**TESTIMONY OF PAUL J. HASTINGS, CHAIRMAN & CEO,**
**ONCOMED PHARMACEUTICALS**

**ON BEHALF OF THE BIOTECHNOLOGY INDUSTRY ORGANIZATION**

**U.S. HOUSE OF REPRESENTATIVES**
**COMMITTEE ON OVERSIGHT & GOVERNMENT REFORM**
**SUBCOMMITTEE ON ENERGY POLICY, HEALTH CARE & ENTITLEMENTS**

**DECEMBER 12, 2013**

***"FDA CHECK-UP: DRUG DEVELOPMENT AND MANUFACTURING CHALLENGES"***

Chairman Lankford and Ranking Member Speier, Members of the Committee, my name is Paul Hastings, Chairman and Chief Executive Officer of OncoMed Pharmaceuticals headquartered in Redwood City, CA. I also serve as Chairman of the Biotechnology Industry Organization (BIO) Emerging Companies Section Governing Board, which represents the smaller, emerging biotechnology companies that often do not yet have a product on the market.

BIO represents more than 1,000 biotechnology companies, academic institutions, state biotechnology centers, and related organizations across the United States and in more than 30 other nations – the majority of which are small and emerging companies, with 90% having fewer than 100 employees. BIO members are involved in the research and development of innovative health care, agricultural, industrial, and environmental biotechnology products, thereby expanding the boundaries of science to benefit humanity by providing better health care, enhanced agriculture, and a cleaner and safer environment.

I have over 27 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: tumor initiating cells, which drive the growth of the 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 these 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 the 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. We currently have five products in clinical development in 13 completed or ongoing clinical trials, with hundreds of patients having received our experimental therapies, and we are pursuing the discovery of additional novel anti-tumor initiating product candidates.

I would like to thank the Committee for holding this timely and important Congressional hearing. The U.S. biotechnology industry is working on treatments and therapies that have the potential to deliver new solutions to our most pressing health care needs and is a key element of an innovation-driven economy.

## I. UNLEASHING THE PROMISE OF BIOTECHNOLOGY TO IMPROVE HUMAN HEALTH

Currently, there are nearly 1,000 biotech drugs and vaccines under development for more than 100 diseases.[1] By harnessing the power of molecular biology and genomics, we have come a long way in turning incurable diseases into treatable diseases, increasing the ability of patients to maintain independent lives, and generally improving the quality of life for many patients suffering from chronic and life-threatening diseases. Improving quality of life, decreasing hospitalizations, and allowing patients to live longer and more independent lives is not only a public health goal – it is a national imperative.

Approximately 60% of individuals between the ages of 50 and 64 have at least one chronic disease and the Baby Boomer population is projected to double the number of individuals that are 65 or older to 71.5 million by 2030.[2] In fact, chronic medical conditions account for more than 75% of total health care spending.[3] If we consider that the projected cost to care for a single chronic disease, Alzheimer's, is projected to increase from $203 billion in 2013 to $1.2 trillion per year in 2050, and that developing a treatment that would delay the onset of Alzheimer's by just five years would reduce that projected increase in cost by $447 billion – it is clear that we need to promote and implement policies that enable the effective development and approval of innovative treatments and therapies.[4, 5]

In addition to the primary mission of developing and providing new medicines and improving the lives of patients, the biopharmaceutical industry is and will be an important sector in a 21st century innovation-driven U.S. economy. In 2011, the U.S. biopharmaceutical sector directly and indirectly supported approximately 3.4 million U.S. jobs and accounted for $789 billion in economic output.[6] However, this is an industry that continues to face intense competition from other countries, as well as increasing research and development costs, regulatory challenges, and a contracted funding environment. While outside the scope of this particular hearing, it is vital to the success of the industry that our nation's policies protect the intellectual property of these

[1] "Innovation in the Biopharmaceutical Pipeline: A Multidimensional View." Analysis Group. January 2013. http://phrma.org/sites/default/files/pdf/2013innovationinthebiopharmaceuticalpipeline-analysisgroupfinal.pdf
[2] CNN Library, "Baby Boomer Generation Fast Facts," November 6, 2013, http://www.cnn.com/2013/11/06/us/baby-boomer-generation-fast-facts/
[3] National Center for Chronic Disease Prevention and Health Promotion, Center for Disease Control, "The Power of Prevention," 2009, http://www.cdc.gov/chronicdisease/pdf/2009-power-of-prevention.pdf
[4] http://www.alz.org/alzheimers_disease_facts_and_figures.asp#quickFacts
[5] http://www.alz.org/documents_custom/trajectory.pdf
[6] Battelle/PhRMA, The Economic Impact of the U.S. Biopharmaceutical Industry, July 2013. http://phrma.org/sites/default/files/pdf/The-Economic-Impact-of-the-US-Biopharmaceutical-Industry.pdf

companies, as any weakening of those protections will have a deleterious impact on the ability to attract the necessary and long-term investment required to research, develop, and ultimately make new medicines available to the public. We also ask Congress to support funding for NIH, which supports the basic research that industry depends on to discover and develop drugs that will benefit the public.

## II. BIOTECHNOLOGY INDUSTRY: SIGNS OF RECOVERY, BUT CHALLENGES REMAIN

This year we have seen positive signs that the biotechnology industry is recovering from the economic crisis of 2007 and 2008. There have been 39 biopharmaceutical companies that have gone public this year, including my own company, OncoMed, marking the most active IPO market in a decade.[7] Additionally, in 2012 the FDA approved 39 new molecular entities, the most approvals we had seen in 16 years and up from 35 approvals in 2011.[8,9] CDER has approved 25 new molecular entities so far this year.[10] This number is still higher than the average of 24 drugs per year we saw from 2003-2011.[11] While this is good news, the financial and regulatory environment continues to pose significant challenges to innovative drug and biologic developers.

In 2012 we saw a 15% decrease from 2011 in venture capital dollars invested in the biotechnology industry.[12] The majority of this decrease was seen in first-time financings, which were the lowest they have been since 1995.[13] This is a trend that has continued in 2013. In the first three quarters of 2013, first-time venture deals in biotechnology were the lowest they have been in 17 years.[14] And while the number of first-time financings increased in the third quarter of this year, the overall dollar value decreased 56%.[15] This means that start-up companies, working on the next generation of medicines, are competing for a limited amount of funds from fewer venture capital firms, as well as non-venture funding mechanisms from angel investors, venture philanthropies, and non-traditional equity deals.

The regulatory environment has improved in recent years, but there continues to be a need to improve the efficiency, timeliness, and consistency of the U.S. drug development and evaluation enterprise. The number of drug approvals has increased, yet so too have the research and development costs. According to a 2013 study from Deloitte and Thompson Reuters, which analyzed the 12 largest life science companies' R&D spend,

7 FierceBiotech, "UPDATED: Fresh burst of biotech IPO pitches launches a busy Q4 season," October 21, 2013, http://www.fiercebiotech.com/special-reports/biotech-ipo-frenzy-headed-crack
8 http://www.ey.com/Publication/vwLUAssets/Beyond_borders/$FILE/Beyond_borders.pdf
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11 http://www.fda.gov/downloads/drugs/developmentapprovalprocess/druginnovation/ucm337830.pdf
12 MoneyTree Report PWC/NVCA Full-year 2012, https://www.pwcmoneytree.com/MTPublic/ns/moneytree/filesource/exhibits/Q4%202012_Full%20Year%202012_MoneyTree_Summary_Report.pdf
13 MoneyTree Report PWC/NVCA Full-year 2012, https://www.pwcmoneytree.com/MTPublic/ns/moneytree/filesource/exhibits/Q4%202012_Full%20Year%202012_MoneyTree_Summary_Report.pdf
14 FierceBiotech, "As VC falters, early-stage biotechs look elsewhere for cash," October 21, 2013 http://www.fiercebiotech.com/story/vc-falters-early-stage-biotechs-look-elsewhere-cash/2013-10-21
15 FierceBiotech, "As VC falters, early-stage biotechs look elsewhere for cash," October 21, 2013 http://www.fiercebiotech.com/story/vc-falters-early-stage-biotechs-look-elsewhere-cash/2013-10-21

the cost of developing a single drug from discovery to the market increased 18% from $1.1 billion in 2010 to $1.3 billion in 2013.[16] The average annual R&D spend for a biopharmaceutical company (both small and large) in 2012 was $54 million, up from $48 million in 2010.[17]

The rising costs of drug development and the resulting decrease in R&D efficiency are complex, multi-faceted problems, but increased cost, complexity, and duration of clinical trials are widely accepted to be critical contributing factors.[18] A study conducted by the Manhattan Institute found that as much as 90% of the development costs for many drugs ultimately approved by the FDA were incurred during Phase III clinical trials.[19]

Additionally, the duration of the clinical phase of approvals for biopharmaceuticals has steadily increased from an average of 4.6 years in the early 1990s to 7.1 years in 2005-2009.[20] Concomitant with the increase in clinical trial duration are the rising protocol complexities and requirements. In fact, by the early 2000s the average clinical trial required enrollment of 2-3 times more patients than comparable trials in the previous decade.[21] Median unique procedures per protocol increased from 105.9 in 2000-2003 to 166 in 2008-2011, an increase of more than 57% in an 11-year window.[22]

And lastly, almost 60% of all clinical trial protocols are amended at some point during the trial, taking more than 60 days to identify and correct, with one-third of those amendments being avoidable.[23]

## III. ADVANCING A REGULATORY ENVIRONMENT THAT FOSTERS BIOMEDICAL INNOVATION

While developing medicines that treat serious and life-threatening diseases is a complicated and high-risk endeavor, the importance of increasing the efficiency and effectiveness of the research and development process is clear. To that end, the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA) focused on enabling FDA to be an agency that advances innovation by implementing review processes designed to promote the effective review of innovative products in a timely manner and that promotes a consistent, science-based decision-making process reflective of patient needs. It is yet to be seen if the regulatory flexibility afforded by FDASIA is being fully embraced at the FDA reviewer level to advance the development of new therapies for

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[16] Deloitte, Thompson Reuters, "Measuring the Return From Pharmaceutical Innovation 2013," http://www.deloitte.com/assets/Dcom-UnitedKingdom/Local%20Assets/Documents/Industries/Manufacturing/uk-manufacturing-measuring-the-return-from-pharmaceutical-innovation-2013v1.pdf

[17] John Carroll, "Biotech R&D spending roars ahead as Big Pharma grimly holds the line," FierceBiotech, 12 September 2013, http://www.fiercebiotech.com/story/biotech-rd-spending-roars-ahead-big-pharma-grimly-holds-line/2013-09-12

[18] See, Scannell JW, Blanckley A, Boldon H, and Warrington B, "Diagnosing the decline in pharmaceutical R&D efficiency," Nature Reviews: Drug Discovery 11, 191-200 (2012). See also, Ruffolo RR, "Why has R&D productivity declined in the pharmaceutical industry?" Expert Opin. Drug Disc. 1(2):99-102 (2006).

[19] Avik R, "The Stifling Cost of Lengthy Clinical Drug Trials," Manhattan Institute, 2012, http://www.manhattan-institute.org/pdf/fda_05.pdf.

[20] Allison M, "Reinventing clinical trials," Nature Biotechnology 30(1):41-49 (2012).

[21] Vogelson CT, "We are the world?" Modern Drug Discovery 4(6):36-38, 40, 42 (2001).

[22] Allison M, "Reinventing clinical trials," Nature Biotechnology 30(1):41-49 (2012).

[23] Tufts Center for the Study of Drug Development, "Majority of Clinical Trial Protocols are Amended, But One-Third of Those Changes Are Avoidable," September 13, 2011, http://csdd.tufts.edu/news/complete_story/pr_ir_sep-oct_2011.

unmet medical needs, and significant challenges must be overcome in order to fully implement FDASIA in the spirit Congress intended.

### A. Eliminate the Sequestration of Industry User Fees

Under FDASIA, which also reauthorized the Prescription Drug User Fee Act (PDUFA V), industry agreed to significant increases in user fee funding for the FDA to help support FDA's drug review activities and advance regulatory science. However, as a result of budget sequestration, a portion of the user fees paid by private industry are being diverted and held in an "escrow" account that has no practical purpose for FDA, industry, or patients. This has severely hindered FDA's ability to add the capacity and infrastructure necessary to implement FDASIA and meet its commitments under PDUFA V. To make matters worse, the $82 million in user fee funding that was sequestered in FY 2013 cannot be released to FDA without forcing corresponding cuts elsewhere in the FDA budget.

BIO urges Congress to rectify this counter-productive situation by passing the Food and Drug Administration Safety Over Sequestration (SOS) Act of 2013 (H.R. 2725), sponsored by Representatives Leonard Lance (R-NJ) and Anna Eshoo (D-CA) with broad bipartisan support. In addition to clarifying that sequestration should not apply to industry-paid user fees, we encourage Congress to continue to support FDA through the annual appropriations process.

### B. Expedite Drug Development for Serious and Life-Threatening Diseases

FDASIA also encourages FDA to expedite the development of modern medicines for serious and life-threatening conditions by expanding the existing Accelerated Approval pathway and enacting a new Breakthrough Therapy Designation process.

The Accelerated Approval pathway has historically been very successful in accelerating the development, review, and availability of innovative medicines to treat HIV/AIDS and cancer. Congress recognized that modern drug development has changed substantially since the initial implementation of Accelerated Approval in 1992 and that the pathway should be expanded to additional diseases and better leverage recent scientific improvements. Specifically, the Congressional findings included in FDASIA provided a detailed description of what Congress intends to achieve by expanding Accelerated Approval, and what it expects FDA to accomplish when applying these expanded authorities:

> *"FDA should be encouraged to implement more broadly effective processes for the expedited development and review of innovative new medicines intended to address unmet medical needs for serious or life-threatening diseases or conditions, including those for rare diseases or conditions, using a broad range of surrogate or clinical endpoints and modern scientific tools earlier in the drug development cycle when appropriate. This may result in shorter clinical trials for*

*the intended patient population or targeted subpopulation without compromising or altering the high standards of the FDA for approval of drugs."*

In August of 2013, FDA released *Draft Guidance for Industry on Expedited Programs for Serious Conditions—Drugs and Biologics*. While this guidance is helpful in explaining the characteristics and features of FDA's four expedited approval pathways, greater clarity in several areas is still needed. In particular, FDA should establish a systematic framework and evidentiary criteria for discussing Accelerated Approval and endpoint selection earlier in drug development, which would foster predictability and stimulate greater Sponsor confidence in the process. Additionally, the guidance inadequately addresses the unique issues associated with rare diseases under Accelerated Approval, which should be the focus of future guidance. BIO is closely evaluating the modernization of the program to track how it is being utilized in additional therapeutic areas by leveraging novel surrogate and intermediate clinical endpoints.

The new Breakthrough Therapy designation program is one of the most publicly discussed provisions of FDASIA. The criteria for this designation require that the drug may be a substantial improvement over existing therapies, based on preliminary clinical evidence from one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The benefit of this program is increased interactions with FDA in order to expedite the development and review process. As of December 10, 2013, the FDA website listed a total of 121 requests for a Breakthrough designation with 34 requests granted, 61 requests denied, and three breakthrough-designated products approved.[24] A majority of the designations thus far have been for products in the Phase III stage of development.[25]

While clearly the Breakthrough Therapy program has been successful in generating interest and granting several requests, BIO is in the process of tracking the success of this program and analyzing specifically how this program is expediting the development and review of these drugs, such as increased interactions with senior FDA staff and utilization of modern tools and approaches such as adaptive clinical trials to clinical development.

Additionally, it is important that non-clinical aspects of drug development also be expedited to keep pace with an accelerated clinical program. For example, we have urged FDA to adopt a risk-based, life-cycle approach to the review of Chemistry, Manufacturing, and Controls (CMC) data and inspectional activities. Additionally, for Breakthrough Therapies and expedited program products with companion diagnostics, Center for Devices and Radiological Health (CDRH) senior staff should be involved in cross-disciplinary engagement during drug development.

### C. Advance Scientific Dialogue and Interactive FDA-Sponsor Communication

[24] Friends of Cancer Research, http://www.focr.org/breakthrough-therapies.

[25] http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FDASIA/ucm341027.htm

There were several provisions in PDUFA V and FDASIA designed to improve the opportunities for biopharmaceutical companies, patients, and FDA to engage in timely, scientific dialogue in order to facilitate efficient and effective drug development programs. For example, a centerpiece of PDUFA V is a new review program for New Molecular Entities intended to reduce unnecessary delays in the review process by improving FDA-Sponsor communication and transparency.

To improve communication during the drug development phase, PDUFA V also created an Enhanced Communications Liaison Office tasked with two primary objectives: facilitate general, and, in some cases, specific interactions with Sponsors and FDA review teams; and develop training for CDER staff and communication of best practices to the Sponsor community. Unfortunately, due to sequestration, FDA has been unable to fully staff this office and thus is likely limited in its ability to conduct training and communication of best practices. As it is a new program, BIO will be working with the FDA to educate the biotechnology community about this new office.

BIO recently completed a survey of BIO member companies focusing on communications between FDA and companies during the drug development process. We are in the process of completing our analysis and will be releasing our findings to the public in the coming weeks. In general, we found that companies believe that communications with FDA have improved since 2007. However, when we asked more specific questions based on type of application (NME vs. BLA), type of review (Priority, Fast Track, Accelerated Approval, Breakthrough Therapy), type of communication (formal vs. informal), and, most importantly, the review division, the level of satisfaction with communications varied significantly. Additionally, while conditions have been improving and culture shifting happening, a significant amount of companies cited miscommunication with FDA as a major factor in delays of one or more products in the past.

### D. Incorporate Patient Perspectives when Balancing Benefits and Risks

FDASIA and PDUFA V also take unprecedented steps to incorporate the patient voice into FDA regulatory decisions. By definition, all prescription drug products offer both therapeutic benefits and potential adverse events. The FDA drug review process must be grounded in a careful evaluation and balance of these benefits and risks made in the broader context of disease severity, patient perspectives, and the body of available scientific evidence. Therefore, it is essential for the public to understand that safety is not an absolute; rather, the acceptability of the safety of a drug is assessed in the context of whether its benefits outweigh its risks.

FDA is taking several important steps under PDUFA V to incorporate greater patient involvement, transparency, and consistency in this benefit-risk assessment. The Patient-Focused Drug Development initiative will carefully assess patient perspectives in 20 therapeutic areas to better understand the patient community's views on the severity of the underlying condition, current treatment options, potential benefits, and anticipated risks. This information will help to inform FDA's proposed *Structured Approach to*

*Benefit-Risk Assessment in Drug Regulatory Decision Making*, a grid-style framework released in May that will be integrated into FDA's approval decisions over the course of PDUFA V. BIO supports FDA's continuing efforts to enhance the clarity of this complex and critical process of benefit-risk assessment, both internally and for the public, throughout the lifecycle of drug evaluation, and will continue to work with FDA on this important issue.

Additionally, there are provisions in PDUFA V designed to increase patient participation in medical product discussions and better enable FDA to engage with external experts on the development and review of targeted therapies and drugs designed to treat rare diseases. BIO will be tracking these activities to determine if they are being successfully implemented.

## IV. CONCLUSION

Ours is an industry that is working to provide better medicines that can improve the lives of patients and bring new solutions to our country's critical health care needs. There have been many positive indicators over the past two years demonstrating that the biotechnology industry is rebounding, but significant challenges on both the financial and regulatory fronts remain. The key provisions of PDUFA V and FDASIA discussed in this testimony, if implemented successfully, could significantly improve the efficiency and effectiveness of the clinical development of innovative drugs by increasing scientific dialogue and enabling the utilization of modern tools and approaches to drug development. BIO is committed to working with FDA and Congress to ensure these goals are achieved.

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**Paul J. Hastings**
Chairman and Chief Executive Officer

Mr. Hastings is the Chairman and CEO of OncoMed Pharmaceuticals. Prior to joining OncoMed in 2006, Mr. Hastings was President and Chief Executive Officer of QLT, Inc. Previous to that, Mr. Hastings served as President and Chief Executive Officer of Axys Pharmaceuticals, which was acquired by Celera Corporation in 2001. From 1999 to 2001, Mr. Hastings served as the President of Chiron BioPharmaceuticals, a division of Chiron Corporation. Prior to that, he was President and Chief Executive Officer of LXR Biotechnology. Mr. Hastings also held a series of management positions of increasing responsibility at Genzyme Corporation, including serving as President of Genzyme Therapeutics Europe as well as President, Genzyme Therapeutics Worldwide. Mr. Hastings also served as Vice President, Marketing and Sales and General Manager, Europe for Synergen, Inc., and previously held a series of marketing and sales management positions with Hoffmann-La Roche.

Mr. Hastings was recently Chairman of the Board of Proteolix (sold to Onyx Pharmaceuticals in 2010), and served on the boards of ViaCell (sold to Perkin-Elmer in 2007). He is currently Lead Director of Pacira Pharmaceuticals and on the board of Relypsa. He also serves as Chairman of the Emerging Companies Section of the Biotechnology Industry Organization, and serves on the board of the Bay Area Biosciences Association (BayBio) and the California Healthcare Institute (CHI).

Mr. Hastings received a Bachelor of Science degree in pharmacy from the University of Rhode Island.

Committee on Oversight and Government
Reform Witness Disclosure Requirement –
"Truth in Testimony" Required by House
Rule XI, Clause 2(g)(S)

Name: Paul J. Hastings, Chairman and CEO, OncoMed Pharmaceuticals

I. Please list any federal grants or contracts (including subgrants or subcontracts) you have received since October I, 2011. Include the source and amount of each grant or contract.

NONE

2. Please list any entity you are testifying on behalf of and briefly describe your relationship with these entities.

1. Biotechnology Industry Organization
2. California Healthcare Institute
3. BayBio
4. OncoMed Pharmaceuticals

3. Please list any federal grants or contracts (including subgrants or subcontracts) received since October I, 2010, by the entity(ies)
you listed above. Include the source and amount of each grant or contract.

None

*I certify that the above information is true and correct.*
Signature: Date: