. Public policy will need to respond to this new paradigm and find even faster ways to enable innovation while keeping patients safe. With this in mind, however, we believe that the NIH will continue to play a key role in our nation's health care landscape, as the proprietor for the nation's science. Although we recognize the need for private industry to do more, particularly in such tough fiscal times, Onyx urges policymakers to support current NIH funding levels to maintiain our economic and innovative competitive edge in life science. The NIH serves as a vital partner to the private sector, without which we cannot do our essential work and funding cuts here would have a devastating impact on innovation for years to come.

An example of one NIH program driving innovation is the Cancer Therapy Evaluation Program (CTEP), whose mission is to improve the lives of cancer patients by finding better ways to treat, control, and cure cancer. CTEP accomplishes this mission by funding an extensive national program of cancer research and by sponsoring clinical trials to evaluate new anti-cancer agents, with a particular emphasis on translational research to elucidate molecular targets and mechanisms of drug effects. CTEP uses a scientific process to accomplish its mission. Promising basic science findings are identified and translated into clinical research, both by identifying new agents for evaluation and by identifying biologic characteristics of tumors that may be clinically exploited.

CTEP attempts to forge collaborations within the broader research community and works extensively with the pharmaceutical/biotechnology industry to effectively develop and advance new cancer treatments. CTEP also seeks to involve outside experts and patients or their advocates in the formulation of research priorities. In the selection of clinical research for National Cancer Institute sponsorship, CTEP attempts to fill critical gaps in the national cancer research effort and to avoid duplication of ongoing private sector efforts. In further efforts to control cancer, active new anticancer agents are made available as rapidly and widely as possible for patients.

Onyx views CTEP as a potentially valuable partner in furthering the medical community's understanding of multiple myeloma, for which Onyx is developing treatments. Currently, African Americans are twice as likely to be diagnosed with myeloma and twice as likely to die from the disease, but the cause of this disparity remains unknown. More research is needed to understand the cause of this disparity and to improve treatments for African American myeloma patients. This is the perfect opportunity for a NIH funded program such as CTEP to partner with industry to improve treatments for African Americans who are disproportionately affected with myeloma. As part of building a blueprint for a bioeconomy, the Office should explore expanding or adding additional public-private partnerships between academia, industry and the government, such as CTEP.

Building an Integrated National Health Database:

An integrated national health database would be a transformational effort with broad benefits across the research and healthcare systems. We are at a point where digital information exists on many aspects of health care: birth, death, disease occurrence, ethnicity, and sometimes environmental and work exposures to health altering agents. An integrated national health database would combine this information into a single source enabling research to address questions including the relationship between disease and environment, such as childhood illnesses, obesity, premature birth, and smoking. Additionally, such a database would allow further exploration into patterns of medication use and capture rare or late side effects not captured during clinical trials.

To develop a database, challenges would need to be addressed including how best to de-identify data so that trends can be analyzed without jeopardizing the confidentiality and privacy of patients and how to best to integrate different data fields and systems. Nearly every database is handled differently, whether they belong to hospitals, pharmaceutical companies, private payers, government health records, etc.

The integration task is enormous, but would be an investment that will pay dividends in the future and one that can leverage much of the work completed by the Office of the National Coordinator for Health Information Technology. Such an effort would tap into the strength that the United States has in informatics and potentially lead to new opportunities for careers and jobs in the computer science and life science informatics.

Regulations Fostering Innovation—Exemptions for Orphan Drugs:

Oftentimes in the case of a rare disease, there is little incentive for a pharmaceutical company to invest in developing a cure. The Orphan Drug Act allows for the FDA Office of Orphan Products Development (OOPD) to give grants to companies that are committed to the development of treatments for rare diseases. OOPD provides incentives for sponsors to develop products for rare diseases and the program has successfully enabled the development and marketing of more than 350 drugs and biologic products for rare diseases since 1983. In contrast, the decade prior to 1983 saw fewer than ten such products come to market. It is estimated that rare diseases affect more than 25 million Americans.

The Orphan Drug Designation program provides orphan status to drugs and biologics that are intended for the safe and effective treatment, diagnosis, or prevention of rare diseases/disorders that affect fewer than 200,000 people in the U.S., or that affect more than 200,000 persons but are not expected to recover the costs of developing and marketing a treatment drug. Government assistance for orphan drugs is designed to reduce cost and balance the economy-of-scale for the product.

The Patient Protection and Affordable Care Act imposes an annual fee on manufacturers and importers of branded prescription drugs in the U.S. The law establishes an overall aggregate fee ($2.5 billion in 2011, rising to $4.1 billion in 2018 and dropping to $2.8 billion for 2019 and following years), which will be annually apportioned by the Secretary of the Treasury based on

each manufacturer or importer's relevant market share of covered domestic sales of branded prescription drugs. The only drug sales considered are those made to or offered pursuant to coverage under government health care programs (e.g. Medicare Parts D and B, Medicaid, Veteran's health plans, Department of Defense coverage, and TRICARE).

Importantly, the provision includes a specific exemption for orphan drugs: the calculation of drug sales for any given year *excludes* the sale of any drugs for which the manufacturer received an orphan drug tax credit (a "section 45C credit"). On October 3, 2011, the Internal Revenue Bulletin: 2011-40 included a section outlining the Department of Treasury's interpretation of the law establishing the new Branded Prescription Drug Fee. In its interpretation, the agency outlined several exclusions to this exemption, specifically a drug is not considered an orphan drug if:

1. the 45C credit for orphan drugs was allowed, but the manufacturers did not claim the credit,
2. a final assessment or court order disallowed the full section 45C credit taken for the drug, or
3. the drug was allowed a 45C credit, but subsequently, the FDA approved the drug for an indication to treat a disease or condition that is not rare. (Note: the drug may be approved for use in multiple rare or orphan diseases and still qualify for this exemption.)

Public comments encouraged Treasury to classify orphan drugs based on whether the 45C credit was allowed, and not on whether it was claimed. This inconsistency in defining an orphan drug poses many challenges to the industry developing orphan drugs and could hinder innovation. The regulation should be modified to state that being eligible to receive a 45C credit is sufficient in determining orphan drug status. A company's decision to act on that credit depends on numerous factors, and a choice to not claim an allowed credit does not change or otherwise influence whether or not a drug is indicated for the treatment of a rare disease. In developing a blueprint for a bioeconomy, Onyx asks the White House to consider modifying this interpretation of the classification of an orphan drug so that it is consistent across regulations and based on whether or not a drug was eligible for a 45C credit.

Moreover, the temporary regulation issued in October states that the exemption of orphan drugs from the fee will not apply if the drug is later approved by the FDA for a non-orphan use. It states, "if a drug is *ever approved* for an indication other than the treatment of a rare disease or condition for which a section 45C credit was allowed, *whether before, during, or after a section 45C credit was allowed* for the drug, sales of that drug are not considered sales of an orphan drug." The Orphan Drug Designation Program was designed to create an incentive to developing a treatment for a rare disease or condition, and this interpretation potentially undermines the overall goal of the program. Additionally, Onyx believes this is contrary to the drafters' intent, and that if a drug is approved for a non-orphan use, any subsequent orphan designation should qualify the product for the exclusion. To prevent this, Treasury should change its interpretation to mean that the sales of the drug for the orphan disease should be exempt from being included in the calculation of the manufacturer's fee, but the sales of the

drug for non-orphan disease indications should be considered in the fee's calculation. This fair approach would continue to protect and promote the goals of the Orphan Drug Designation Program. This issue has bipartisan support; in April 2011, 12 Members of the House (seven Republicans and five Democrats) wrote to Secretary Geithner on this issue.

Conclusion:

Thank you very much for the opportunity to submit these comments for consideration as you draft a national blueprint to build a bioeconomy. Onyx believes that sustained investment in funding of the NIH, support for public-private partnerships, building an integrated health database, and incentives such as those for the development of orphan drugs, will help drive innovation forward, lead to economic growth and ensure that America retains its leadership position in life science innovation.