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Edison Explains

Antibiotics

With instances of antibiotic resistance on the rise, why is the antibiotic market stagnant?

Why do we need new antibiotics?

Early in their development, new antibiotics were being produced at a copious rate, with 14 new classes of drugs entering the market between 1935 and 2003.

With so many new treatments, bacterial resistance was of little concern to the healthcare community, but as development tapered, drugs were no longer produced quickly enough to match the spread of antibiotic-resistant bacteria.

The UK's 2016 Review on Antimicrobial Resistance reported that antimicrobial resistance (AMR) causes 700,000 deaths each year worldwide. This is a health burden not likely mitigated by the few antibiotics in Phase I to III trials, most of which are for follow-up compounds, without novel mechanisms for treating infection.

Why are companies uninterested in developing antibiotics?

Today it takes over a decade and billions of dollars to develop a new antibiotic, an initial investment unlikely to see a return, as only 6.5% of those antibacterial drugs for which approval was sought from the FDA were granted it in 2017.

Even when approval is given to a newly developed antibiotic, the market does not compare favourably to other therapeutic fields. This is partly because a wide variety of cheap and effective generics creates a highly competitive market.

It is also due to the growing fields of oncology, neurology and cardiovascular disease providing a more fertile field for profit with consistent, sometimes lifelong, treatment regimes. By comparison, antibiotics have an expected treatment lifespan of 12 days.

A short lifespan is made worse by attempts to curb over-prescription, ensuring that doctors save new antibiotics for emergencies when cheaper and widely available drugs are ineffective, creating an unprofitable market for new products.

How large is the market for antibiotics?

Research by the University of Illinois, in partnership with the Centers for Disease Control and the Department of Veterans Affairs, found that antibiotics cost the US $56bn between 2020 and 2015. Of this, $8.8bn was spent in 2015, down from $10.6bn in 2010, a trend of antibiotic use that the Journal of Clinical Infectious Diseases reports decreased US spending on antibacterials by 16.6% over the same period.

What are the regulatory requirements of antibiotics?

Like all drugs, antibiotics must go through rigorous approval procedures before they are sold or marketed. However, the FDA has shown signs of softening the approval process for antibiotics through the Qualified Infectious Disease Product (QIDP) designation.

As a result of Congress's GAIN Act, QIDP drugs receive expedited approval for antibacterial and antifungal drugs that treat life-threatening infections.

Europe has yet to create a designation specific to antibiotics, but many antibiotics do apply for other fast track designations. And in 2016 the EMA agreed in a joint session with the FDA and the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) that abbreviated clinical development programmes for antimicrobials should be considered in the future.

Edison's Insight:

"Many have argued that the golden age of antibiotic discovery is over. To some extent that's true and to combat the issues, companies developing new antimicrobial agents will have to take advantage of new incentives, look towards preventative indications but, above all, bring new agents without resistance to the market." Andy Smith, Edison healthcare analyst

How are institutions incentivising antibiotic research?

In addition to expediting regulatory approval, governments are increasingly eager to help make antibiotic development more profitable. The Organisation for Economic Co-operation and Development (OECD) estimates that countries are investing around $550m in grant funding every year to antibiotic development.

Even so, the consensus remains that more will have to be invested into the market if it is to reach the level of innovation required to outpace bacterial resistance.

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Drive-AB, an antibiotic advocacy group, estimates that an additional $1.5bn a year over the next 30 years would be required to meet the production rates of the early to mid-1990s that stymied antibiotic resistance.

Which companies are developing new antibiotics?

As of September, 48 new antibiotics treatments for serious bacterial infection were in clinical development.

Of these, Basilea's Ceftobiprole was recently awarded QIDP status in the US and is preparing for a Phase III study on acute bacterial infection, following approval in 12 European countries and Canada for the treatment of pneumonia.

Shionogi has begun Phase II trials on two Cephalosporin-based drugs and Toyama/Fujifilm has licensed Solithromycin in Japan, following successful Phase II trials.

The UK's Destiny Pharma is developing a completely new antibiotic, which is not associated with resistance and is active against sensitive and resistant Gram-positive strains for a new preventative indication that has been endorsed by the FDA. The preventative aspect is important since the business case for new antibiotics is limited by their short courses, and the tendency to reserve new agents for those infections that fail to respond to cheaper (generic) agents. A preventative agent addresses these challenges.

In the preclinical space, two new compounds have generated some interest. Of these, Nosopharm recently discovered symbiotic bacteria in soil that have antibiotic properties, while the new drug Teixobactin has been shown to be effective against resistant bacteria.

Novobiotic Pharmaceuticals is currently pre-trialling a Teixobactin derivative, but it is important to note that the new class of drug is not effective against Gram-negative bacteria, like the E.coli or Pseudomonas strains, where new antibiotics are most needed.