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REDWOOD CITY, CA

ON BEHALF OF THE BIOTECHNOLOGY INDUSTRY ORGANIZATION

BEFORE THE U.S. HOUSE OF REPRESENTATIVES
ENERGY AND COMMERCE SUBCOMMITTEE ON HEALTH HEARING

PDUFA V: MEDICAL INNOVATION, JOBS, AND PATIENTS

JULY 7, 2011

Chairman Pitts, Ranking Member Pallone, and Members of the Subcommittee, my name is Paul Hastings and I am the President and Chief Executive Officer of OncoMed Pharmaceuticals. I am here testifying on behalf of the Biotechnology Industry Organization where I serve as the Vice-Chairman of its Emerging Companies Section, comprised of more than 480 companies. BIO represents over 1,100 members involved in the research and development of innovative healthcare, agricultural, industrial, and environmental technologies.

Ninety percent of BIO's research and development company members have fewer than 100 employees. Additionally, 43 percent of typical biotech companies have less than a year's worth of cash on hand and 48 percent are at least three years away from having product revenue.[1]

I have over 25 years of experience in the biotechnology and pharmaceutical industry. My current company, OncoMed Pharmaceuticals, is working at the cutting edge of oncology research, focusing on a specific set of cells within tumors that drive the growth of the

[1] BIO Emerging Companies Section Membership Survey, 2011.

tumor and can morph into various cell types within the tumor. We have developed the ability to isolate and monitor these tumor initiating cells using specific surface markers and technologies. Our studies have shown that tumor initiating cells are more resistant to standard chemotherapy agents and radiotherapy. So, some current treatments may succeed at initially decreasing the size of a cancer, but leave behind an increased proportion of the most malignant cells. We have developed a portfolio of antibodies and have tested them within xenograft models derived from freshly resected human cancers. These antibodies target biologic pathways critical for survival of tumor initiating cells. We believe these models are more representative of the effects of these treatments in cancer patients than traditional models using cancer cell lines, which may no longer accurately reflect the properties of the original tumor. Currently we have one antibody that targets tumor initiating cells in Phase I and are developing other promising therapeutic candidates.

The U.S. biotechnology industry is poised to be a major driver in an innovation-driven economy. And while we are currently the global leader in the development of biotechnology treatments and therapies, intense competition from China and India means this a position we have to fight to keep. Indeed, when it comes to venture-backed start up biotechnology discovery companies, our industry is facing a crisis. Regulatory uncertainty, longer drug development timelines, and an increasing regulatory and Congressional focus on risk instead of reward in pharmaceutical innovation deters limited partners from investing in biotech venture capital firms and subsequently deters venture capitalists from investing in biotechnology discovery companies.

Today, I will briefly discuss PDUFA, but the focus of my testimony will be on developing a policy environment that will support the one industry, biotechnology, which is offering real solutions to our most pressing health care needs: curing disease, reducing costs, increasing quality, and ensuring that people enjoy not only longer lives, but better and more productive lives. Despite the extraordinary promise offered by biotechnology, government policies restrain our industry's ability to meet its full potential to serve patients.

The bioscience sector accounts for over 7 million direct and related jobs.[2] Not only do we create high paying jobs for scientists, clinicians, manufacturing technicians, and support staff internally at our companies, we also create jobs and vital revenue for our universities and medical centers through the clinical trials we conduct.[3]

We are also innovators. Of the 172 scientifically novel and orphan drugs approved from 1998-2007, 52% were discovered and/or developed by biotechnology companies.[4] We offer tremendous hope to patients with over 3,700 new biotherapies in development that have the potential to offer significant advances in treatments for patients suffering from cancer, diabetes, Alzheimer's, cardiovascular disease, and rare genetic disorders.

The public benefit of medical innovation is well-documented.

- Medicines can help offset overall medical costs by preventing or delaying the need for other costly services, such as emergency room visits and hospitalizations. For example, a 2009 Medicare study found that use of prescription drugs reduced hospitalization costs for Medicare beneficiaries.[5]
- Medicare ultimately saves $2.06 for every additional dollar it spends on drugs.[6]
- Reducing cancer deaths by 10% would be worth approximately $4 trillion in economic value.[7]
- Medicare spends $91 billion each year caring for individuals suffering from Alzheimer's disease and delaying the onset of Alzheimer's by just five years would save $50 billion per year.[8]

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[2] The Batelle Technology Partnership Practice. 2010. "Gone Tomorrow? A Call to Promote Medical Innovation, Create Jobs and Find Cures in America." Prepared for the Council for American Medical Innovation.
[3] Battelle Technology Partnership Practice. 2010. Battelle/BIO State Biosciences Initiatives.
[4] Kneller, Robert. 2010. "The Importance of New Companies for Drug Discovery: Origins of a Decade of New Drugs." Nature Reviews/Drug Discovery.
[5] B. C. Stuart, J. A. Doshi, and J. V. Terza. 2009. "Assessing the Impact of Drug Use on Hospital Costs." *Health Services Research* 44, no. 1: 128–144.
[6] Shang, Baoping and Dana P. Goldman. 2007. "Prescription Drug Coverage and Elderly Medicare Spending." NBER Bulleting on Aging and Health.
[7] Murphy, K.M. and R.H Topel, 2003. "Measuring the Gains from Medical Research." University of Chicago Press
[8] Alzheimer's Association

We have a national imperative to foster the development of innovative treatments and therapies. Baby boomers are now entering into the Medicare system. By 2030, almost one out of every five Americans – some 72 million people – will be 65 years or older.[9] Currently, Medicare is projected to equal 5.1% of the U.S. GDP by 2030.[10] One of the main drivers of rising health care costs is treating chronic disease, with approximately 75 cents of every health care dollar spent on taking care of individuals suffering from a chronic disease.[11] This is even more concerning when you take into account that 45% of the population (133 million Americans) has at least one chronic disease.[12]

Developing innovative treatments and cures is a time- and capital-intensive endeavor reliant on private investment. It generally costs over $1 billion and 8-10 years to research and develop an FDA-approved drug.[13] In order to encourage innovation, we must have an FDA that is empowered and able to effectively and consistently review breakthrough treatments and therapies. There are several troubling trends that threaten to severely hamper our ability to innovate. For example, only half of the products submitted to the FDA are approved on the first submission.[14] From the average of the previous PDUFA rounds of 2003-2007 to today, drug and biologics approval times have increased 28 percent.[15] Between 1999 and 2005, the average length of clinical trials grew by 70%.[16] And despite the extraordinary advances in science over the last two decades, the number of new drug approvals per year remains flat (i.e., an average of 23 NME approvals per year over the past decade).[17]

[9] Alliance for Aging Research
[10] 2010. Medicare Trustees' Report
[11] Partnership for Chronic Disease
[12] Partnership for Chronic Disease
[13] J Dimasi and H. Grabowski, "The Cost of Biopharmaceutical R&D: is Biotech Different?" Managerial and Decision Economics No 28 (2007): 469–79
[14] BIO. Biomed Tracker. 2011.
[15] CHI. BCG. 2011. "Competiveness and Regulation: The FDA and the Future of America's Biomedical Industry."
[16] Tufts Center for the Study of Drug Development. 2008. "Growing Protocol Design Complexity Stresses Investigators, Volunteers." Impact Report. 10.1.
[17] FDA. http://www.fda.gov/downloads/AboutFDA/Transparency/Basics/UCM247465.pdf

We are in danger of losing our position as a global leader in medical innovation and our ability to keep private investment dollars and jobs in the United States as Europe, China, and India continue to develop aggressive strategies to entice companies to take their research and development enterprises abroad. In 2007, the European Union and the European Pharmaceutical Industry Association (EFPIA) sought to attract life sciences companies to Europe by establishing the $2 billion Innovative Medicines Initiative (IMI), which is described as "Europe's largest public-private initiative aiming to speed up the development of better and safer medicines for patients…[which] supports collaborative research projects and builds networks of industrial and academic experts in order to boost pharmaceutical innovation in Europe." A March 2011 press release indicates that the IMI has recently launched a second wave of research projects (focusing on areas including cancer, infectious disorders and electronic health), with a total of 23 current research projects and over €450 million (approximately USD $658 million at the time of publishing) committed by the European Commission and the EFPIA. In 2010, while the amount of capital invested in private U.S. biotechnology companies declined 3.2%, Europe saw a 29% increase.[18]

Additionally, last year, the Chinese government unveiled a 5-year plan for national economic and social development, and the biopharmaceutical industry was identified as one of the seven strategic emerging industries that China would target. The plan includes a $1.5 billion commitment and the establishment of new venture funds to invest in emerging start-up companies. India has similar plans to expand biopharmaceutical activities and in 2010 announced a plan to establish a $2.2 billion venture fund for supporting drug discovery and research infrastructure development projects.[19]

We as a nation need to focus policy discussions on how to unleash the promise of biotechnology so that the American public can realize the benefits it has to offer. Small biotechnology companies like my own depend on private investment to advance our innovative treatments and therapies programs and ultimately make it through the FDA

[18] Ernst & Young. Beyond Borders. Global Biotechnology Report. 2011
[19] Ernst & Young. Beyond Borders. Global Biotechnology Report. 2011

approval process. A fundamental part of our ability to innovate and raise private investment is having an FDA with the resources and mechanisms required to effectively and consistently review and approve innovative products in a timely manner. These decisions must be understood by stakeholders – industry, investors, patients, and physicians – and then must be made in the context of patients and diseases being treated. The FDA is rarely praised for approving a novel therapy, yet they are often maligned if there are unforeseen adverse events that occur once a product is approved. It is imperative that policymakers understand the scientific realities of approving novel medicines. When determining if the benefits of a novel product outweigh the risks, examination of current standard of care and what level of risk patients and physicians find acceptable must be part of the analysis. It is important to maintain a functioning regulatory system. Increasing requirements and associated costs without a balanced assessment of what is reasonable to accomplish and in the best interest of patients risks slowing innovation in the U.S.

The remainder of my testimony will focus on solutions. I will discuss some of the positive outcomes of the PDUFA technical negotiations as well as describe a set of policy proposals/recommendations BIO has developed to address a key policy area required to encourage innovation: the creation of a 21st century FDA. Commissioner Hamburg said it best – "Discoveries in biomedical research are slow to find their way into patient care because the agency relies on 20th century methods to evaluate 21st century science." It is imperative that we have an FDA that is empowered and able to consistently and effectively review innovative treatments and therapies. It must be an agency which has review processes and requirements that are understood by patients, physicians, industry, investors, and policymakers. And lastly, it must be an agency that takes the diseases and patients being treated into account when evaluating innovative treatments and therapies.

PDUFA TECHNICAL RECOMMENDATIONS

As you are aware, the PDUFA V technical discussions between the FDA and industry have concluded. FDA, BIO, and PhRMA have agreed on a package

of proposed technical recommendations that seek to restore FDA's review performance and get "back to basics" for patients by strengthening scientific dialogue and transparency between FDA and the Sponsor with the goal of minimizing review issues that can delay patient access to novel treatments.

Among BIO's top priorities throughout the technical discussions was to promote innovation by fostering scientist-to-scientist dialogue between FDA and Sponsors concerning high-priority rate-limiting scientific issues that arise during drug development. We are pleased that FDA agreed to adopt a new philosophy that timely interactive communication with sponsors during drug development is a core Agency activity to help achieve the Agency's mission.

BIO also supports enhancements under PDUFA V that will strengthen the timeliness, transparency, and predictability of the review of novel medicines, advance regulatory science initiatives, and enhance post-market safety surveillance. Through increased FDA-Sponsor scientific dialogue and interaction during the review process, the proposed New Molecular Entity (NME) review program will help to identify and resolve issues earlier in the review and reduce the potential for a second review cycle, thereby facilitating earlier patient access to needed treatments.

PDUFA V also makes significant contributions in the field of regulatory science. Modern approaches to drug development and evaluation, such as through the application of new tools for rare disease drug development, greater utilization of biomarkers and patient reported outcome scales, and structured benefit/risk assessment, will introduce new efficiencies in the drug development enterprise and provide FDA with additional tools to evaluate the benefits and risks of pharmaceutical products.

Additionally, PDUFA V continues industry's commitment to a lifecycle approach to product evaluation by strengthening FDA's post-market surveillance and benefit/risk management capacity. Earlier discussion of risk management, standardized approaches

to Risk Evaluation and Mitigation Strategies (REMS), and further validation of the Sentinel Network will promote patient confidence in drug and biologics.

BIO believes that PDUFA should be reauthorized in a timely and expeditious manner because the program supports the patients that the biotechnology industry serves.

POLICY PROPOSALS TO RE-INVENT THE IDEA-TO-MARKET PATHWAY

In addition to work that was accomplished within the confines of PDUFA technical discussions, last year BIO began the process of interviewing thought leaders in our industry with the purpose of envisioning game-changing strategies. Following those conversations, BIO began a rigorous policy development process to develop a forward-thinking set of policies focused on revamping incentives for investment and improving the regulatory approval pathway. As part of this process, BIO sought, and will continue to seek, input from Members of Congress, federal agencies and institutes, patient organizations, former high-level government employees, former Members of Congress, and other policy experts. The culmination of all of these efforts to date are described in a document entitled "*Unleashing the Promise of Biotechnology: Advancing American Innovation to Cure Disease and Save Lives*," which was unveiled last week during BIO's 2011 International Convention and is the focus of my testimony today.

The policy recommendations we developed are designed to ensure a clear and effective pathway for turning ideas into realities that will benefit patients and improve public health. The proposals are focused on creating a 21st century FDA and creating more effective clinical research and development processes. With an increasingly aging population, it has never been more critical to support an American industry that offers solutions to the most pressing health care needs of today and tomorrow. It is imperative that FDA be an agency that recognizes its national role in advancing innovation, maintains the ability to effectively review innovative products in a timely manner, and promotes a consistent and science-based decision making process that is reflective of patient needs. The proposals described below are designed to address each of these

principles. They are organized under three main headings: Elevating FDA and Empowering Operational Excellence; Advancing Regulatory Science and Innovation; and Enabling Modernized Patient-Centric Clinical Development.

ELEVATING FDA AND EMPOWERING OPERATIONAL EXCELLENCE

Update the FDA Mission Statement

FDA needs a clear mandate to encourage the development of innovative products. In addition, FDA must have the capacity and commitment to incorporate the latest scientific advances into its decision making so that regulatory processes can keep pace with the tremendous potential of companies' leading edge science. Congress can help by updating FDA's statutory mission to underscore the need for FDA to advance medical innovation by incorporating modern scientific tools, standards, and approaches into the Agency's work, so that innovative products can be made available to those who need them and in a timely manner.

Establish a Fixed Term of Office for the Commissioner of Food and Drugs

The Commissioner of Food and Drugs is charged with leading a science-based regulatory agency to advance the public health. As required by statute, the President appoints the Commissioner with the advice and consent of the U.S. Senate. However, a presumption of replacement with each new President has politicized the appointment and confirmation process. The Federal Food, Drug, and Cosmetic Act (FFDCA) should be amended to provide that the President appoint the Commissioner to a six-year term of office. Once confirmed, the Commissioner would be removable by the President only for pre-specified reasons – neglect of duty, malfeasance in office, or an inability to execute the agency's mission. Encouraging consistent and stable leadership at FDA, with protection from political influence that typically occurs during a presidential administration transition, better equips the Agency to fulfill its mission to protect and promote the public health.

Grant FDA Status as an Independent Agency

FDA regulates nearly a quarter of the consumer goods supplied to the American public. As such, the Agency should have the same authorities to make budget, management and operational decisions as afforded other independent agencies such as the Environmental Protection Agency. This would empower the Agency to work more effectively with the President and Congress to carry out its mission to promote and protect the public health. Creating an independent agency would also enhance the Agency's ability to obtain quality and consistent leadership.

Establish an External Management Review Board for FDA

FDA is a large, complex organization, and in order to fulfill its responsibilities effectively, it must be well-organized and well-managed. It is critical that the Agency's organization and management capabilities be periodically analyzed, and that the Commissioner of Food and Drugs be provided with fresh, visionary, and independent thinking on how to improve the ability of the Agency and its centers to promote and protect the public health, as well as the support necessary to implement recommendations. An external advisory board composed of individuals with experience in organizational management could help the Agency address operational challenges. Current law should be amended to establish a Management Review Board (MRB) to conduct periodic reviews of FDA's management and organizational structure, and to provide recommendations to the Commissioner about ways to improve FDA operations. This idea is modeled upon the Scientific Management Review Board at the National Institutes of Health, which was developed and passed by this Committee and the Congress as part of the NIH Reform Act of 2006.

ADVANCING REGULATORY SCIENCE & INNOVATION

Support Regulatory Science Public-Private Partnerships

Under the Food and Drug Administration Amendments Act of 2007 (FDAAA), Congress established the Reagan-Udall Foundation for the Food and Drug Administration, an independent non-profit organization intended to support public-private partnerships for the purpose of advancing the mission of FDA to "modernize medical [and other] product

development, accelerate innovation, and enhance product safety." The Foundation could, for example, form collaborations to advance the use of biomarkers, surrogate markers, and new trial designs to improve and speed clinical development. However, Congressional appropriations bills for the Agency have subsequently restricted FDA's ability to transfer federal funding to the Foundation. These funding restrictions should be lifted so that the Reagan-Udall Foundation can fulfill its promise.

Create an FDA "Experimental Space," led by a Chief Innovation Officer, to Pilot Promising New Scientific and Regulatory Approaches

FDA has developed several initiatives to advance regulatory science. These include the FDA/NIH Joint Leadership Council, the academic Centers of Excellence in Regulatory Science, and FDA's Critical Path Initiative. However, FDA's ability to incorporate modern science into its regulatory processes has been limited because there is no entity within the Agency with unified responsibility for systematically analyzing the findings and recommendations from these groups, and with clear authority to pilot promising scientific and regulatory approaches. An FDA "Experimental Space," led by a new Chief Innovation Officer, should be established with the responsibility and authority to ensure that promising new approaches are integrated into Agency operations at all levels.

Enhance FDA's Access to External Scientific and Medical Expertise

FDA is the preeminent federal agency charged with evaluating cutting-edge science as it is applied to the prevention, diagnosis, and treatment of human disease. FDA also has been perceived by many as the global standard bearer for regulatory review of drug and biologic applications. However, scientific and medical knowledge, techniques, and technology are advancing at a more rapid pace today than at any other time, and FDA's capacity to access information about these advances has not kept pace. It is essential that FDA's access to scientific and medical advice be enhanced by improving the operations of FDA Advisory Committees, establishing Chief Medical Policy Officers in the immediate offices of the Center Directors, and providing FDA staff with additional avenues for accessing external scientific and medical expertise.

ENABLING MODERNIZED PATIENT-CENTRIC CLINICAL DEVELOPMENT

Increase Access to Innovative Treatments and Therapies through Progressive Approval

Patients, industry, Congress, and others are eager to find ways to deliver safe and effective new drugs and biologics to patients. Patients, particularly those with illnesses for which no adequate therapy exists, want access to promising new therapies earlier in the drug development process. Smaller biopharmaceutical companies that develop those therapies are sometimes unable to maintain operations through extensive phase III testing without revenue from the sale of products. Expanding and improving the accelerated approval pathway into a progressive approval mechanism would help provide patients more timely access to needed therapies. This pathway would be limited to innovative products for unmet medical needs, significant advances to standard of care, targeted therapies, and those that have been approved by the European Medicines Agency (EMA) or other mature regulatory agencies. This pathway also would ensure risk-benefit analysis that incorporates the safety and needs of patients in the real world.

Empower FDA to Utilize a Weight-of-Evidence Approach

FDA's current statutory authority requires that the Agency approve applications for new drugs when they have been demonstrated to be safe and effective under the intended conditions of use. The law provides that effectiveness is established where FDA is satisfied that there is "substantial evidence" that the new drug has the intended effect that it is purported to have. FDA typically requires two "adequate and well controlled" studies under this standard. A weight-of-evidence approach to data analysis, however, would allow the decision-maker to look at all data and information, whatever its value, and give each appropriate consideration.

Leverage Electronic Health Records to Facilitate Clinical Research

Every new drug's sponsor spends years designing and conducting clinical trials to show their drug is safe and effective. Using health information technology (IT) such as electronic health records (EHRs) in clinical research will improve and speed up the drug development process, and decrease costs. However, there are significant barriers

preventing wide-spread use of health IT in clinical research, including slow adoption by providers and lack of standards development. FDA can help remove those barriers. Congress should create a Clinical Informatics Coordinator in the Office of the Commissioner of Food and Drugs charged with developing processes to validate and encourage the use of health IT in clinical research, and establishing pilot projects to use health IT in clinical research.

Require FDA to Disclose to the Sponsor Reasons for Non-Approval

The FFDCA implies that licensing or approval applications contain a binary question – approve or deny – due to phased, investigational review of applications; however, there is in practice a third response. In this case, FDA neither approves nor officially denies the application (which would require FDA to give the sponsor specific procedural rights such as a hearing); rather it finds the application to be incomplete in some way that makes the application ineligible for approval. When FDA makes such a finding, it should communicate to sponsors in clear terms why risk was determined to outweigh benefits, and why other Agency authorities such as Risk Mitigation and Evaluation Strategies (REMS) – which are designed to mitigate risk for approved products – are insufficient (in addition to indicating what must be done to address any deficiencies). Such an approach would help create a consistent and transparent evaluation of risk-benefit, and provide the sponsor with better information on what, if any, additional studies are required to achieve approval.

Conclusion

We have a national imperative to support and foster advances in medical innovation. The full potential of biotechnology industry to cure disease and offer real solutions to our nation's most pressing health care needs has yet to be realized. We look forward to working with you on developing policies for a 21st century FDA that will serve to unleash the promise of biotechnology in the United States.