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LONDON, UK (GlobalData), 3 July 2012 - While the world focused on the fate of the **Affordable Care Act**, another important piece of **healthcare** **legislation** worked its way through Congress, the Prescription **Drug** **User** **Fee** **Act** (PDUFA) V. First introduced in 1992, PDUFA authorizes the **FDA** to collect fees from companies seeking approval of new drugs. The FDA uses these **funds** to **hasten** the **drug** **review** **process**. PDUFA must be approved every five years, and the fifth iteration has to be renewed by this October. PDUFA V has been approved by both houses of Congress and awaits President Obama's signature. As with most pieces of legislation, PDUFA V is multifaceted, but the Generating Antibiotic Incentives Now (GAIN) Act alone could dramatically influence the pharmaceutical industry.

The GAIN Act outlines enticements for pharmaceutical companies to develop novel antibiotics. Antibiotics have saved countless lives since their implementation in the 1940s, but the emergence of microorganisms that have developed antibiotic resistance has been an escalating medical concern. Drug-resistant infections are difficult to treat and have resulted in an increase in medical costs and mortality. Despite the escalating need for novel antibiotics, Big Pharma has been decreasing, or even eliminating, internal antibiotic R&D. The expensive, lengthy drug approval process, low price and short duration of antibiotic therapy, and competition from generics culminated in pharmaceutical companies shifting their focus to more profitable therapies (e.g. cancer and cholesterol therapeutics). The GAIN Act hopes to buck this trend by outlining various incentives meant to spur antibiotic drug discovery and approval to combat the various drug-resistant pathogens. These pathogens include Methicillin-Resistant Staphylococcus aureus (MRSA), Vancomycin-Resistant Staphylococcus aureus (VRSA),

Vancomycin-Resistant *Enterococcus,* Multidrug-Resistant *Acinetobacter,* Multidrug-Resistant *Klebsiella,* Multidrug-Resistant *Pseudomonas,* Multidrug-Resistant *Escherichia coli* (*E. coli*), Multidrug-Resistant *Tuberculosis,* and *Clostridium difficile (C. diff).*

Incentives outlined in the GAIN Act include:

1. Companies developing a novel antibiotic will be eligible for fast track status. This will increase the level of communication between the FDA and the company, decreasing the time required for filing a New Drug Application (NDA).
2. The novel antibiotic NDA would then qualify for priority review, thereby shortening the FDA review period from ten to six months.
3. Once approved, the antibiotic would receive five additional years of market exclusivity.

These carrots will not be large enough to entice Big Pharma to revive its antibiotic R&D, but they could increase interest in smaller companies with novel antibiotic pipelines. Examples of leading biotechnology companies with promising antibiotics are listed in the table attached. The GAIN Act acknowledges the need for novel antibiotics, but does little to address the underlying issues affecting drug discovery and antibiotic drug resistance.

Pharmaceutical companies decreased antibiotic discovery due to a low ROI. The incentives outlined in the GAIN Act do little to truly increase the profitability of antibiotics. While the FDA review process is hastened, the GAIN Act does nothing to increase the chance of approval for a given antibiotic candidate. Therefore, there is still considerable risk associated with antibiotic drug discovery. Big Pharma had shifted this risk to smaller firms, which has provided a short-term fix. Collaboration between public and private sectors would provide a more viable long-term solution for fostering antibiotic drug discovery. Establishing partnerships between academia and industry would reduce cost, increase access to compound libraries, and broaden expertise associated with antibiotic drug discovery. The GAIN Act also does nothing to prevent the spread or emergence of drug-resistant organisms. Without the implementation of antibiotic stewardship and surveillance, any novel antibiotics developed as a result of the GAIN Act will

only provide temporary relief before microbes develop resistance.

Ultimately, the GAIN Act represents a stopgap solution. Establishing a pricing incentive that reflects the high cost associated with bringing a drug to market would increase the profitability of antibiotics. Changing the FDA safety threshold for antibiotics to align closer to other life-threatening indications (e.g. cancer) would decrease review time and cost, increase the probability of FDA approval, and enable doctors and patients to assess risks when treating a deadly, drug-resistant infection. Without lasting reform like the aforementioned examples, the need for antibiotics will only escalate, and Big Pharma will continue to pursue more profitable therapeutic avenues.