IDSA Headquarters
1300 Wilson Boulevard
Suite 300
Arlington, VA 22209
TEL: (703) 299-0200
FAX: (703) 299-0204
EMAIL ADDRESS:
info@idsociety.org
WEBSITE:
www.idsociety.org

IDSA
Infectious Diseases Society of America

June 10, 2014

Representative Fred Upton
2183 Rayburn House Office Building
Washington, DC 20515

Representative Diana DeGette
2368 Rayburn House Office Building
Washington, DC 20515

Submitted electronically to cures@mail.house.gov

RE: 2nd White Paper — 21st Century Cures: An Update on the President's Council of Advisors on Science and Technology 2012 Report on Propelling Innovation

Dear Chairman Upton and Representative DeGette:

On behalf of the Infectious Diseases Society of America (IDSA), thank you for this second opportunity to comment on the 21st Century Cures Initiative. IDSA shares your commitment to fostering greater drug innovation and development, particularly for urgently needed new antibiotics. We agree that many of the recommendations set forth in the President's Council of Advisors on Science and Technology (PCAST) 2012 Report to the President on Propelling Innovation in Drug Discovery, Development, and Evaluation can inform the Committee's efforts to stimulate pharmaceutical research and development (R&D). Below we offer specific comments and recommendations about how the Committee can apply PCAST's recommendations to incentivize antibiotic R&D.

As IDSA explained in our response to the 21st Century Cures first white paper, the rapidly increasing rates of antibiotic resistance and the nearly dry antibiotic pipeline constitute a public health crisis in need of urgent federal action. While the Generating Antibiotic Incentives Now (GAIN) Act has provided a valuable incentive, as evidenced by Roche recently re-entering antibiotic R&D, key stakeholders agree that much more must be done to rebuild the necessary antibiotic R&D enterprise to produce the variety of new antibiotics that patients desperately need to treat serious or life-threatening infections.

PCAST Recommendation: Support Federal Initiatives to Accelerate Therapeutics

IDSA strongly agrees with the PCAST recommendation for increasing funding for the National Institutes of Health (NIH) to allow for new and further research on the underlying basis of disease and therapeutics. Sustained, robust funding is needed not only to spur research today, but also to encourage the younger generations to pursue careers in research to ensure the future of our nation's biomedical research enterprise. IDSA urges the Committee to work with your colleagues on the Appropriations Committee and in congressional leadership to better prioritize funding for the NIH, and specifically the National Institute for Allergy and Infectious Diseases (NIAID).

Between Fiscal Year (FY) 1998 and FY 2003, Congress doubled the funding for NIH. Since that time, NIH has received very modest increases some years and even cuts in FY 2011 and FY 2013. For FY 2015, the President proposed a $200 million increase for NIH. However, NIH estimated that the Biomedical Research and Development Price Index for 2015 would be 2.9%. As such, the 0.7% increase requested for NIH in the President's budget continues the 10-year downward trend in purchasing power at the NIH. The overall NIH grant success rate for FY 2013 is likely to be reported as falling to 15%, its lowest level in history. The latest funding line reported by investigators for investigator initiated grants (R01s) is the 9th percentile.

Depressed NIH funding is having a chilling effect on research, causing established researchers to scale back or completely discard promising research, lay off laboratory staff and dismantle research infrastructure that took years to build. Young people are so discouraged by the lack of NIH funding that they are abandoning potential careers in research entirely, seriously jeopardizing our nation's ability to remain a leader in biomedical innovation.

Weakened NIAID funding comes at a particularly problematic time as we are facing an onslaught of emerging, growing and re-emerging infectious disease threats for which patients need researchers to help develop cures. In addition to infections caused by multi-drug resistant pathogens, U.S. patients have now experienced our first cases of the Middle East Coronavirus (MERS). Dengue and chikungunya are becoming more prevalent. We are also seeing a resurgence of measles. College campuses are struggling with meningitis cases. Of course seasonal and pandemic influenza remain a serious concern.

In the area of infectious diseases, we are facing urgent needs and opportunities that require a well-funded NIH in order to advance scientific discovery in life-saving ways. IDSA specifically supports increased funding for NIAID, which funds a variety of critical infectious diseases research efforts. For example, the NIAID recently established the Antibacterial Resistance Leadership Group (ARLG) to develop, design, implement, and manage a clinical research agenda to increase knowledge of antibacterial resistance. The ARLG will focus on antibacterial drug and diagnostic development, optimal usage strategies, infection control and activities to limit the development of resistance. If properly supported, the ARLG is well poised to help catalyze efforts to bring new antibiotics to patients.

While the PCAST report does not focus on the need to increase funding for the Centers for Disease Control and Prevention (CDC), IDSA argues that strong funding for this agency is equally important. CDC has an important role in research and innovation. For example, CDC's proposed Detect and Protect Against Antibiotic Resistance initiative – which has broad support – includes the establishment of a bacterial isolate library that could be useful to researchers and companies for the development of new antibiotics. Unfortunately, CDC funding has suffered dramatic cuts in the last several years—most notably a $740 million cut in FY 2011 and an additional $300 million cut in FY 2013 due to sequestration.

PCAST Recommendation: Catalyze the Creation of a Broad-Based Partnership to Accelerate Therapeutics

IDSA wholeheartedly agrees with PCAST's assessment that a high-level public private partnership (PPP), with representation from the federal government, academia, industry, physicians and other key stakeholders, is needed to promote innovation and improvement in the discovery, development, and evaluation of new medicines for important public health needs. As PCAST correctly asserts, this mission cannot be appropriately performed by existing federal entities. Given the urgent need for new antibiotics, and the significant scientific, economic and regulatory challenges these products face, these areas are well suited for a PPP to tackle. The European Commission (EC) has a successful PPP that should serve as a strong example for the U.S.

In 2012, the EC launched their ground-breaking New Drugs For Bad Bugs (ND4BB) PPP. PPPs are essential to furthering the discovery process for new antibiotics because they convene the required diverse stakeholders to tackle the complex scientific and economic challenges facing antibiotic R&D. For example, ND4BB brings together government leaders, academia, industry and other experts for an unprecedented sharing of information and multi-disciplinary collaboration. The focus of the overall program is to develop better networks of researchers, create fluid and innovative clinical trial designs and provide incentives for companies to meet the challenges of antibiotic resistance quickly and efficiently. Initial funding for ND4BB (approximately $300 million for the first phase) was nearly equally split between government and industry sources.

The U.S. has begun recognizing the importance of PPPs for antibiotic development, though US efforts have been much more limited in scope than EU activities. For example, the Biomedical Advanced Research and Development Authority (BARDA) has become a critical source of funding for companies developing novel antibiotics. However, discreet projects, while valuable, will likely not yield as powerful an impact as a large-scale, well-coordinated PPP similar to the ND4BB initiative.

IDSA urges U.S. government leaders to establish a large scale PPP, similar to the European effort, to ensure that we do not continue falling further behind. Industry leaders at the forefront of ND4BB have noted that government initiative was vital to the creation of these valuable partnerships.

PCAST Recommendation: Create a New Pathway for Initial Approval of Drugs Shown to be Safe and Effective in a Specific Subgroup of Patients

IDSA urges the Committee to swiftly act upon the Antibiotic Development to Advance Patient Treatment (ADAPT) Act, H.R. 3742, which would follow PCAST's recommendation to establish a new approval pathway for new antibiotics to treat infections that are resistant to current available treatments. Under ADAPT, companies could study new antibacterial or antifungal drugs to treat serious or life-threatening infections for which there is an unmet medical need in smaller clinical trials and receive approval for the limited population in most need of the therapy. The European Union is already developing regulatory schemes to allow for this type of limited population antibacterial drug development, and we strongly urge the U.S. to follow suit.

Clinical trials for antibacterial and antifungal drugs to treat serious or life-threatening infections face significant challenges. Some of the most dangerous pathogens are to date occurring in relatively small numbers of patients, making it difficult to impossible to populate traditional, large scale clinical trials. It is important to develop drugs to treat infections caused by these deadly pathogens before they infect larger numbers of people. Moreover, when a pathogen is resistant to all approved antibiotics, there is no effective antibiotic against which to compare the new antibiotic, which is the standard procedure for clinical trials. Compounding the problem is the lack of rapid diagnostic tests to identify patients infected with certain pathogens who may be eligible for antibiotic or antifungal clinical trials.

The ADAPT Act would speed patient access to desperately needed, life-saving new antibiotics and antifungals, and it includes important provisions to help guide the appropriate use of these drugs. IDSA recommends that one additional provision be added to require a prominent and conspicuous visual element, such as a logo, on the labeling of ADAPT drugs to make it as simple as possible for the health care community (including those conducting educational campaigns, such as the CDC Get Smart program) to easily recognize that these drugs have been approved in a different manner than traditional antibiotics and must be used appropriately. As PCAST noted, a limited population drug approval pathway must be implemented in such a way as to strongly influence behavior. Lastly, a visual element would help give the Food and Drug Administration (FDA) the comfort level it needs to approve new drugs under this pathway, thus increasing the potential success of the ADAPT Act in bringing lifesaving new antibiotics to patients. We believe this issue can be easily addressed as the legislation moves forward.

We are pleased that the ADAPT Act has garnered broad bipartisan support among Committee members. Numerous medical societies and public health organizations share IDSA's view of this important legislation. Given the urgent need for new antibiotics and the broad stakeholder support for a limited population antibacterial drug pathway, we believe that the ADAPT Act should move forward right away.

PCAST Recommendation: Improve FDA's Tools for Monitoring and Communication of Clinical Benefits and Risks

IDSA has long called for data on antimicrobial drug use to be collected in real time and made publicly available on a regular basis. PCAST specifically recommended that Congress increase FDA funding to expand post-marketing surveillance activities, such as the Sentinel System, to better identify and evaluate the potential benefits and risks of drugs and the populations at highest risk for adverse events. IDSA agrees with the potential value of Sentinel, and would also alert the Committee to another important, but underfunded, tool for monitoring antimicrobial drug use and resistance rates — CDC's National Healthcare Safety Network (NHSN). NHSN's antibiotic use module and antibiotic resistance module provide important opportunities for collecting critical data. But NHSN has been flat funded for years, despite repeated requests from the Administration for funding increases. Additional support for this program would allow and encourage more healthcare facilities to report important antibiotic use and resistance data through NHSN. IDSA urges the Committee to authorize funding in this area and to work with

your colleagues on the Appropriations Committee and in congressional leadership to provide more robust resources for antimicrobial use and resistance monitory and data collection.

While the FDA Sentinel System and other programs, such as the Antibiotic Use and Antibiotic Resistance modules of CDC's NHSN provide valuable data and should be better funded in order to expand their reach, the U.S. still lacks a comprehensive system for collecting in real time data on antimicrobial drug use and resistance rates. Specific data on the type and quantity of antimicrobial drugs used in patient care are needed, not only to evaluate effectiveness and identify adverse outcomes (key areas of focus for Sentinel), but also to determine antimicrobial drug overuse patterns and their impact on the development of resistance. Only by understanding the scope and severity of the problem can we develop, implement and evaluate effective interventions to prevent and control resistance. Regarding antimicrobial drug use data, at a minimum IDSA recommends collection of the following data: specific drug, indication, site of infection, organism, basic patient demographics, treatment duration, and outcomes (efficacy and side effects).

As the Committee considers PCAST's recommendation regarding the Sentinel System, IDSA urges you to consider the European Union's (EU) successful system across all member countries for collecting antimicrobial drug use data and tracking antimicrobial resistance trends. The European Surveillance Antimicrobial Consumption (ESAC) and the European Antimicrobial Resistance Surveillance Network (EARS-Net) are funded by the European Centre for Disease Control (ECDC) and serve as a strong example of the type of comprehensive data collection needed in the U.S.

PCAST Recommendation: Reform Management Practices at FDA

IDSA agrees with PCAST's recommendations that FDA seek to make the approval process for drugs more transparent, predictable, responsive, and efficient through a variety of means including addressing regulatory barriers, advancing regulatory science and issuing guidance documents in a timely manner that is in accordance with national priorities.

IDSA strongly supports collaborative regulatory science efforts underway among FDA, NIAID and the Foundation of the NIH (FNIH) along with industry and academia to develop new endpoints for antibacterial drug trials, as well as the Clinical Trials Transformation Initiative (CTTI), established by Duke University and the FDA to engage patients and experts in discussions of current practices and challenges in the design and conduct of antibiotic trials and to develop novel approaches to overcome these challenges.

IDSA has long called for clear and feasible regulatory guidances for antibiotic clinical trials. In setting regulatory guidance for antibiotic development, FDA must balance the public health risks of approving a potentially less effective drug with the risk of having no new, critically needed antibiotic available to treat patients infected with resistant pathogens. While significant work remains, we note that FDA has made recent progress in this area. In 2013, FDA sought public comment on new approaches to antibacterial drug development, and specifically requested input on prioritizing new and updated clinical trial guidance documents. Also in 2013, FDA published

draft guidance for industry on antibacterial therapies for patients with unmet medical need for the treatment of serious bacterial diseases. IDSA offered comments on this draft guidance which overall was thoughtful and provided useful information that we hope will stimulate more antibacterial drug development. FDA also published draft guidance for industry on pulmonary tuberculosis (TB): developing drugs for treatment in 2013. In light of the urgent need for new drugs to treat TB, particularly drug-resistant TB, this guidance provides much-needed clarity for sponsors interested in TB product development. FDA has continued its progress this year, issuing draft guidance on community-acquired bacterial pneumonia: developing drugs for treatment. IDSA noted that this document was a good faith effort by FDA to address concerns raised about previous guidance documents, but additional changes are needed, including allowing a greater percentage of patients with prior antibacterial drug therapy, expanding the non-inferiority margin in certain circumstances, and providing greater clarity on multiple issues.

PCAST Recommendation: Study Current and Potential Economic Incentives to Promote Innovation in Drug Development

PCAST correctly asserts that current economic incentives are insufficient to meet the need for new antibiotics to treat infections caused by drug-resistant bacteria. However, IDSA disagrees with PCAST's recommendation to study incentives for antibiotic R&D. Numerous studies on this issue have already been commissioned and completed. Real world experience, including widespread company exits from the antibiotic market over the last few decades and a sharp decline in FDA approvals of new antibiotics, clearly demonstrate a market failure and the need for new incentives. Numerous factors make antibiotics an unattractive economic prospect for companies: Antibiotics are typically priced low compared to other products, taken for a short duration, and held in reserve to protect against the development of resistance.

The Committee recognized the need for Congress to incentivize antibiotic R&D in 2012 when it led the successful effort to enact the Generating Antibiotic Incentives Now (GAIN) Act. As IDSA and other key stakeholders have asserted, the GAIN Act was a critical first step, but more work remains to sufficiently stimulate antibiotic R&D. Waiting for the results of another study to once again demonstrate the need for antibiotic incentives will waste valuable time, and patients will continue dying as they wait for desperately needed new antibiotics.

IDSA urges you to continue developing and advancing policies to stimulate antibiotic R&D and recognizes this effort may include collaborative work with colleagues on other committees (particularly Ways & Means and Appropriations). For example, reimbursement mechanisms can be used to help stimulate antibiotic R&D, such as through the Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms (DISARM) Act, H.R. 4187. The bill would provide Medicare add-on payments for antibiotics used in inpatient settings to treat infections associated with high rates of mortality. Strong communication between the Centers for Medicare and Medicaid Services (CMS) and FDA is critical for the success of such efforts, to help ensure that criteria to determine a drug's coverage and payment are applied in a scientifically appropriate and consistent manner that provides companies with the certainty and predictability they need in order to develop life-saving new antibiotics.

IDSA is also working on proposals for targeted and transferrable R&D tax credits to further stimulate antibiotic R&D, and hopes the Committee will collaborate with other committees to include such tax credits as a complimentary provision to the 21st Century Cures Initiative. While the GAIN Act and DISARM Act provide valuable incentives, companies must fully develop a product before receiving the benefits from increased exclusivity or reimbursement. Economic modeling has indicated that financial support during expensive clinical trials, as provided through tax credits, would be a powerful incentive to complement enhanced exclusivity and reimbursement. In fact, Ernst & Young analysis estimated that our tax credit proposal would result in an additional 5-7 new antibiotics or antifungal drugs to treat serious or life-threatening infections in the pipeline every year.

Lastly, IDSA supports increased direct federal funding to spur antibiotic R&D through NIAID, BARDA, CDC, the Defense Threat Reduction Agency (DTRA), and the Defense Advanced Research Projects Agency (DARPA).

Again, IDSA thanks you for this opportunity to comment. The Society is eager to maintain an ongoing dialogue with you regarding the 21st Century Cures Initiative and policies to incentivize antibiotic R&D. If you would like any additional information, or if IDSA can assist you in any way, please contact Jonathan Nurse, IDSA's Director of Government Relations, at [redacted]

Sincerely,

[redacted]

Barbara E. Murray, MD, FIDSA
President

June 10, 2014

The Honorable Fred Upton
2183 Rayburn House Office Building
Washington, DC 20515

The Honorable Diana DeGette
2368 Rayburn House Office Building
Washington, DC 20515

Submitted electronically to cures@mail.house.gov

RE: IDSA Members' Group Response to 2nd White Paper — 21st Century Cures: An Update on the President's Council of Advisors on Science and Technology (PCAST) 2012 Report on Propelling Innovation

Dear Chairman Upton and Representative DeGette:

As infectious diseases physicians and scientists, we applaud the House Energy & Commerce Committee for launching its 21st Century Cures initiative. Further, we appreciate your review of the recommendations provided in the 2012 President's Council of Advisors on Science and Technology (PCAST) *Report to the President on Propelling Innovation in Drug Discovery, Development, and Evaluation*. As you know, we are in the midst of the public health crisis of rapidly rising antibiotic resistance. Many of us who work in clinical settings see increasing numbers of patients who have infections that we cannot effectively treat with current antibiotics. Additionally, economic and regulatory disincentives continue to keep pharmaceutical companies on the sidelines of antibiotics research and development (R&D). For these reasons, we ask that you act without delay on the 2012 PCAST recommendation of a limited population drug approval pathway by advancing the widely supported Antibiotic Development to Advance Patient Treatment (ADAPT) Act, H.R. 3742.

The bipartisan ADAPT Act establishes a new limited population approval pathway for antibiotics to treat serious or life-threatening infections where an unmet medical need exists. The legislation would allow the Food and Drug Administration (FDA) to approve ADAPT drugs based upon smaller clinical trials. It is often not feasible for these drugs to be developed using traditional, large clinical trials due to the limited numbers of patients in whom these infections currently occur. ADAPT drugs would need to meet FDA standards of evidence for safety and effectiveness for the limited indicated population. ADAPT would guide proper stewardship of covered drugs with numerous mechanisms, including a statement on the label that the "drug is indicated for use in a limited and specific population." This provision could be strengthened by including a prominent visual element, such as a logo, to make it simple for the health care community to quickly recognize that these drugs are approved for a limited population and must be used prudently.

The 2012 PCAST report is joined by the 2013 Centers for Disease Control and Prevention report on antibiotic resistant threats in the United States, 2014 World Health Organization global report on antibiotic resistance, and the 2014 progress report of the Transatlantic Taskforce on Antimicrobial Resistance in stressing the urgency of the crisis and calling for the development of new drugs. The

threat from antibiotic resistance and the lack of new drugs is well documented. However, we are increasingly concerned that a lack of action is costing lives.

According to CDC, approximately 23,000 Americans will die this year due to antibiotic-resistant infections. This is a very conservative estimate due to limited surveillance and data collection capabilities. The economic costs of antibiotic resistance are high as well. Antibiotic resistant infections cost the U.S. health care system an estimated $20 billion annually (including 8 million additional hospital days) and $34 billion in societal costs.

We urge the House Energy & Commerce Committee to move quickly to advance the ADAPT Act. The legislation has bipartisan support and fits well within the scope of the 21st Century Cures initiative. With patients losing their lives to multi-drug resistant infections, we don't have a day to waste.

Sincerely,

ALABAMA

Glenn D. Bedsole, MD, FACP
2257 Taylor Rd
Suite 200
Montgomery, AL 36117
[redacted]

Suresh B. Boppana, MD
Professor, Pediatric Infectious Disease
University of Alabama at Birmingham
CHB 114, 1600 7th Avenue South
Birmingham, AL 35233
[redacted]

Cecelia Hutto, MD
Professor of Pediatrics
UAB School of Medicine
1600 Seventh Avenue South
Birmingham, AL. 35294
[redacted]

ARIZONA

Maria Teresa A. Seville, MD
Mayo Clinic in Arizona
Consultant Division of Infectious Diseases
Assistant Professor of Medicine
5777 E. Mayo Boulevard
Phoenix, AZ 85054
[redacted]

CALIFORNIA

Bonnie V. Bock, MD
Newport Beach, CA
[redacted]

Michael Butera, MD, FIDSA
Pulmonary Medicine and
Infectious Diseases Medical Group
San Diego, CA
[redacted]

Henry F. "Chip" Chambers, MD
Professor of Medicine
Director, Clinical Research Services
UCSF Clinical and Translational Sciences Institute
Room 3400, Building 30
San Francisco General Hospital
1001 Potrero Avenue
San Francisco, CA 94110
[redacted]

Gerald N. DeLorenze, PhD
Research Scientist
Division of Research
Kaiser Permanente Northern California
2000 Broadway
Oakland, CA 94612
[redacted]

Continues on the next page

Stan Deresinski, MD
Clinical Professor of Medicine
Division of Infectious Diseases and
Geographic Medicine
Stanford University
Stanford, CA
[redacted]

Daniel Gluckstein, MD
Inland Valley Infectious Disease Medical
Group, Inc.
Claremont, CA 91711
dglucker@gmail.com

Matthew Bidwell Goetz, MD
Professor of Clinical Medicine
David Geffen School of Medicine at UCLA
11310 Wilshire Blvd (111-F)
Los Angeles, CA 90073
[redacted]

Martin Hoenigl, MD
University of California, San Diego
AntiViral Research Center (AVRC)
220 Dickinson Street, Suite A
San Diego, CA 92103-8208
[redacted]

Lily Horng, MD
Fellow in the Department of Infectious Diseases
& Geographic Medicine
Stanford University, School of Medicine
[redacted]

Susan S. Huang, MD, MPH
Associate Professor
Medical Director of Epidemiology and
Infection Prevention
Division of Infectious Diseases and
Health Policy Research Institute
University of California
Irvine School of Medicine
101 The City Drive South
City Tower Suite 400, ZC 4081
Orange, CA 92868
[redacted]

Scott T. Johns, PharmD, BCPS(ID)
ID Pharmacist
VASDHS
3350 La Jolla Village Drive (119)
San Diego, CA 92161
[redacted]

Jane E. Koehler, MA, MD
Professor of Medicine
Division of Infectious Diseases
513 Parnassus Avenue, Room S-380
University of California-San Francisco
San Francisco, CA 94143-0654
[redacted]

David W. Martin, Jr., MD
Chairman and CEO
AvidBiotics Corp.
100 Kimball Way
South San Francisco, CA 94080
[redacted]

Wilbert Mason MD, MPH
Emeritus Professor of Pediatrics
Keck School of Medicine at USC
Attending Physician
Children's Hospital Los Angeles
4650 Sunset Blvd.
Los Angeles, CA 90027
[redacted]

Gregory P. Melcher, MD
Professor of Clinical Medicine
University of California, Davis
4150 V St., Suite 500
Sacramento, CA 95817
[redacted]

Lawrence Mintz, MD, FIDSA
3533 21st Street
San Francisco. CA 94114
[redacted]

Continues on the next page

Jim Nomura, MD
Chief, Infectious Diseases
Kaiser Los Angeles Medical Center
1505 Edgemont St
Los Angeles, CA 90027
[redacted]

Suzanne Sincavage, PhD
CEO: IDIQ INC.
3245 Sumac Rd.
Fallbrook, CA 92028
[redacted]

Upinder Singh, MD
Division Chief
Infectious Diseases and Geographic Medicine
Associate Professor
Departments of Internal Medicine and Microbiology and Immunology
Stanford University School of Medicine
Suite 134, Lane Building, Room 121
300 Pasteur Drive
Stanford, CA 94305-5107
[redacted]

Harris R. Stutman, MD, FIDSA
Executive Director, Clinical Informatics (CMIO)
MemorialCare Health System
Fountain Valley, CA
[redacted]

Alan M. Sugar, MD
Sansum Clinic
317 W Pueblo ST
Santa Barbara, CA 93001
Professor of Medicine (retired)
Boston University School of Medicine
[redacted]

Townson Tsai, MD
Kaiser Permanente Los Angeles
Division of Infectious Diseases
1505 North Edgemont Street, 2nd Floor
Los Angeles, CA 90027
[redacted]

COLORADO

John Hammer, MD, DTM&H
Denver Infectious Disease Consultants
4545 East Ninth Ave. Suite 120
Denver, CO 80220
[redacted]

Kati Shihadeh, PharmD
Clinical Pharmacy Specialist – Infectious Diseases
Denver Health Medical Center
790 Delaware St.
MC0056
Denver, CO 80204
[redacted]

Michael L. Vasil, MT(ASCP), PhD
Professor of Microbiology
MS8333, RC-1 North, Room P18-9132
12800 East 19th Avenue
Aurora, CO 80045
[redacted]

Brent Wieland, MD
Western Infectious Disease Consultants
3885 Upham St. Suite 200
Wheat Ridge, CO, 80033
[redacted]

CONNECTICUT

Sheela Shenoi, MD, MPH
Yale University School of Medicine
Section of Infectious Disease
135 College Street
New Haven, CT 06510
[redacted]

Continues on the next page

FLORIDA

David M Berman, DO
Assistant Professor, Part time
Johns Hopkins University
School of Medicine
All Children's Hospital
St Petersburg, FL
[redacted]

Winston B. Bokor, MD
East Tennessee State University
Graduating Chief Fellow
216 Blanca Ave.
Tampa, FL 33606
[redacted]

George L. Drusano, MD
Professor of Medicine
Director
Institute for Therapeutic Innovation
College of Medicine
University of Florida
6550 Sanger Road
Lake Nona, FL 32827
[redacted]

Moises Feldman, MD
21230 NE 23rd Ct
Miami, FL 33180
[redacted]

Sandra G. Gompf, MD, FACP, FIDSA
Infectious Diseases Subspecialist
James A. Haley Veterans Hospital
13000 Bruce B. Downs Blvd. #111J
Tampa, FL 33612
[redacted]

Charles D. Mitchell, MD
Professor
Division of Infectious Diseases and Immunology
Department of Pediatrics
University of Miami Miller School of Medicine
1580 NW 10th Avenue
Miami, FL 33133
[redacted]

GEORGIA

James M. Hughes, MD, FIDSA
Professor of Medicine and Public Health
Emory University
1462 Clifton Rd NE, Suite 446
Mailstop 1370/004/1AD
Atlanta, GA 30322
[redacted]

Alvaro J. Lopez, MD
Infectious Disease Consultants, P.C.
1370 Montreal Road
Suite 130
Tucker GA 30084
[redacted]

David S. Weiss, PhD
Assistant Professor of Infectious Diseases
Emory University
School of Medicine
954 Gatewood Road, Room 2028
Atlanta, GA 30329
[redacted]

ILLINOIS

Nina M. Clark, MD
Associate Professor
Division of Infectious Diseases
Department of Medicine
Loyola University Medical Center
Fahey Building, Rm 112
2160 S. First Ave.
Maywood, IL 60153
[redacted]

Continues on the next page

Bill Muller, MD, PhD
Assistant Professor, Pediatrics
Northwestern University
Feinberg School of Medicine
Attending Physician
Ann & Robert H. Lurie
Children's Hospital of Chicago
310 East Superior Avenue
Morton 4-660
Chicago, IL 60611
[redacted]

Constance T. Pachucki, MD, FACP
Medical Director, Open Door Clinic
164 Division St, Suite 607
Elgin, IL 60120
[redacted]

Gary D. Rifkin, MD
Professor of Medicine
University of Illinois College of Medicine
[redacted]

David C. Slagle, MD, FACP
Associate Professor of Clinical Medicine
Interim Chair, Section of Infectious Diseases
University of Illinois College of Medicine at Peoria
[redacted]

INDIANA

Daniel A. Nafziger, MD, MS
Health Officer
Elkhart County Health Department
608 Oakland Avenue
Elkhart, IN 46516
[redacted]

LOUISIANA

Raymond A. Coghlan, MD, FRCPC, FIDSA
Willis-Knighton Health System
Shreveport/Bossier City, LA
[redacted]

MARYLAND

Larry William Chang, MD, MPH
Assistant Professor
Infectious Diseases
Johns Hopkins School of Medicine
[redacted]

Emil Lesho, DO, FACP
IDSA & Antimicrobial Resistance Committee Member
Maryland, US

Michael T. Melia, MD
Assistant Professor of Medicine
Division of Infectious Diseases
Johns Hopkins University School of Medicine
1830 E. Monument St., Rm. 448
Baltimore, MD 21287
[redacted]

Kayvon Modjarrad, MD, PhD
Bethesda, MD 20892

Chloe L. Thio, MD
Professor of Medicine
Johns Hopkins University
855 N Wolfe Street
Suite 520
Baltimore, MD 21205
[redacted]

MASSACHUSETTS

Helen W. Boucher, MD, FACP, FIDSA
Director, Infectious Diseases Fellowship Program
Associate Professor of Medicine
Division of Geographic Medicine and Infectious Diseases
Tufts Medical Center
800 Washington Street, Box 238
Boston, MA 02111
[redacted]

Continues on the next page

Stephen M. Brecher, PhD
Director of Microbiology
VA Boston Health Care System
1400 VFW Parkway
West Roxbury, MA 02132
[redacted]

Michael S. Calderwood, MD, MPH
Associate Director of Antimicrobial Stewardship
Brigham and Women's Hospital
Division of Infectious Diseases
181 Longwood Ave.
MCP Building
5th Floor
Boston, MA 02115
[redacted]

Robert A. Duncan, MD, MPH
Associate Professor of Medicine
Tufts University School of Medicine
Hospital Epidemiologist
Center for Infectious Diseases
Lahey Hospital & Medical Center
41 Mall Road
Burlington, MA 01805
[redacted]

Joyce Fingeroth, MD
Professor of Medicine
Division of Infectious Disease
University of Massachusetts Medical School
LRB323
364 Plantation Street
Worcester, MA 01605-4321
[redacted]

George A. Jacoby, MD
Research Associate
Lahey Hospital and Medical Center
Burlington, MA 01805
[redacted]

Ellen Kulp
Associate Managing Editor
Journal of Infectious Diseases
65 Landsdowne Street #412
Cambridge, MA 02139
[redacted]

Joanne Levin, MD
Medical Director
Infection Prevention
Cooley Dickinson Hospital
Northampton, MA 01060
[redacted]

Stuart M. Levitz, MD
Professor of Medicine and Microbiology and Physiological Systems
University of Massachusetts Medical School
364 Plantation Street, LRB 317
Worcester, MA 01605
[redacted]

Paul F. Miller, PhD
Vice President, Infection Biology
AstraZeneca Pharmaceuticals, LP
35 Gatehouse Drive
Waltham, MA 02451
[redacted]

Anna Thorner, MD
Infectious Diseases Attending
Brigham and Women's Hospital
Boston, MA
Assistant Clinical Professor
Harvard Medical School
Boston, MA
Brigham and Women's Hospital
Division of Infectious Diseases
75 Francis St., PBB-A4
Boston, MA 02115
[redacted]

Continues on the next page

Jatin M. Vyas, MD PhD
Assistant Professor of Medicine
Harvard Medical School
Massachusetts General Hospital
Department of Medicine
Division of Infectious Disease
55 Fruit Street
Gray-Jackson Building Room 504
Boston, MA 02114
[redacted]

MICHIGAN

Donald P. Levine, MD
Professor of Medicine
Associate Vice Chair for
Continuing Medical Education and
Community Affairs
Wayne State University
University Health Center
Suite 2E
4201 St. Antoine
Detroit, MI 48201
[redacted]

Eric McGrath, MD
Assistant Professor of Pediatrics
Division of Infectious Diseases
Carman and Ann Adams Department of
Pediatrics
Wayne State University School of Medicine
Children's Hospital of Michigan
3901 Beaubien Blvd., Detroit, MI 48201
[redacted]

Rosemary Olivero, MD
Helen DeVos Children's Hospital
35 Michigan St NE
Grand Rapids, MI 49503
[redacted]

Maria Jevitz Patterson, MD, PhD, FIDSA, FAAP
Professor Emerita
Michigan State University
Departments Microbiology/Molecular Genetics and Pediatrics
Biomedical Physical Sciences Room 2209
567 Wilson Road
East Lansing, MI 48824
[redacted]

MINNESOTA

Johan S. Bakken, MD, PhD, FIDSA
Vice President IDSA
St. Luke's Infectious Disease Associates
1001 E. Superior Street, Suite L201
Duluth, MN 55802
[redacted]

Mark R. Eckman, MD, FACP
University of Minnesota, Duluth
3809 Rockview Court
Duluth, MN 55804
[redacted]

Andrew Thompson, MD
St. Luke’s Hospital
1001 E Superior St.
Duluth, MN 55802
[redacted]

MISSOURI

Nirav Patel, MD
Assistant Professor of Internal Medicine
Infectious Diseases and Critical Care Medicine
Saint Louis University School of Medicine
Infection Control Officer
Director of Antibiotic Stewardship
Saint Louis University Hospital
3635 Vista Ave
St. Louis, MO 63110
[redacted]

Continues on the next page

William L Salzer MD
Professor of Clinical Medicine
Division Director, Program Director
University of Missouri-Columbia School of Medicine
Columbia, MO 65212
[redacted]

Marcia L. Sokol-Anderson, MD
Director, New Hope Clinic
Professor of Internal Medicine
Division of Infectious Diseases
St. Louis University Medical Center
St. Louis, MO 63110
[redacted]

MONTANA

George F. Risi, MD, MSc, FIDSA, FACP
President, Infectious Disease Specialists, PC
902 N. Orange St
Missoula, MT 59802
[redacted]

NEBRASKA

Sandra L Reis Crosara, MD
Adult Infectious Diseases Fellow
University of Nebraska Medical Center
985400 Nebraska Medical Center
Omaha, NE 68198-5400
[redacted]

NEVADA

F. Kevin Murphy, MD, FACP
Clinical Associate Professor
University of Nevada School of Medicine
[redacted]

NEW JERSEY

Fernando Barahona, MD
Saint Michael's Medical Center
111 Central Av, Newark, NJ 07102
[redacted]

Richard H. Ebright, PhD, FIDSA
Board of Governors Professor of Chemistry and Chemical Biology, Rutgers University
Laboratory Director, Waksman Institute of Microbiology
190 Frelinghuysen Road
Piscataway NJ 08854
[redacted]

William E. Farrer, MD, FACP, FIDSA
Academic Chief of Infectious Diseases and Hospital Epidemiologist
Trinitas Regional Medical Center
225 Williamson St.
Elizabeth, NJ 07207
[redacted]

NEW MEXICO

Joel E. Gallant, MD, MPH
Chair, HIV Medicine Association
Associate Medical Director of Specialty Services
Southwest CARE Center
Santa Fe, NM 87505
[redacted]

Anuj Malik, MD, MS
Infectious Diseases Fellow
University of New Mexico
Albuquerque, NM
[redacted]

Jeffrey Ross, MD
Infectious Diseases & Internal Medicine Associates
Albuquerque, NM 87102
[redacted]

NEW YORK

Maria C Abelardo, MD
Woodside, NY 11377
[redacted]

Continues on the next page

Edward Chapnick, MD, FACP, FIDSA, FSHEA
Vice Chair for Education and
Program Development
Department of Medicine
Director
Division of Infectious Diseases
4802 Tenth Avenue
Brooklyn, NY 11219
[redacted]

Louis Z. Cooper, MD
Professor Emeritus of Pediatrics
Columbia University
80 Central Park West
New York, NY 10023
[redacted]

Anne A. Gershon, MD
Professor of Pediatrics
Columbia University Medical Center
[redacted]

Joy H. Glaser, MD, FAAP
Professor of Pediatrics
Albert Einstein College of Medicine
Bronx, NY
[redacted]

Joel Greenspan, MD, FACP
44 S Bayles Ave
Port Washington, NY 11050-3765
[redacted]

Shirish Huprikar, MD
Director, Transplant Infectious Diseases
Program
Icahn School of Medicine at Mount Sinai
New York, NY
[redacted]

Chester W. Lerner, MD, FIDSA, FACP,
FSHEA
Associate Chief of Infectious Diseases
Hospital Epidemiologist
New York-Presbyterian/Lower Manhattan
Hospital
Assistant Professor of Clinical Medicine
Weill Cornell Medical College
[redacted]

Nathan Litman, MD
Vice Chair, Clinical Affairs
Chief, Section of Pediatric Infectious Diseases
Children's Hospital at Montefiore
Professor, Pediatrics
Albert Einstein College of Medicine
111 East 210th Street
Bronx, NY 10467
[redacted]

Stephanie M. Pouch, MD, MS
Fellow, Division of Infectious Diseases
Columbia University Medical Center
630 W. 168th Street
P&S Box 82
New York, NY 10032
[redacted]

NORTH CAROLINA

Elias Ashame, MD
Infectious disease consultants
W.G (Bill) Hefner VA Medical Center
Salisbury, NC 28144
[redacted]

John Boreyko PharmD, BCPS
Duke Regional Hospital
Durham, NC 27704
[redacted]

David T Durack MD
Consulting Professor of Medicine
Duke University
[redacted]

Continues on the next page

James E Peacock, Jr MD
Professor of Medicine/Infectious Diseases
Wake Forest Health Sciences
Medical Center Boulevard
Winston-Salem, NC 27157
[redacted]

OHIO

Kevin Downes, MD
Fellow, Division of Infectious Diseases
Cincinnati Children's Hospital Medical Center
3333 Burnet Avenue, MLC 7017
Cincinnati, OH 45229-3026
[redacted]

Barbara M. Gripshover, MD FIDSA
Associate Professor of Medicine
Case Western Reserve University
Cleveland, OH 44106-5083
[redacted]

Mark Herbert, MD
President, ID Med Inc.
777 West State Street, Suite 308
Columbus, OH 43222
[redacted]

Thomas Herchline, MD
Professor of Medicine
Boonshoft School of Medicine, WSU
Weber CHE Building, 2nd Floor
128 E. Apple St.
Dayton, OH 45409-2902
[redacted]

Ravi K. Kamepalli MD, CWS
Regional Infectious Diseases and Infusion Center, Inc.
830 West High St., Suite 255
Lima, Ohio 45801
[redacted]

Robert Munson, PhD
Professor of Pediatrics
Professor of Microbiology
The Research Institute at
Nationwide Children's Hospital and
The Ohio State University
[redacted]

Rebecca Schein, MD
Pediatric Infectious Diseases
MetroHealth Medical System
2500 Metrohealth Drive
Pediatrics H455
Cleveland, OH 44109
[redacted]

Denise J. Signs, MS, MD
President of the Infectious Diseases Society of Ohio
Suite 3D
Wooster Community Hospital
Wooster, OH 44691
[redacted]

Scott W. Sinner, MD, FACP
Hyperbaric Medical Director
Mercy Health - Clermont Hospital
Wound Care Center
3020 Hospital Drive
Batavia, OH 45103
[redacted]

Richard R. Watkins, MD, MS, FACP
Associate Professor of Internal Medicine
Northeast Ohio Medical University
Rootstown, OH
Division of Infectious Diseases
Akron General Medical Center
224 W Exchange St. Suite 290
Akron, OH, 44302
[redacted]

Continues on the next page

Harrison G. Weed, MD, MS, FACP
Professor of Internal Medicine
Chair, Pharmacy and Therapeutics
Executive Committee
The Ohio State University
College of Medicine
Division of General Internal Medicine
Suite 2250
Morehouse Pavilion
Room 2275
2050 Kenny Road
Columbus, OH, 43221
[redacted]

OREGON

Matthew Labreche, PharmD, MSc, BCPS
NW Regional Antimicrobial Stewardship Program
Infectious Diseases Therapeutic Lead
Kaiser Permanente
1836 SW Cable Ave, Apt 1 (Home Address)
Portland, OR 97201
[redacted]

Donald Venes, MD, CCHP, FACP
NDCC of Brookings, OR
PO Box 41327
Eugene, OR 97415
[redacted]

PENNSYLVANIA

Lewis Barrett
Senior Vice President
Synthetic Biologics
Lansdale, PA 19446
[redacted]

John Bartels, MD
Thorndale, PA 19372
[redacted]

Alan T. Evangelista, PhD, D(ABMM)
Director of Microbiology, Virology,
& Molecular Diagnostics
St. Christopher's Hospital for Children
Department of Pathology &
Laboratory Medicine
3601 A Street
Philadelphia, PA 19134-1095
[redacted]

Neil Fishman, MD
Associate Chief Medical Officer
University of Pennsylvania Health System
3400 Convention Center Blvd.
706 Penn Tower
Philadelphia, PA 19104
[redacted]

Jason C. Gallagher, PharmD, FCCP, BCPS
Professor
Temple University
3307 North Broad Street
Philadelphia, PA 19140
[redacted]

Jane M. Gould, MD
Associate Professor of Pediatrics
Drexel University College of Medicine
Hospital Epidemiologist
Attending Physician
Section of Infectious Diseases
St. Christopher's Hospital for Children
Erie Avenue at Front Street, Suite 1112
Philadelphia, PA 19134-1095
[redacted]

Brandon Palermo, MD, MPH
Adjunct Assistant Professor of Medicine
Division of Infectious Diseases
Temple University School of Medicine
3401 North Broad Street
Parkinson Pavilion
Suite 500
Philadelphia, PA 19140
[redacted]

Continues on the next page

Kathleen E. Squires, MD
Havens Professor of Infectious Diseases
Thomas Jefferson University
1015 Chestnut Street
Suite 1020
Philadelphia, PA 19107
[redacted]

PUERTO RICO

Doris Perez, MD
Infectious Disease Physician
Hospital del Maestro
San Juan, PR
[redacted]

RHODE ISLAND

Lalitha. Koduri, MD
Atwood Medical Associates
North Providence, RI 02911
[redacted]

Steven M. Opal, MD
Professor of Medicine
Alpert Medical School of Brown University
Providence, RI
Chief, Infectious Disease Service
Memorial Hospital of RI
111 Brewster Street
Pawtucket, RI 02860
[redacted]

SOUTH CAROLINA

Katherine A Minnick, MD
Director, Antimicrobial Stewardship Program
Roper Saint Francis Healthcare System
306 Geddes Ave
Charleston SC, 29407
[redacted]

TENNESSEE

Elisabeth Adderson, MD
Department of Infectious Diseases
St. Jude Children's Research Hospital
Memphis, TN
[redacted]

TEXAS

Cesar A. Arias, MD, MSc, PhD
Associate Professor of Medicine
Director Laboratory for Antimicrobial Research
Division of Infectious Diseases
University of Texas Medical School at Houston
6431 Fannin St. MSB 2.112.
Houston, TX 77030
[redacted]

Andres Gutierrez, MD
Post-Doctoral Fellow
PGY-5
Department of Medicine
Section of Infectious Diseases
Baylor College of Medicine
One Baylor Plaza
Houston, TX, 77030
[redacted]

Gary P. Holmes, MD, FSHEA, FIDSA
Chief, Division of Infectious Diseases
Department of Medicine
Carl R. Darnall Army Medical Center
Adjunct Associate Professor
Texas A&M Health Science Center
School of Rural Public Health
Department of Epidemiology and Biostatistics
College Station, TX 77843-1266

Continues on the next page

Brian Metzger, MD MPH
Austin Infectious Disease Consultants
1301 W. 38th St.
Suite 403
Austin, TX 78759
[redacted]

UTAH

Sankar Swaminathan, MD, FIDSA
Don Merrill Rees Presidential Endowed Chair
Chief of Infectious Diseases
Department of Medicine
University of Utah School of Medicine
30 N. 1900 E.
Room 4B319 SOM
Salt Lake City, UT 84132
[redacted]

VIRGINIA

Michael Edmond, MD
Hospital Epidemiologist
VCU Medical Center
Richmond, VA 23298-0019
[redacted]

Frederick G. Hayden, MD
Stuart S. Richardson Professor of
Clinical Virology
Professor of Medicine
Division of Infectious Diseases
and International Health
University of Virginia
School of Medicine
Charlottesville, VA 22908
[redacted]

WASHINGTON

Mary S. Campbell, MD
Clinical Assistant Professor
University of Washington
Seattle, WA
[redacted]

LEUKEMIA & LYMPHOMA SOCIETY®
fighting blood cancers

www.LLS.org

June 10, 2014

The Honorable Fred Upton
Chairman
House Energy & Commerce Committee
2183 Rayburn HOB
Washington, DC 20515

The Honorable Diana DeGette
Member
House Energy & Commerce Committee
2368 Rayburn HOB
Washington, DC 20515

Dear Chairman Upton and Congresswoman DeGette:

The Leukemia & Lymphoma Society (LLS) appreciates this opportunity to comment on the *21st Century Cures: an Update on the President's Council of Advisors on Science and Technology 2012 Report on Propelling Innovation* whitepaper. As the world's largest voluntary health agency dedicated to the needs of blood cancer patients, LLS is a strong supporter of action that will facilitate the discovery, development and delivery of new, safe, effective therapies for blood cancer patients. This year, we estimate that more than 150,000 Americans will be newly diagnosed with a blood cancer, accounting for nearly 10 percent of all new U.S. cancer diagnoses. Our mission is to cure leukemia, lymphoma, Hodgkin's disease and myeloma and improve the quality of life of patients and their families. We advocate on behalf of all blood cancer patients to ensure they have sustainable access to quality, affordable, coordinated healthcare.

LLS is a significant stakeholder in the drug and device development process, and has provided more than $1 billion for research aimed at discovering, developing and delivering blood cancer cures since its founding. LLS-funded research has been part of nearly all of the FDA-approved therapies for blood cancer treatment. As such, we appreciate the opportunity to comment and provide our unique perspective as both a large funder of research and an organization that represents patients.

Though the FDA has made many strides in addressing PCAST report recommendations, much work remains to be done. Our comments below focus on Recommendations numbered 1, 2, 3, 4, 5, 6, and 8.

Recommendation 1: Support Federal Initiatives to Accelerate Therapeutics

The Federal Government must strongly support the funding of basic biomedical research. As we noted in our comments to the first White Paper, 21st *Century Cures: A Call to Action*, (submitted May 30, 2014 – attached) restoring adequate funding to the National Institutes of Health (NIH) and its individual research centers should be a top priority for the Congress and the Administration. Targeted funding like the Gabriella Miller Kids First Research Act (GMKFRA) is a step in the right direction, but is insufficient to restore funding to adequate levels. The 21st Century Cures initiative should inject increased funds into the NIH in a strategic manner to promote promising research at early stages.

The Committee should ensure policies that adequately fund all stages of research, but pay special attention to those that promote translational science research. Translational science is essential to the development of new cures, because it bridges the gap between basic scientific discoveries and applied treatments. Through

our own Translational Research Program (TRP), LLS funds new and innovative research that shows high promise for translating basic biomedical knowledge to clinical application.[1]

Major gaps in funding exist at all stages of the discovery process. Although LLS and other private stakeholders have developed innovative programs that attempt to fill the gaps (please see discussion of the LLS project Beat AML in our comments submitted on May 30. 2014), the overarching economic incentives create an environment where a shortage of federal funds may lead to a shortage of scientific discoveries. Adequately funding the discovery process is essential to keeping the United States at the forefront of biomedical innovation.

Recommendation 2: Catalyze the Creation of a Broad-Based Partnership to Accelerate Therapeutics

LLS partners with numerous organizations, working together to help accelerate the process of developing new drugs and making them available to patients. By combining the resources of biotechnology and pharmaceutical companies, private-sector and public firms and academic institutions, we are able to see faster and more efficient results in the development of new drug therapies to benefit blood cancer patients.

Given our success with multi-stakeholder initiatives, LLS supports the concept of a broad-based partnership to accelerate therapeutics. LLS sees numerous benefits to engaging a range of stakeholders on a regular basis to tackle the challenges of transforming drug development.

The PCAST report suggests that such a partnership would need an annual budget of at least $10-15 million to fulfill the outlined goals, with funding coming primarily from key corporate and non-profit organizations. Given the importance of the projects that such an umbrella organization would tackle, and the long range nature of these projects, it is critical to ensure that the partnership has sufficient long-term funding. The Committee should explore incentives that will foster investment and funding of the partnership, and to the extent possible, long range funding should be secured through a variety of methods, allowing the partnership to focus on accelerating therapeutics rather than funding.

Recommendation 3: Expand the Use in Practice of FDA's Existing Authorities for Accelerated Approval and Confirmatory Evidence

LLS recognizes the importance of alternative and expedited approval pathways and the positive impact these pathways have on the blood cancer community. For example, Gleevec was granted accelerated approval for the treatment of CML in 2001, and has now saved thousands of lives. Making effective use of the FDA's existing authorities has the potential to save additional lives. For example, the large sample sizes, long follow-up durations, and considerable costs and effort invested in completing clinical trials could be reduced if valid alternative or surrogate end points to overall survival (OS) were identified and validated by the FDA. In acute myeloid leukemia (AML), a disease that causes over 10,000 American deaths a year, OS is the endpoint generally accepted by the FDA to approve a new agents, as opposed to

[1] http://www.lls.org/#/researchershealthcareprofessionals/academicgrants/translationalresearch/

progression free survival (PFS), an endpoint in clinical trials generally accepted by researchers. By considering PFS as an appropriate endpoint, many AML patients could benefit from extended time in remission.

Our patients have also benefited from the "Breakthrough Therapy" designation. This new pathway has already led to the approval of three medications for the hematological malignancies – Imbruvica, Gazyva and Arzerra. These therapies offer promise for patients with limited alternatives. The FDA should be given the tools and funding to continue and expand this program.

While accelerated approval and breakthrough designation offer incredible opportunities for patients with the greatest medical needs, LLS agrees that regulations requiring pharmaceutical and biotechnology companies to follow through on postmarketing studies to confirm data in a timely fashion should be strictly enforced and that the FDA should continue to ensure compliance with these regulations. In previous comments to the FDA, LLS requested clarity in regards to how the agency would monitor products given breakthrough therapy designation following approval. LLS recognizes the need to avoid unforeseen safety issues in products with breakthrough therapy designation.

Recommendation 4: Create a New Pathway for Initial Approval of Drugs Shown to be Safe and Effective in a Specific Subgroup of Patients

Our understanding of the molecular drivers of blood cancer is at the cutting edge. Building upon breakthroughs in genomics, epigenomics, and proteomics, we have identified the critical pathways amenable to therapeutic intervention. Despite these insights, there are many obstacles that still remain, such as the high cost and extended timelines of developing drugs for small patient populations.

The novel precision medicines being developed to treat the hematological malignancies will inherently benefit small subpopulations of patients. There are numerous unmet medical needs and novel therapies currently in development that may be accelerated by a special approval pathway. For example, there is the pioneering immunotherapy research being done at the University of Pennsylvania (led by Carl June and funded by LLS), using genetically engineered autologous T-cells for patients with leukemia who have relapsed after standard treatments. Of 59 cancer patients treated to date, 26 have experienced sustained, complete remissions. One of those patients, Emily Whitehead, was a six year old near death from relapsed acute lymphoblastic leukemia (ALL). Emma is now 9 years old, cancer free and in remission for over 2 years. In another example, researchers at MD Anderson Cancer Center are developing anti-cancer vaccines for patients with follicular lymphoma. The program includes individualized anti-tumor vaccines, based on the unique proteins produced by each patient's particular lymphoma.

There are times when large, randomized trials are simply not feasible; therefore an expedited pathway for initial approval could greatly accelerate the availability of these treatments to all patients who meet the diagnostic criteria of the particular subpopulation. However, it will be critical such a pathway define terms such as "limited-use," "serious conditions," and "well-defined subpopulations" in order to understand how inclusive this pathway will be. Every blood cancer is a serious or life-threatening condition; many of the

therapies in development will be used in small, well-defined patient populations, many of whom share a risk tolerance that is much higher than in the overall population.

As previously noted, LLS recognizes that blood cancer patients have benefited from the "breakthrough therapy" designation created under FDASIA following the PCAST report. As such, LLS believes that further experience with the breakthrough designation, and other expedited approval pathways following FDASIA, will be helpful in determining the design of any additional pathways.

Recommendation 5: Explore Approaches for Adaptive Approval Via Pilot Projects Under Existing Pathways, but Do Not Create New Adaptive Approval Pathways Through Legislation

Adaptive approval provides a mechanism for new drugs to be approved in iteratively expanded patient populations as additional evidence from clinical studies is collected. In short, this would permit the initial approval of a drug for a small population and then gradually broaden the indication for additional patient populations as more data becomes available. LLS would support the exploration of such an approval process, given the potential of such a pathway to reduce the time and expense required to complete premarket trials and ensure earlier access for patients with severe and lifethreating diseases.

However, if such an approval process is considered, the impact of adaptive approval on coverage decisions and payment must also be considered. The availability of any new treatment is tempered by a patient's ability to access and pay for that treatment. Coverage determiniations for new therapies are often based on the assumption that pre-approval trials have demonstrated a clinical benefit to that treatment over existing therapies. All stakeholders must understand how coverage and payment decisions will be altered due to an expedited pathway that could likely produce less confirmatory information. The PCAST report mentions payors in its discussion of adaptive approval, but does not adequately address this important piece of the puzzle.

Recommendation 6: Improve FDA's Tools for Monitoring and Communication of Clinical Benefits and Risks

LLS has made an exceptional investment in the collection, monitoring and communication of information regarding clinical benefits and risks to our patient population through our Information Resource Center. LLS's staff of Information Specialists are master's level oncology social workers, nurses and health educators who help patients deal with the challenges of their diagnosis, provide information about treatment options, help patients map the best route from diagnosis through treatment and survivorship, conduct individual clinical trial searches, and provide general education materials for patients.

Building upon these efforts, LLS is embarking upon the creation of a patient registry to collect, aggregate and analyze patient reported outcomes and perspectives, including clinical manifestations of the diseases, impact upon daily life, disease progression, effectiveness and clinical impact of therapies, as well as variances within different subpopulations. The registry will also help LLS provide the FDA with accurate, aggregated patient data that communicates their collective risk-benefit tolerance. Although this registry is

still in its early early stages of planning, the ultimate goal is to monitor response to and potential side effects of therapies that can only be captured by aggregating large numbers of cases from large cancer centers as well as community settings.

As we move these important initiatives forward, LLS would appreciate the opportunity to work with the Committee and the FDA to identify ways for us to further the goal of monitoring and communicating clinical benefit and risk information to the medical community and to patients.

Recommendation 8: Study current and potential economic incentives to promote innovation in drug development

The PCAST report stated that, "there is currently insufficient knowledge on which to base wise policy decisions," in regard to determining the economic incentives needed to promote innovation in drug development. The PCAST report recommended that a study be commissioned to examine:

- The utility of various types of incentives (such as exclusivity periods, voucher for priority review, market commitments, tax credits), including economic analysis of the impact of current and potential incentives on drug developers and on Federal costs;
- Whether current incentives promote adequate investment in general and in specific areas of important public health need (such as antibiotics for drug-resistant bacteria, prevention for chronic diseases, and underserved diseases affecting the developing world); and
- Whether targeted changes to economic incentives would serve national needs.

LLS supports a study examining these issues. However, LLS requests that any such study also take a holistic review of the challenges associated with bringing innovative products to market. Specifically, the study should include an examination of how to balance the need for innovation with the ability to provide sustainable patient access to quality, affordable healthcare.

The Leukemia & Lymphoma Society thanks the committee for engaging all stakeholders, in particular patient groups, in this important discussion. Should you or your staff have any questions regarding our comment, please do not hesitate to contact me at [redacted]. Thank you.

Sincerely,

[redacted]

Brian Rosen
Senior Vice President, Public Policy & Advocacy
The Leukemia & Lymphoma Society

June 10, 2014

The Pharmaceutical Research and Manufacturers of America (PhRMA) believes that the challenges affecting the ability to provide life-saving and life-enhancing new medicines to patients in an efficient and timely manner are significant, and addressing them will require the involvement of and partnerships among all members of the biomedical innovation ecosystem. PhRMA appreciates the Committee's interest and attention to accelerating the discovery, development, and delivery of innovative new treatments and cures.

In September 2012, the President's Council of Advisors on Science and Technology (PCAST) issued a *Report to the President on Propelling Innovation in Drug Discovery, Development, and Evaluation* (http://www.whitehouse.gov/sites/default/files/microsites/ostp/pcast-fda-final.pdf) that detailed many of the challenges in the discovery, development, and delivery process. PhRMA's comments below focus on four specific recommendations from the PCAST report that we feel are most relevant to the intent of the 21st Century Cures initiative. Our comments are offered as a contribution to the dialogue about how to spur innovation to address a broad range of health challenges, grow jobs and the U.S. economy, and ensure the U.S. remains a global leader in research and development (R&D).

PhRMA is a voluntary, non-profit association that represents the country's leading pharmaceutical research and biotechnology companies. PhRMA members are dedicated to developing medicines that allow patients to live longer, healthier, and more productive lives. In 2013 alone, PhRMA's member companies invested an estimated $51.1 billion in the research and development of new medicines.

Recommendation 2: Catalyze the Creation of a Broad-Based Partnership to Accelerate Therapeutics

PhRMA concurs that the challenges to the efficient production of innovative therapeutics are significant and cannot be solved by any one sector. Hence, PhRMA supports the need to foster the development of effective public-private partnerships among the National Institutes of Health (NIH), the U.S. Food and Drug Administration (FDA), academia, patient groups, and the biopharmaceutical industry to address a range of scientific and technological challenges and make significant progress in areas such as target validation, qualification of drug development tools, and modernization of clinical trials, including the establishment of sustainable networks to improve efficiency and connectivity in the ecosystem.

According to report by the Tufts Center for the Study of Drug Development, "[a]s the scope of some of the scientific challenges is so large, collaboration is viewed as increasingly important to making significant progress."[i] The report found that partnerships and other forms of collaboration are growing in number and importance as the translational gap between discovery and clinical development has become increasingly difficult to bridge. Sustaining productivity in

medical research is critical for the health of the economy as well as U.S. competitiveness in the global marketplace, which underscores the importance of fostering partnerships to harness the full potential of new scientific discoveries.

Congress should explore policies to foster and expand such collaborative efforts, including assessing whether and how existing regulatory policies need to be adapted to ensure consistent and predictive regulatory adoption of the output of collaborations.

Recommendation 4: Create a New Pathway for Initial Approval of Drugs Shown to be Safe and Effective in a Specific Subgroup of Patients

Recommendation 5: Explore Approaches for Adaptive Approval Via Pilot Projects Under Existing Pathways, but Do Not Create New Adaptive Approval Pathways Through Legislation

Congress highlighted the need for FDA to exercise creativity and flexibility conducive to promoting and incentivizing the development of innovative medicines for unmet medical needs when it enacted the Food and Drug Administration Safety and Innovation Act in 2012. Specifically, Congress included enhancements of FDA's existing accelerated approval pathway and fast track designation procedures, and it created a new "breakthrough therapy" designation. PhRMA supports FDA's use of these and other tools, such as priority review. Biopharmaceutical companies are committed to helping ensure that patients have access to safe and effective new medicines, and we recognize the particular importance of developing and securing the approval of drugs and biologics for patients with unmet medical needs.

Although PhRMA believes that FDA's existing regulatory armamentarium and statutory flexibility to determine appropriate evidence of safety and efficacy are strong, we also recognize that development of innovative, safe, and effective medicines for serious or life-threatening diseases represents an urgent and unique challenge that requires special attention. For this reason, PhRMA stands ready to continue its work with all stakeholders, including FDA, patients, healthcare providers, and legislators toward ensuring that there are appropriate and targeted regulatory approaches that will continue to accelerate the development and availability of innovative medicines. PhRMA believes that FDA could initiate a new program using a combination of (i) its existing broad regulatory flexibility granted under the Federal Food, Drug, and Cosmetic Act and (ii) an expansion of its ability to make decisions regarding therapeutic benefit based on real-world evidence used as a supplement or potentially as a replacement for randomized controlled trials, as appropriate.

Recommendation 8: Study Current and Potential Economic Incentives to Promote Innovation in Drug Development

We concur with the PCAST report recommendation of the need to examine the adequacy of current economic incentives and to assess whether current incentives are aligned to promote innovation generally and in specific areas of public health priority. We think it is important to fully consider how the nature of innovation has evolved and how the environment for innovation has changed, particularly since the passage of the Hatch-Waxman Act. To ensure that the U.S.

remains a global leader and able to bring new medicines to patients, a range of policies are needed to sustain and grow the U.S. biopharmaceutical sector:

- To foster a favorable environment for innovation, we need an intellectual property (IP) environment that provides strong protections for both patents and data generated during the regulatory approval process to help drive medical innovation in the U.S. and around the world. In terms of IP protections, as noted in our prior submission, industry dynamics have changed dramatically over time creating substantial uncertainties for industry, particularly in terms of IP. PhRMA supports the need to assess the adequacy of current IP incentives. PhRMA also supports robust enforcement of IP rights in the U.S. and abroad and increasing efforts to remove trade barriers to expand open markets for U.S. products and services. IP incentives and the ability to enforce IP rights are critical to allow the sector to continue attracting the resources needed for a large-scale biomedical research enterprise that can deliver the medical advances society needs and desires.
- PhRMA supports strengthening and making permanent the R&D tax credit. Doing so would help the biopharmaceutical R&D enterprise continue to grow and flourish in the U.S., both economically through high-wage, high-value jobs and in benefits to patients realized through continued innovation in the industry.
- PhRMA supports policies to help strengthen state and regional innovation clusters, including expanding the scope of current federally supported innovation collaborations funded by the Small Business Administration and Economic Administration to include the life sciences industries, particularly the innovative biopharmaceutical industry.
- PhRMA supports policies to help expand the pool of qualified workers in the biosciences to help grow the U.S. economy through worker skills building and training efforts, including policies to attract and retain foreign students and highly skilled foreign workers in science, technology, engineering, and mathematics (STEM) fields. A range of federal worker training and skills building currently exist but few specifically include the biosciences. Existing federal workforce programs should be expanded to include a specific focus on the biosciences. To fulfill the U.S. long-term potential for economic growth, it is critical that we advance and improve knowledge in STEM fields and grow the 21st century workforce needed by the increasingly knowledge-based economy. There is increasing concern that the U.S. will lose its competitive edge in STEM occupations, which will result in a loss of innovative capacity and related economic contributions. This underscores the need to assess the adequacy of federal STEM programs and to promote best practices and reduce duplication.

PhRMA welcomes the opportunity to further explore the issues raised in the report and achieve the shared goal of accelerating the discovery, development, and delivery of treatments and cures to patients.

[i] C.P. Milne, et al., "Academic-Industry Partnerships for Biopharmaceutical Research & Development: Advancing Medical Science in the U.S.," Tufts Center for the Study of Drug Development, April 2012.

GPhA Comments to "21st Century Cures: President's Council of Advisors on Science and Technology - Report To The President On Propelling Innovation In Drug Discovery, Development, and Evaluation"

The Generic Pharmaceutical Association (GPhA) appreciates the opportunity to provide comments regarding the May 1st white paper, "21st Century Cures: An Update on the President's Council of Advisors on Science and Technology (PCAST) 2012 Report on Propelling Innovation." GPhA's core purpose is to improve the lives of patients by providing timely access to affordable pharmaceuticals. We applaud the Committee for the 21st Century Cures initiative and look forward to working with you to accelerate patient access to life-saving cures.

Our member companies manufacture more than 90% of all generic pharmaceuticals dispensed in the United States, and their products fill nearly three billon prescriptions per year. Members of GPhA have also produced safe and effective biosimilars for sale outside the United States for more than seven years. Today's generic industry is innovative – from the processes used to manufacture generic drugs, to the new methods of delivering high-quality products, to the development of innovative, less costly ways of bringing biologics to patients with biosimilars. This innovation will only continue in the future as more complex generic drugs and biosimilars come onto the market.

This response addresses several of the recommendations in the PCAST report and offers suggestions on other ideas discussed in the report.

Recommendation 1: Support Federal Initiatives to Accelerate Therapeutics

GPhA and its member companies strongly support federal initiatives to accelerate therapeutics. It is imperative that Congress provide sufficient funding for the National Institutes of Health (NIH). NIH's research has led to the discovery and development of hundreds of novel therapies that have enhanced the lives of millions of Americans and people around the world. GPhA and its members recognize that in tough budgetary times, it may difficult to fund the NIH at recommended levels. However, NIH funding helps supplement private investment from biopharmaceutical companies and allows for the exploration of certain issues where return on investment is insufficient, such as methodologies to develop drugs for currently "undruggable" targets, new techniques for drug screening, new approaches to predictive toxicology and pharmacogenomics, and improved statistical methods. NIH's research in these and other areas is necessary to accelerate patient access to life-saving medicines. GPhA and its member companies support a predictable and steady stream of funding for NIH, which would allow them to undertake certain projects without the threat of being subject to budgetary politics.

Recommendation 6: Improve FDA's Tools for Monitoring and Communication of Clinical Benefits and Risks

Patient safety is of paramount importance to GPhA and its membership. When patients take their medications as directed by their health care provider, the therapy most often produces the

intended clinical benefit. However, it is important to keep in mind that prescription drugs are inherently dangerous if not used as directed and there are instances when adverse events occur. Generic manufacturers comply with the letter of the law and report these adverse events to the FDA through their quarterly and yearly reporting, and for serious unknown adverse events, within 15 days.

FDA has enhanced its position as the primary repository of safety information for pharmaceutical products through creation of the Sentinel System. FDA utilizes their national electronic Sentinel System to track the safety of marketed drugs, biologics, and medical devices. FDA launched the Sentinel System in 2008 with the goal of developing and implementing a proactive system to complement existing systems the Agency has in place to track reports of adverse events linked to the use of regulated products.[1]

Monitoring the safety of its regulated products is a major part of FDA's mission to protect public health. The Sentinel System enables FDA to actively query diverse automated healthcare data holders—like electronic health record systems, administrative and insurance claims databases, and registries—to evaluate possible medical product safety issues quickly and securely.

FDA contends that the Sentinel System has many advantages over the traditional approach to monitoring and evaluating drug safety. Active surveillance by the Sentinel System will allow FDA to identify an increased risk of common events that healthcare providers may not suspect are related to medical products. Therefore, by using the Sentinel System and relying far less on the historical passive reporting processes, FDA can protect public health more effectively.

GPhA and its members strongly support the recommendation that Congress appropriate additional funding to the FDA for the specific purpose of carrying out and enhancing the Sentinel System. GPhA also supports the recommendation that FDA should develop improved systems to communicate risks and benefits of drugs to the public. In most instances, the onus falls on the patient to ask questions about the prescription drug their provider prescribed them. Patients oftentimes are too embarrassed to ask their physician or pharmacist about the potential side effects of a drug, and rely on the hope that the principal-agent relationship holds up. Similarly, health care providers are facing more demands each day, which constrain the amount of time they can spend with each individual patient and discuss their treatment options. Pharmaceutical manufacturers, the FDA, pharmacists and health care providers need to foster an environment where it becomes commonplace to discuss the risks and benefits of a specific therapy. GPhA and its members stand ready to help.

Another commonsense approach to increasing public health and making sure that patients and providers have up-to-date information on the risks and benefits of prescription drugs is for FDA to finalize their rule on electronic labeling or e-labeling. E-labeling allows for the prompt dissemination of new labeling. The public health benefit of e-labeling is clear as it will speed up the availability of accurate, real-time, and consistent labeling of marketed products for pharmacists, physicians, and patients.

[1] There are reported to be over 100 million patients in the Sentinel database. It is recognized that Sentinel is still emerging but nevertheless offers opportunity for monitoring drug safety that is expected to far exceed today's passive reporting procedures since it could be used as a general screening tool for product safety information.

Although tangentially addressed in the report, Congress designed the Risk Evaluation and Mitigation Strategies (REMS) Program to provide patients and health care providers additional information about drug products beyond what is included in the professional labeling. When used appropriately, REMS programs are helpful in conveying pertinent safety information to both patients and providers. Pharmaceutical companies may achieve this by creating a medication guide or patient package insert, a communication plan, or Elements to Assure Safe Use (ETASU).

Unfortunately, NDA and BLA holders are using the REMS programs and other restricted access programs to deny ANDA/ABLA applicants access to product samples they need in order to conduct bioequivalence testing, which is a necessary component in order for the FDA to approve a biosimilar or a traditional small molecule generic product. This is not a brand/generic dynamic either; brands are employing these tactics against other brand companies. Certain companies engage in this behavior with more frequency, especially in the biologics/biosimilars sphere. When Congress passed Hatch-Waxman and the Affordable Care Act, which established the biosimilars pathway, they did so with the intent of providing patients access to safe, low-cost versions of small molecule and expensive biologic drugs. Denying samples to biosimilar applicants undermines Congressional intent and hinders patient access to these life-saving therapies.

From an innovation perspective, many of the companies that are exploring getting into the biosimilars sector may forgo the opportunity if these potentially anticompetitive practices continue. Several of those companies are using cutting-edge technologies and methods to develop biosimilars – true innovation. This behavior could stymie innovation with respect to biosimilars. GPhA and its members urge Congress to pass legislation that clarifies the existing REMS statute to disincentivize REMS manipulation, but also create a process to help facilitate the provision of samples to ANDA/ABLA applicants.

Recommendation 7: Reform Management Practices at FDA

The generic pharmaceutical industry and the FDA share the view that the Generic Drug User Fee Act (GDUFA) and its obligations are a public health priority. GPhA commends the FDA for committing to making the Abbreviated New Drug Application (ANDA) process more timely and predictable and for taking the appropriate steps to meet GDUFA goals, which will be measured in years 3-5.

In January 2014, FDA demonstrated its commitment to continuous improvement of the approval process by announcing communication enhancements to the ANDA review process. These changes are positive steps that can make it significantly easier for industry to assess the status of submissions and improve market launch planning. FDA is also working quickly to achieve its commitment under GDUFA to reduce the backlog of generic drug applications at FDA. As the agency does so, it is vital that FDA approves first-to-market generic applications on the very same day as patent expiration. It is also critically important that FDA work expeditiously to approve subsequent generics to the market since increasing number of competitors help drive greatest savings to the health care system.

In order for our health care system to continue to realize these savings, and to provide greater choice and affordable access to patients, it is critical that first generics and subsequent generics are prioritized in the agency's review process and approved as soon as legally possible. GPhA and its members support the recommendation of improving FDA communication to the external community. As part of the GDUFA negotiations, the generic industry highlighted the need to increase communication between industry and the FDA. While communication between industry and FDA has improved, it needs to continue to expand and broaden to ensure transparency – one of the main goals of GDUFA – as both parties are committed to building upon these advancements. Better communication between the Agency and industry will eliminate redundant and needless activities on both ends and streamline the review and approval process.

GPhA and its members share similar views with the PCAST report that FDA can improve its internal process for issuing guidance documents and clearing current guidance backlog. This is important as it relates to the review and approval of biosimilars and interchangeable biologics. While FDA has released some guidance with respect to biosimilars, several outstanding issues remain, such as interchangeability and naming. Biosimilars represent a tremendous opportunity to provide a less-costly version of biological drugs, which are one of the fastest growing segments of health care spending. A more transparent and efficient guidance process could provide GPhA member companies more business certainty. GPhA agrees with the report about providing, "…adequate clarity about the pathways and standards of evidence that the FDA will require in evaluating those products."[2] GPhA continues to work with FDA to ensure that the approval process for biosimilars is workable and provides for timely access of biosimilar medicines.

Recommendation 8: Study Current and Potential Economic Incentives to Promote Innovation in Drug Development

The Drug Price Competition and Patent Term Restoration Act, otherwise known as Hatch-Waxman, has been a resounding success. This landmark legislation struck the appropriate balance between access and innovation – patients gaining timely access to low-cost versions of branded drugs and providing innovator companies marketing exclusivity and recouping patent protection. This tradeoff has worked. Generic competition spurred greater investment in R&D and the development of hundreds of novel products. PhRMA reports that, "In the last ten years, more than 300 new medicines have been approved by the FDA, helping patients live longer, healthier lives. Medications are transforming many cancers into treatable conditions, reducing the impact of cardiovascular disease, offering new options for patients with hard-to-treat diseases like Alzheimer's and Parkinson's, and fighting even the rarest conditions."[3] The 2009 Medco Drug Trend Report reported that "about one-third to one-half of the products in Phase III development are new molecular entities (NMEs), new therapeutic biologics, or new

[2] President's Council of Advisors on Science and Technology. *Report to the President on Propelling Innovation in Drug Discovery, Development, and Evaluation.* (September 2012). Retrieved from http://www.whitehouse.gov/sites/default/files/microsites/ostp/pcast-fda-final.pdf

[3] Pharmaceutical Research and Manufacturers of America (2014). "Explore the Latest Progress on Medicines in Development." Retrieved June 4, 2014, from http://www.phrma.org/innovation/meds-in-development

vaccines/blood products; the remainder involve new indications for existing drugs, new combination products, new dosage forms, or new routes of administration."[4]

With respect to generic medicines, they now account for 84 percent of the prescriptions dispensed, up from 20 percent when Congress passed Hatch-Waxman. A December 2013 analysis by the IMS Institute for Healthcare Informatics showed that over the 10-year period 2003 through 2012, generic drug use has generated more than $1.2 trillion in savings to the U.S. health care system. In 2012 alone, generics saved $217 billion. The federal government reaped 31 percent of the 10-year savings, which included $180 billion for Medicaid, $96 billion for Medicaid, and more than $78 billion for out-of-pocket cash payers.[5] Generic versions of brand name drugs provide consumers with affordable alternatives to prescribed medicines. A 2012 report from the National Association of Chain Drug Stores showed that the average retail price for a generic prescription was $35.22, while the average retail price for a brand-name prescription was $121.18, a difference of more than 70 percent.[6]

GPhA and its members recognize the importance of marketing exclusivity and patent protection. These economic incentives play a key role in bringing novel therapies to patients. However, for some, the mechanistic response for ideas on how to spur investment and drug development is increased market exclusivity. GPhA and its members urge caution when evaluating proposals to add additional years of market exclusivity for novel therapies and new conditions of use. As the PCAST report correctly points out, excluding generic competition results in higher drug prices and could possibly put life-saving therapies out of reach for patients and a higher prescription drug bill for federal, State, and local governments. An unintended consequence of excessive periods of exclusivity is that it could actually discourage innovation because of the lack of competition.

When looking at economic and other types of incentives to spur drug development, it is important to take a holistic approach and focus on the specific reasons why companies are not getting involved in certain drug spaces. Is it because the cost to conduct clinical trials continues to grow? Are there regulatory barriers? Reimbursement issues? Pinpointing the reasons for lack of investment can help isolate the appropriate incentive. GPhA and its members understand that the generic and biosimilar industry is dependent upon the development of new therapies, which is why a measured approach should be taken to determine the appropriate incentives to spur innovation

[4] Medco (2009). "Drug Trend Report." Retrieved June 5, 2014, from http://www.medco.com/art/drug_trend /pdf/DT_2009_Drug_Trend_Report.pdf

[5] Generic Drug Savings in the United States (5th ed. 2013). Retrieved June 4, 2014, from http://www. gphaonline.org/media/cms/2013_Savings_Study_12.19.2013_FINAL.pdf.

[6] National Association of Chain Drug Stores Foundation (2012). "2010-2011 Chain Pharmacy Industry Profile." Retrieved from Statistical Abstract of the United States Vol. 129 at http://www.books.google.com/books?id=zgsBn_F81Q0C&pg=PA139&lpg=PA139&dq=National+Association+of+Chain+Drug+Stores+average+retail+price+generic+34.34&source=bl&ots=Ok_DEaGZKr&sig=YNCjEKvi8lz2Lfq29gfdhyJBslo&hl=en&sa=X&ei=vdSPU6i8NZGayATKrYK4Dw&ved=0CCIQ6AEwAQ#v=onepage&q=National%20Association%20of%20Chain%20Drug%20Stores%20average%20retail%20price%20generic%2034.34&f=false

Conclusion

GPhA appreciates the opportunity to provide comments on ways to assure patient access to affordable life-saving cures. We look forward to continuing to work with the Committee on this important initiative and developing legislation to achieve our shared goals.

SAREPTA
THERAPEUTICS

June 10, 2014

The Honorable Fred Upton, Chairman
The Honorable Diana DeGette
Committee on Energy and Commerce
United States House of Representatives
2125 Rayburn House Office Building
Washington, DC 20515

Re: 21st Century Cures Initiative, Combined Comments- PCAST Report and Call to Action

Dear Chairman Upton and Representative DeGette:

Sarepta Therapeutics thanks the United States House of Representatives Committee on Energy and Commerce for its leadership in calling to action "A Path to 21st Century Cures."

We applaud the Energy and Commerce Committee for its interest and dedication to accelerating the pace of cures in America. As the Committee looks to support the interests of patients and families in obtaining the treatment options they urgently seek, we are pleased to submit our own ideas for your consideration.

Our input is driven by: (1) our recent experience working with FDA to apply novel regulatory approaches, as provided by the FDA Safety and Innovation Act of 2012 (FDASIA), in order to speed the availability of drugs to children with a rare and fatal disease – Duchenne muscular dystrophy (DMD); and (2) the rapid advances in scientific knowledge and personalized medicine that will require further advances in FDA's regulatory processes and policies. Toward this end, we would like to suggest consideration of a novel regulatory framework to facilitate the review of technology platforms that utilize a standard approach across multiple products.

We look forward to working with you and the other members of the Committee in your efforts to further streamline drug development and evaluation.

About Sarepta Therapeutics & Our Technology

Sarepta Therapeutics is a leading biotechnology company whose workforce of over 150 employees operates principally in two offices; our headquarters in Cambridge, MA, and a research facility in Corvallis, OR. Our company's goal is to harness the power of cutting-edge RNA technologies to improve the lives of people affected by serious and life-threatening diseases. Sarepta's RNA technology offers a versatile platform that can be customized so as to target the root cause of a patient's individual variant of a disease.

We believe that our platform approach to RNA-based therapies is uniquely suited for the treatment of many rare genetic disorders and emerging infectious diseases, including serious and life-threatening diseases that otherwise could not be treated with traditional small molecule or biologic drugs.

About our Duchenne muscular dystrophy (DMD) Pipeline

Sarepta is currently applying its RNA technology platform to the development of life-saving treatments to halt the progression of DMD, a devastating, degenerative, rare, and fatal genetic muscular disease that predominantly affects boys and young men. There are currently no commercially available treatments in the United States indicated to treat DMD, representing a significant unmet medical need. Sarepta's DMD drug candidates act directly on the underlying cause of DMD by restoring production of the dystrophin protein that is lacking in Duchenne patients. Because numerous known mutations in the dystrophin gene can lead to DMD, the ability to treat the majority of DMD patients, and not just a select few, will require drugs that target each mutation. Sarepta's DMD "targeted therapies" based on a common platform are just one example of this new era of personalized medicine.

Importantly, after a year-long dialogue with the agency, Sarepta recently received guidance from FDA on the path forward for its lead DMD drug candidate, eteplirsen, and also initial guidance for its follow-on DMD drug candidates. While this guidance is allowing Sarepta to move forward and is an encouraging sign that FDA is adhering to the spirit of FDASIA, we believe the FDA will need to continue to think and act with flexibility, creativity, transparency and urgency in order to accelerate access to these DMD drugs for all boys who may potentially benefit. Moreover, we anticipate along with our industry peers that the pace of innovation will continue to challenge the conventions of regulatory science in its present form.

As the Committee continues its landmark work to advance the pace of cures in the 21st century, we respectfully encourage you to consider our company's recent experience as it may serve as a compelling and illustrative example of areas for improvement in the status quo- the current arc of discovery, development, regulation, and delivery of personalized rare disease therapies.

The President's Council of Advisors on Science and Technology (PCAST) 2012 Report on Propelling Innovation in Drug Discovery, Development, and Evaluation

While we are generally supportive of the spirit and tenor of all recommendations contained within the PCAST report, our remarks herein focus specifically on recommendations 2-3 and 7.

- **Recommendation 2: Catalyze the Creation of a Broad-Based Partnership to Accelerate Therapeutics.** This high level partnership should engage a range of stakeholders to promote innovation and improvement in the discovery, development, and evaluation of new medicines for important public health needs. As innovation advances and industry is incentivized to develop an increasing number of drugs for unmet medical needs, we believe FDA would benefit from new tools and funding that helps it to anticipate new approaches and therapeutics on the horizon, with which they may be unfamiliar. As science advances rapidly, it will be critical for FDA to have new tools to fill these inevitable scientific

knowledge gaps. In addition, as FDA evolves its thinking about the clinical trial paradigm, the agency could encourage innovation by allowing new, more flexible approaches that reflect advances in our understanding of disease and our ability to target particular subpopulations.

Filling key knowledge gaps. To address knowledge gaps in DMD, FDA appears to have utilized multiple mechanisms to obtain expert input, including through direct interaction with key opinion leaders and through meetings facilitated by patient advocacy organizations. This outreach to understand the science is extremely important; however, if such outreach is intended to inform regulatory decision making, it would be helpful to ensure that the process is transparent to all who are working in the space. As a broad-based partnership takes shape, we believe it will be necessary to make sure that FDA's engagement with all outside organizations and key opinion leaders occurs in an open and transparent process. This is especially the case for rare diseases where the paucity of expertise inherently limits the number of experts available to inform the agency's efforts to advance product development.

Often for rare diseases like DMD, there is also a need for validated biomarkers that can serve as surrogate endpoints. FDA has shown a willingness to work collaboratively with companies to better understand the methodology underlying the biomarker measurements used in clinical trials; we think this is an important activity that the agency should be encouraged to continue. Sarepta also believes that it is especially important for FDA to reach out to a diversity of players that make up the patient voice; it is important that patient views and preferences be included in any such effort, at all levels of planning, governance, and policy development. The patient voice has many layers; the more FDA reaches out to these many different layers, the better input the agency will receive. In DMD, the patient community has been especially instrumental in helping the FDA understand the preferences of patients and family members and guiding the FDA in determining meaningful benefit, risk tolerance, and acceptable tradeoffs. FDA has done an admirable job of reaching out to different voices in the DMD community, and this may be a model for outreach to other patient communities in the rare disease space.

Improving clinical trials capabilities. FDA has a role in helping the clinical trial paradigm to evolve. DMD is an example of a rare disease that encompasses a small population, yet there is interest across multiple companies to conduct clinical trials. The traditional approach of one compound and one trial at a time is not sufficient. New models need to be employed that will help overcome potential bottlenecks such as with protocol standardization and effective patient accrual.

FDA is partnering in other spaces, such as lung cancer, to explore new approaches to clinical trial protocols; this is a great example of FDA innovation that could provide an effective model for DMD and other rare diseases. The "Master Protocol" approach first used in lung cancer may serve to speed clinical trials of targeted therapies in other disease settings such as DMD where the population is segmented into smaller and smaller subsets. The protocol would take a broad-based "all comers" approach and use a standing infrastructure that prevents re-creating the wheel each time a new therapy enters late-stage development.

Clarifying the development pathway for innovative medicines. One of the most important PCAST recommendations from an innovator standpoint is that FDA should partner with companies to clarify the pathway for innovative medicines early, and to the fullest extent possible. For a rare disease company, this could mean the difference between developing or not developing a new medicine. It is significant to note that while Sarepta received inconsistent guidance from FDA over the course of the past year related to development and approval of our lead DMD drug candidate, the most recent comprehensive drug-specific guidance has enabled Sarepta to commit to a plan forward and the creation of jobs to help execute this plan. **We cannot overemphasize the importance of having clear and consistent guidance from the FDA.** Having clear pathways for innovative technology will help our nation maintain its role as the innovation capital of the world and strengthen the economic viability of the biotech industry.

In the DMD space, FDA is testing a novel approach to gathering patient input; the agency has reached out to specific patient groups to prepare draft guidance for FDA's consideration, and to quantify patients' benefit/risk tolerance. This innovative pilot has significant upside for helping to clarify a development pathway for innovative medicines. With that said, FDA needs to make sure it has balanced the many voices from the patient community, innovators and scientific experts to reflect the range of viewpoints.

- **Recommendation 3: Expand the Use in Practice of FDA's Existing Authorities for Accelerated Approval and for Confirmatory Evidence.** As is widely recognized, this recommendation is similar to the related FDASIA provision encouraging FDA to "implement more broadly effective processes for expedited development and review of innovative medicines for unmet medical needs, including those for rare diseases." We wholeheartedly are aligned with this recommendation and believe it is consistent with the Committee's goals for the Cures initiative.

  Our engagement with FDA to explore new regulatory approaches toward accelerated approval of personalized rare disease therapies for DMD has put us and the DMD community at the forefront of the implementation of FDASIA on several levels. Here are a few steps we have taken that have advanced our progress, and that could be instructive as the Committee looks for ways in which to streamline the Agency's interaction with innovators:

  - We are working with FDA to achieve regulatory flexibility that will allow use of novel surrogate endpoints, intermediate clinical endpoints, and efficient clinical trial designs[1] to advance our DMD drugs through the accelerated approval pathway;
  - FDA has been consulting with DMD medical experts to enhance its understanding of the disease, the science, and methodologies[2], although as mentioned previously the transparency and accountability of this process could be improved upon; and
  - The patient community has engaged FDA to a great extent in order to inform the FDA's calculus with regard to benefits and risks of a prospective therapy as well as

[1] See FDASIA Sec. 901 - P. L. 112-144; FFDCA- 21 U.S.C. § 356
[2] See FDASIA Sec. 903 - P. L. 112-144; FFDCA- 21 U.S.C. § 360bbb-8

alternatives or the absence of therapy[3], as it is ultimately the patient community, in close consultation with their clinical care providers, who must weigh the potential benefits and risks for the chance of stopping the progression of disease.

- Additionally, while we find the Agency's recent industry guidance[4] for expedited review programs to be an encouraging step forward**, there remains a high degree of uncertainty as to how sponsors may approach validation of a biomarker as a surrogate endpoint that is "reasonably likely to predict clinical benefit."** Much of this uncertainty can be attributed to inconsistent views and use of the accelerated approval authority across FDA staff and divisions, both horizontally and vertically. As you reflect on policies that could strengthen FDA, we suggest the Committee explore options for addressing this issue.

- **Recommendation 7: Reform Management Practices at FDA**

  Establish a Regulatory Innovation Program. Though we realize there are ongoing efforts within the Center for Drug Evaluation and Research's Office of Pharmaceutical Quality to address this PCAST recommendation, we believe that FDA will need additional resources to implement this to the extent -- and at the more senior level -- recommended by PCAST. In addition, one area of focus should encompass creating a meaningful dialogue with those on cutting edge of the technology development including academics and industry experts.

Regulatory Framework for Platform Technologies

We are very supportive of the Committee leadership's efforts to explore new drug review and approval pathways that will help regulatory policies keep pace with innovation. **As science and technology advance over the next decade, especially in the area of personalized medicines, one of most significant trends we believe FDA will see is the proliferation of platform technologies - technologies that use common or standardized approaches and tools across multiple products.** Platform technologies have the power to reduce costs, increase efficiencies, and, in general, accelerate drug development programs – all goals of the 21st Century Cures initiative. To realize the benefits of platform technologies, new thinking is needed about how to approach the regulatory review of such technologies.

We have some detailed thoughts as to how this might work; we will submit these ideas to the Committee as a separate document.

Conclusions

The PCAST report featured many significant recommendations that could be bolstered by Congressional interest and involvement. We believe the Committee should consider prioritizing recommendations 2, 3, and 7. Furthermore, we urge the Committee to consider putting additional focus on how platform technologies may allow for important benefits for all stakeholders; recognizing the value of platform technologies may save agency resources and speed the delivery of treatments to patients by avoiding duplicative reviews.

[3] See FDASIA Sec. 905 - P. L. 112-144; FFDCA- 21 U.S.C. § 355(d)(7)
[4] See FDA Guidance for Industry "Expedited Programs for Serious Conditions - Drugs and Biologics".

At Sarepta, we stand ready to work with the Committee as it looks at streamlining drug development and review. Our recent regulatory experience, though not completely smooth, shows FDA is willing to work with innovators in addressing drug development for life threatening diseases. FDA has put additional resources toward trying to address DMD, and this may be a place for significant learnings that can be applied to other rare diseases.

For questions regarding Sarepta or the above comments, please contact Diane Berry, Ph.D., Vice President, Global Health Policy and Government Affairs, at [redacted]

Sincerely,

Chris Garabedian
President & CEO
Sarepta Therapeutics

UNIVERSITY OF UTAH
HEALTH SCIENCES

Vivian S. Lee, M.D., Ph.D., M.B.A.
A. Lorris Betz Senior Vice President for Health Sciences
Dean, School of Medicine
CEO, University of Utah Health Care

June 10, 2014

The Honorable Fred Upton
Chairman
Energy and Commerce Committee
U.S. House of Representatives
Washington, DC 20515

The Honorable Joe Pitts
Chairman, Health Subcommittee
Energy and Commerce Committee
U.S. House of Representatives
Washington, DC 20515

Dear Chairmen Upton and Pitts,

On behalf of the University of Utah Health Sciences Center (UUHS), thank you for your continued efforts to support medical research and accelerate the paces of cures and medical breakthroughs in the United States. We appreciate your dedication and commitment to improving the health of our nation and ensuring America maintains its position as the top competitor in biomedical research and the innovation capital of the world. We are pleased to respond to the House Energy and Commerce Committee's May 12, 2014 request for input on how the President's Council of Advisors on Science and Technology's (PCAST) proposals on propelling innovation in drug discovery, development, and evaluation can contribute to the 21st Century Cures Initiative.

As the only academic medical center in a region that spans over 10% of the continental United States, and as one of the top 3 employers in the state of Utah, UUHS' impact on the health and economy on the West is unlike most. Through telehealth services, satellite clinics, AirMed helicopters, and fixed-wing aircraft, our 1,200 physicians and more than 12,000 staff impact the lives of more than one-million urban and rural patients across Utah, Idaho, Wyoming, Montana, western Colorado, and much of Nevada each year. We provide these patients access to a range of services, from population health and wellness to high-end specialty care, including a Level 1 trauma center, the region's major burn center,

Clinical Neurosciences Center 5201
175 North Medical Drive East
Salt Lake City, Utah 84132-5901

Phone: (801) 581-7480
E-mail: vivian.lee@hsc.utah.edu
Twitter: @vivianleemd
Blog: www.vivianleemd.org

the region's only designated Comprehensive Stroke Center, and our world-renowned Huntsman Cancer and Moran Eye Centers. We also serve as the safety net for many of our low-income and uninsured populations, providing over $100 million in charity care this year alone.

But our impact is not only local. Our scientists unearth biomedical truths in genetics, cancer, diabetes and metabolism, cardiovascular disease, and neuroscience – just to name a few – that allow us to improve care and save the lives of patients worldwide. These groundbreaking discoveries not only enable us to better understand our world and to build the tools necessary to improve it, they also allow us to train a new generation of teachers and researchers, who work alongside our students in medicine, dentistry, nursing, pharmacy, and occupational health to translate discoveries into improved care.

It is from this unique perspective that we provide comments on several of PCAST's recommendations. Our comments reflect feedback provided by stakeholders in our academic medical center, including senior leadership and clinical and research PI's who have successfully translated discovery to the bedside.

Support federal initiatives to accelerate therapeutics

NIH funding has clearly accelerated the pace of discovery, and the federal government should increase the NIH budget to allow for new and further research on the underlying basis of disease and therapeutics. The impact of NIH funding can be illustrated by Utahn Gregg Johnson.

Gregg's mother died at 47. She followed Gregg's grandmother, who died at 42. Colon cancer, the second deadliest disease in the U.S., killed them both. Gregg, now in his fifties, is much less likely to die from the same colon cancer that killed his family because, in 1987, with the help of NIH funding, University of Utah researchers identified mutations in the APC gene as the underlying cause of an inherited colon cancer predisposition called familial adenomatous polyposis, or FAP. The lifetime risk of FAP for people with this inherited mutation is 100%.

Since then, scientists have determined that an acquired, or non-inherited, mutation of this gene is also found in 80% of other colon cancers; and further discoveries have led to drug trials that target the specific, cancer-causing proteins of these mutations that may have implications in other types of cancer and personalized medicine. Due to discoveries like these, supported in great part by the NIH, Gregg and his family have already succeeded in outliving their family histories.

This University of Utah discovery, and more than 30 genes responsible for breast cancer, atrial fibrillation (long QT syndrome), and dozens of other rare and undiagnosed diseases, all occurred with the help of a Utah state resource called the Utah Population Database that houses massive family genealogies connected to public health and medical records. Today, we can digitize and decode an entire human genome for less than $1000, but searching for the genetic cause of disease is like looking for one misspelled word in all

the books in the Library of Congress. We have built tools that allow us to compare the genetic sequences of other affected and un-affected family members, and to then find these disease-causing genes more easily. Our database currently maps the family genealogies and medical records of almost 7 million people—the next largest database is DECODE in Iceland, now privately owned with about 500,000 records.

Thanks to Francis Collins and the NIH for their commitment to harnessing the power of DNA in biomedical research and to a tradition of large families in Utah, the genetic goldmine in our valleys can be a precious resource to all of humankind; we can leverage our unique American resource to make vital discoveries that transform how we think about and treat diseases from autism to Alzheimer's and from cancer to heart disease. But to tap this crucial resource and realize this impact, we need NIH funding and other direct federal support. With greater federal initiatives like this, we can make the foundational discoveries necessary to develop and accelerate new therapeutic treatments and cures.

Catalyze the creation of a broad-based partnership to accelerate therapeutics

Broad-based partnerships are clearly an answer to the problem of funding shortfalls on the academic side of therapeutic development and discovery, but we should critically consider the regulation of these relationships. Most academic health centers are seeing a significant growth in partnerships with industry. These partnerships, of course, should be handled very carefully because of conflict of interest concerns at both the PI and the institutional level. But, there are some real advantages to looking toward our industry counterparts. Commercialization opportunities ensure that our discoveries are made accessible to patients directly, and these kinds of partnerships can help speed up the process of translation. It will be a delicate balance between the individual PI/research team driven to scientific discovery and the industrial pharmaceutical industry partner driven to profit. Additional consideration must be given to the nature of any partnerships between institutions and their fair share of credit, IP, and reputation in the cases of discovery.

At the University of Utah, the John A. Moran Eye Center recently announced that, Voyant Biotherapeutics, LLC, a company formed out of the Moran Center for Translational Medicine, signed an exclusive R&D Collaboration Agreement with Allergan, Inc., a multi-specialty health care company headquartered in Irvine, California. Under the agreement, the two companies will work together to identify disease-associated pathways and targets for the development of new therapeutic agents to treat ocular disease. A primary effort of this collaboration will be centered on new treatments for age-related macular degeneration (AMD), a leading cause of irreversible vision loss worldwide. The opportunities for such a potentially successful partnership are built on shared resources that protect the interests of all sides.

Voyant Biotherapeutics, LLC was created as a vehicle that could allow both sides to do what they do well and interact and give kind of a flexible space between. Additionally, the partnership doubles our research resources, which allows us to be more strategic and

nimble when it comes to focusing efforts on new pathways and potential discoveries. We have high hopes for the model and are optimistic it will open a host of pipelines for the translation and commercialization of new discoveries.

Create a new pathway for initial approval of drugs shown to be safe and effective in a specific subgroup of patients

Any new pathway of selective distribution could rely heavily on advances to genomic science, big data, and electronic health records. For instance, at our organization, we house a state-owned and protected genetic gold mine called the Utah Population Database. The largest of its kind in the country, our database combines family genealogies with medical and public health records and is a model of the kind of tool we would need to effectively and efficiently identify subgroups of patients and their candidacy for said distribution. However, resources of this nature are expensive to establish and maintain and pose a breadth of unanswered questions regarding utilization and privacy. Pathways that identify subgroups of patients in any manner require financial support and legislative innovation to activate.

Explore approaches for adaptive approval via pilot projects under existing pathways, but do not create new adaptive approval pathways through legislation

When exploring new approaches, we must be careful not to conduct clinical outcomes and cost-effectiveness research in a vacuum. Without doing research to understand the value (cost vs. outcomes) of these "accelerated therapeutics" to society and patients, getting these technologies to the bedside will not happen. The industry experienced a literal turning point this year in the case of Gilead sciences when they brought Sovaldi to market at $84,000 for a 12-week course of therapy to cure HCV. Consideration of how this innovation should be used needs coordinated use and distribution. First use should be focused only in patients with the genotype where it has been shown more effective than the current standard of care. Only after value has been established in this group of patients should we consider expanding the trial to see if there is additional potential value for the broader population.

Study current and potential economic incentives to promote innovation in drug development

To be successful with any "acceleration practices," development must be affordable. We have pushed pharmaceutical companies to be innovative, but we are not sure if those who pay for health care (insurance companies, government, employers, patients) are willing, or can afford, to pay for such innovation. This has to be part of the equation. For example, in the case of Gilead, Forbes recently listed the company as one of the top ten profit margin companies with a 50% profit margin so far in 2014 – no doubt due to Sovaldi sales. The American Association of Health Insurance Plans is trying to meet with pharmaceutical companies to somehow address the conflict of innovation and affordability going forward. This is a critical step to the success of any innovation, and it must become part of the development calculus in the United States, as it is in other

countries. Accordingly, the Committee should not only focus on increasing innovation, as recommended in the PCAST report, but the Committee should also focus on how society will pay for the acceleration or the output of these initiatives.

UUHS appreciates and supports your efforts to address important issues surrounding medical discovery, development, and delivery, and we look forward to working with you to advance the 21st Century Cures Initiative. If you would like to discuss any of these comments in greater detail, please contact me at [redacted]

Respectfully,

[redacted]

Vivian S. Lee, M.D., Ph.D., M.B.A.
Senior Vice President for Health Sciences of the University of Utah
Dean of the School of Medicine
CEO of University of Utah Health Care

June 10, 2014

The Honorable Fred Upton
2183 Rayburn House Office Building
Washington, DC 20515

The Honorable Diana DeGette
2368 Rayburn House Office Building
Washington, DC 20515

Submitted electronically to cures@mail.house.gov

RE: Stakeholder Groups' Response to 2nd White Paper — 21st Century Cures: An Update on the President's Council of Advisors on Science and Technology (PCAST) 2012 Report on Propelling Innovation

Dear Chairman Upton and Representative DeGette:

The undersigned organizations represent health care providers, hospitals, pharmacists, clinical laboratory scientists and medical microbiologists, public health experts, patients and advocates who share a deep concern about the growing threat of antibiotic resistance and the lack of new antibiotics to treat serious or life-threatening infections. Without swift congressional action, we fear that antibiotic research and development (R&D) will continue to struggle, and that patients will continue dying from infections that are resistant to current antibiotics. No one is safe from these infections, but certain populations are at heightened risk, including individuals with weakened immune systems (e.g. chemotherapy patients, transplant patients, the elderly, premature infants, patients with a primary immunodeficiency disease and patients with HIV), soldiers with deep combat wounds, and patients who have had recent surgeries.

We write to thank you for launching the 21st Century Cures Initiative and to offer comments on the initiative's second white paper, ***"21st Century Cures: An Update on the President's Council of Advisors on Science and Technology (PCAST) 2012 Report on Propelling Innovation."*** The 2012 PCAST report recommends the establishment of a new Food and Drug Administration (FDA) pathway in which sponsors could seek approval of a new drug for use in a limited population of patients with a serious disease and unmet medical need. The PCAST report specifically recommends new antibiotics to treat patients with drug resistant infections as one area for which this new pathway would be appropriate.

We urge the Committee to act promptly on the Antibiotic Development to Advance Patient Treatment (ADAPT) Act, which would carry out the PCAST recommendation to establish a new limited population approval pathway for antibiotics to treat serious or life-threatening infections where an unmet medical need exists. This would allow FDA to consider the risk benefit calculation for patients with few or no other options. Under this bill, the FDA could approve ADAPT drugs based upon smaller clinical trials. It is often not feasible for these drugs to be developed using traditional, large clinical trials due to the limited numbers of patients in whom these infections currently occur.

Importantly, ADAPT drugs must still meet FDA standards of evidence for safety and effectiveness for the limited indicated population. ADAPT's provisions aimed at guiding appropriate use of these drugs include a statement on the label that the "drug is indicated for use in a limited and specific population", but could be strengthened by including a prominent visual element, such as a logo, to make it simple for

the health care community to quickly recognize that these drugs are approved for a limited population and must be used prudently. We believe this issue can be easily resolved as the bill advances.

Quick movement on the ADAPT Act is a logical first step for the 21st Century Cures Initiative. This bill already has over two dozen bipartisan cosponsors on the Committee. The limited population approval approach is supported by a wide array of stakeholders, including medical societies, public health organizations and the pharmaceutical industry. Congress, the FDA, the Centers for Disease Control and Prevention (CDC), the Director of the National Institute for Allergy and Infectious Disease, and the Trans-Atlantic Task Force on Antimicrobial Resistance (TATFAR) have all underscored the urgent need for new antibiotics. With more and more patients dying from multi-drug resistant infections every day, we see no reason for the Committee to delay consideration of this thoughtful, widely supported proposal.

As medical, healthcare, public health and patient organizations dedicated to patient care and safety, as well as public health in general, we urge you to move the ADAPT Act now – without waiting for other legislative initiatives that will be in a part of the 21st Century Cures Initiative – given the public health interests at stake. We look forward to working with you toward the establishment of a limited population approval pathway to speed patient access to new life-saving antibacterial drugs.

Sincerely,

AIDS Action Baltimore, Inc.
Alliance for Aging Research
American College of Rheumatology
American Gastroenterological Association
American Society for Microbiology
American Thoracic Society
Association for Professionals in Infection Control and Epidemiology
Cempra Inc.
Harm Reduction Coalition
HIV Medicine Association
Immune Deficiency Foundation
Infectious Diseases Society of America
National Association of County and City Health Officials
National Association of Pediatric Nurse Practitioners
National Foundation for Infectious Diseases
Pediatric Infectious Diseases Society
Society for Healthcare Epidemiology of America
Society of Critical Care Medicine
Society of Infectious Diseases Pharmacists
The Pew Charitable Trusts
Trust for America's Health
UPMC Center for Health Security