



**Statement for the record from Cubist Pharmaceuticals**

**Submitted to the  
U.S. House of Representatives  
Committee on Energy and Commerce  
Subcommittee on Health**

**Hearing on  
21st Century Cures: “Examining Ways to Combat Antibiotic Resistance and Foster New  
Drug Development”  
September 19, 2014**

Chairman Pitts, Ranking Member Pallone, and Members of the Subcommittee, Cubist Pharmaceuticals (Cubist) thanks you for convening today’s hearing to address new ways to combat antibiotic resistance and foster new drug development. Also, we would like to thank Chairman Upton and Representative DeGette for the Committee’s 21<sup>st</sup> Century Cures effort. In the last Congress, this Committee’s leadership and the efforts of Dr. Gingrey and Representative Green, secured passage of the Generating Antibiotic Incentives Now (GAIN) Act—the single most important policy change to date for antibiotic innovation. While a number of approaches will be necessary to address the broken market for antibiotics, the most meaningful next step Congress can and should take is to ensure enhanced reimbursement for new drugs to treat patients with serious and life-threatening infections.

Cubist is a global biopharmaceutical company headquartered in Lexington, Massachusetts. Our company is focused on the research, development and commercialization of pharmaceutical products for use in the acute care environment. Cubist has a growing commitment to global public health through its leadership in the discovery, development and commercialization of novel antibiotics to treat serious and life-threatening infections caused by a broad range of increasingly drug-resistant bacteria. The company hopes to deliver at least four new antibiotics in support of the Infectious Diseases Society of America (IDSA) goal of 10 new antibiotics by 2020. Cubist also expects to invest approximately \$400M USD in 2014 on antibacterial R&D

and approximately 75 percent of its employee base is focused on the research, development, commercialization and support of antibiotics. Our deep experience in this therapeutic area makes us well positioned to comment on the types of incentives that could help companies deliver desperately-needed antibiotics to patients, and we welcome the opportunity to do so.

### **Opportunity to Build on Success of the GAIN Act to Enhance Antibiotic Innovation**

Today's hearing builds on the Subcommittee's bipartisan contributions to what is arguably the most important federal policy adopted in recent history to incentivize antimicrobial innovation. In 2012, Congress took action to address the lack of innovation for antibiotics through enactment of the GAIN Act as part of the Food Drug Administration Safety and Innovation Act (FDASIA), Public Law 112-144. The GAIN Act established a new Qualified Infectious Disease Product (QIDP) designation for antibiotics that treat serious or life-threatening infections, fast tracking their development and regulatory review and allowing manufacturers to apply for extended market exclusivity upon approval. The Food and Drug Administration (FDA) recently approved the first drugs designated as QIDPs under the GAIN Act—including Cubist's SIVEXTRO® (tedizolid phosphate)—and others may reach patients later this year, if approved by the agency.

The Subcommittee should be aware that, in just over two years, the GAIN Act has proven to be an important foundation for renewed investment, research and development in the field of antibiotics. By relying upon its experience with the highly regarded Orphan Drug Act, Congress successfully crafted a set of proven incentives for QIDPs, a special designation for new antibiotics that address the most serious and life-threatening infections faced by patients. The FDA has already approved three new antibiotics as QIDPs, and as of late July, 35 drugs under development have received the designation, according to the agency.<sup>1</sup>

Although the GAIN Act was a critical first step in revitalizing the antibiotic pipeline, it is widely recognized that more needs to be done. As supporters and beneficiaries of this important law, we

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<sup>1</sup> Edward M. Cox, MD, Director, Office of Antimicrobial Products, Center for Drug Evaluation and Research, FDA. "FDA's multi-pronged approach helps meet the challenge of bringing new and innovative antibiotics to patients who need them." July 28, 2014. <http://blogs.fda.gov/fdavoices/index.php/2014/07/fdas-multi-pronged-approach-helps-meet-the-challenge-of-bringing-new-and-innovative-antibiotics-to-patients-who-need-them/> (Accessed on 9/9/2014).

are grateful for the opportunity to contribute to the discussion and provide suggestions on other types of incentives that would build on the success of the GAIN Act to further encourage meaningful development in the antibiotic space.

### **Enhanced Reimbursement for QIDPs Would Expand Innovation**

First and foremost, it is important to ensure that once manufacturers develop novel antibiotics, reimbursement barriers are not an obstacle to patients and providers having access to these important new treatments. Thus, enhanced reimbursement must be the next step to build on the incentives for development embodied in the GAIN Act.

We ask that you consider the following specific actions:

#### **1. Increase reimbursement for antibiotics targeting serious or life-threatening infections by creating a Medicare DRG carve-out or new reimbursement mechanism for antibiotics designated as a QIDP under the GAIN Act.**

Currently, unfavorable reimbursement by Medicare and other providers is a barrier to the development of innovative antibiotics.<sup>2</sup> A mechanism to offset the cost of novel antibiotics that provides an incentive for companies to develop them would be a vital next step in an effort to revive the broken marketplace. Reimbursement should better reflect the life-saving value of antibiotics and should remove the cost barrier to patients getting proper treatment for their specific condition.

Patients with the most serious infections are often treated in the hospital inpatient setting. Existing inpatient payment strategies available through the Centers for Medicare & Medicaid Services (CMS) to allow for adoption of new technology have proven unsuccessful for novel antibiotics. Due to the nature of antibiotic clinical trials that most developers must use for FDA

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<sup>2</sup> Engelberg Center for Health Care Reform at Brookings, *Incentives for Change: Addressing the Challenges in Antibacterial Drug Development*, February 27, 2013. <http://www.brookings.edu/~media/events/2013/2/27%20bcadd%20meeting/meeting%20summary%2020130925%20final.pdf> (Accessed 9/9/2014.)

approval, (data are typically collected in non-inferiority studies for ethical and other reasons)<sup>3</sup> the New Technology Add on Payment (NTAP) program does not apply to most antibiotics. In addition, the short duration of the NTAP program is not well suited to appropriate antibiotic stewardship, and the coding limitations and partial reimbursement provided by NTAP do not effectively provide an enhanced payment system for drugs that reflects the true life-saving value of these medicines.

A carve-out from Medicare's Diagnostic Related Group (DRG) inpatient payment system or new reimbursement mechanism in the hospital (inpatient) setting, specifically for antibiotics designated as QIDPs under the GAIN Act, would alleviate some of the cost pressures that discourage the use of new treatments for serious or life-threatening infections. Removing QIDP reimbursement from the DRG bundle via an enhanced reimbursement mechanism would ensure providers are not adversely financially impacted when using an important new antibiotic and could employ appropriate stewardship without cost concerns. The cost to the government to apply this type of mechanism has been estimated to be very low, but the value as an incentive to antibiotic development would be extraordinarily significant. Reimbursement should be structured in such a way that it removes the financial barrier, allowing physicians to make their decisions based on clinical factors, including the needs of their specific patient and antibiotic stewardship.

Applying reimbursement incentives to antibiotics designated by FDA as QIDPs would ensure that coverage and payment is determined in a consistent manner. QIDP is a narrowly-tailored, carefully-crafted definition of the most critically-needed antibiotics—those targeting serious or life-threatening infections. The QIDP designation is limited in scope and provides the certainty companies must have in order to make business and investment decisions. An enhanced reimbursement should apply for the life cycle of a product and provide a consistent and well-defined pathway for innovators. Improved reimbursement will incentivize pharmaceutical companies to continue in, and even reenter, the antibiotic space to develop the new drugs we so desperately need to combat antibiotic resistant pathogens.<sup>4</sup>

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<sup>3</sup> S. Nambiar et al. *Antibacterial Drug Development: Challenges, Recent Developments, and Future Considerations*. *Clinical pharmacology & Therapeutics* (96): August 2014.

<http://www.nature.com/clpt/journal/v96/n2/pdf/clpt2014116a.pdf> (Accessed 9/15/2014.)

<sup>4</sup> Matthew Herper, *How to Avert an Antibiotic Apocalypse*, *Forbes*. January 27, 2014.

## **2. Establish higher or multiple Medicare DRG rates for resistant infections**

Patients in the acute-care setting with serious or life-threatening antibiotic-resistant infections often suffer from other (comorbid) conditions. The cost of managing these patients can be higher due to the serious infection, but current DRG payment rates may not cover the cost of treating these patients using novel new antibiotics. We urge Congress to establish higher or multiple Medicare DRG rates for resistant infections and/or support the use of major complication or comorbidity (MCC) classifications for such patients to alleviate the cost pressures hospitals face. Without higher DRG rates or MCC classifications, hospitals must utilize existing DRG codes that may or may not account for the higher costs associated with treating patients with resistant infections. Currently, novel treatments may increase treatment costs above the DRG reimbursement amount provided to the hospital, discouraging the use of new antibiotics. Reimbursement should not be a barrier to using the new antibiotics, when appropriate.

### **Modernizing Specific FDA Regulatory Procedures and Adopting Targeted Tax Credits for QIDPs Would Expand Innovation**

It is likely that a variety of incentives will be necessary to jumpstart innovation and restock the antibiotic pipeline.<sup>5</sup> In tandem with enhanced reimbursement, which we believe would provide the biggest incentive to antibiotic innovators, facilitating and lowering the costs of antibiotic development could also encourage more investment and innovation in the field. This aim can be accomplished through a number of means, including: streamlining and modernizing the regulatory process for antibiotics; FDA user fee exemptions; targeted tax credits; and increased investment in research networks to advance the development of antibiotics and rapid diagnostics. Cubist recommends the Subcommittee pursue the following reforms:

#### **1. Modernize the regulatory approval process for establishing and updating susceptibility test interpretive criteria, also known as “breakpoints” for antibiotics and testing devices.**

Cubist strongly supports the regulatory reforms for “breakpoints” proposed in HR 3742, the Antibiotic Development to Advance Patient Treatment (ADAPT) Act, as introduced by

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<sup>5</sup> Aylin Sertkaya, et.al. *Analytical Framework for Examining the Value of Antibacterial Products*, April 2014. [http://aspe.hhs.gov/sp/reports/2014/antibacterials/rpt\\_antibacterials.cfm](http://aspe.hhs.gov/sp/reports/2014/antibacterials/rpt_antibacterials.cfm). (Accessed 9/9/2014.)

Representatives Gingrey and Green last year and co-sponsored by a bipartisan group of over 20 Committee members. However, we recognize that a more comprehensive approach to improve the process for setting and updating antibiotic (and the associated automated testing devices that measure susceptibility) breakpoints would be valuable and understand that FDA has put forward some recommendations. We would support potential changes to the ADAPT Act, including a requirement that breakpoints be updated on an FDA website instead of the drug label and allowing the FDA to recognize breakpoints set by recognized standard setting organizations when appropriate.

## **2. Incorporate Elements of Newly Enacted Breakthrough Therapy Approval Pathway into the GAIN Act's QIDP Framework.**

Cubist is aware that the ADAPT Act, the FDA, IDSA, The Pew Charitable Trusts and others have endorsed creation of a limited population approval pathway for use by antibiotic sponsors. To date, we have collaborated well with the FDA on robust but efficient clinical trials to support the approval and review of QIDPs. Cubist is confident that the FDA will continue to exercise their existing regulatory authority to expedite access of innovative antibiotics for patients. We also commend their efforts to streamline the clinical development of important treatments in order to address antibiotic resistance as described in recent regulatory guidance.<sup>6</sup>

If the Subcommittee elects to pursue a limited population approval pathway, we recommend that it be entirely voluntary and at the sponsor's discretion and that a designation be conferred in advance, much like the fast track and breakthrough drug designations, to allow sponsors to appropriately develop their clinical programs. Cubist also notes that, in addition to defining any pre- and post-market requirements, any proposal should provide for cross-disciplinary review by senior FDA staff (as with the breakthrough designation) and require that the FDA describe the types of clinical development programs that might be considered under this pathway. We believe the latter could be accomplished through regulatory guidance. Finally, the Subcommittee should

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<sup>6</sup> Food and Drug Administration, *Guidance for Industry Antibacterial Therapies for Patients With Unmet Medical Need for the Treatment of Serious Bacterial Diseases*. July, 2013.  
<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM359184.pdf>  
(Accessed 9/9/2014.)

consider inclusion of meaningful incentives, such as orphan drug based policies of exemption from requirements under the Pediatric Research Equity Act (PREA) (including Prescription Drug User Fee (PDUFA) fees, per below), research grants, tax credits or additional exclusivity protection.

Cubist also encourages the Subcommittee to consider an alternative approach of updating the GAIN Act to ensure QIDP sponsors have access to the new breakthrough drug approval pathway and its associated benefits under section 902 of FDASIA, in the same manner that Congress assured QIDP sponsors access to fast track under section 803 of FDASIA.

**3. Provide transferable research and development and manufacturing tax credits to offset the costs of clinical testing for QIDPs.**

While the GAIN Act provides valuable economic incentives, companies must fully develop a product before receiving the benefits from increased exclusivity. Financial support to help offset clinical development costs of QIDPs, including tax credits modeled after the Orphan Drug Tax Credit, would provide an attractive incentive to antibiotic developers. Such a credit should apply to expenses incurred during late-stage (phase 2 and 3) clinical testing. The credits should also be transferable to allow small, pre-revenue companies without tax liability to sell the credit and invest the sales income into additional research and development.

**4. Exempt sponsors from FDA User Fees associated with approval of QIDPs.**

As mentioned above, FDA user fees associated with the approval of QIDPs, including the Application, Product, and Establishment user fees, should be exempted in order to reduce the costs of development for these priority antibiotics.

**5. Consider funding and or expanding existing clinical trials networks for the study of investigational antibiotics.**

We encourage Congress to explore ways to improve clinical trial efficiency by developing a robust infrastructure to facilitate clinical trials for investigational antibiotics.

**6. Invest in the development of rapid diagnostics.**

Rapid diagnostics have the potential to streamline antibiotic development, improve antibiotic prescribing and drive innovation of targeted therapies, but technological and other challenges have slowed their availability. These significant barriers are unlikely to be overcome by any one entity and would benefit from public/private collaboration. Such efforts should aim to address not only the technological and scientific barriers to rapid diagnostic development, such as sample preparation and biomarker validation, but also must consider the significant economic and regulatory barriers to rapid diagnostic development, as well as barriers to uptake of diagnostics in various healthcare settings.

**7. Expand tropical disease priority review vouchers, as established under FDAAA, to apply to QIDPs.**

Section 1102 of the FDA Amendments Act of 2007 (FDAAA) authorizes the FDA to award priority review vouchers to sponsors of certain tropical disease product applications. A priority review voucher may be used by the sponsor who obtains it or may be transferred from the sponsor (including by sale) to another sponsor of a human drug application. This policy is intended to create a positive incentive (that can be monetized) to encourage companies to pursue drug development in neglected global diseases, but is easily extensible to the development of priority antibiotics.

**Conclusion**

Cubist thanks Chairman Pitts and the Subcommittee for holding today's hearing. We are eager to assist the Subcommittee in developing and promulgating new policies that build on the GAIN Act to further incentivize antibiotic research and development.

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