Research and development (R&D) is what has moved society from the pre-antibiotic era, when over 40% of all deaths were due to bacterial infections, to today, a society in which the largest majority of bacterial infections can be treated with antibiotics, saving millions of lives each year. As these antibiotics are gradually rendered obsolete by the emergence of resistance, continued development of novel antibiotics becomes absolutely essential. Hence, R&D is critical to ensure that healthcare professionals are armed with the tools they need to tackle infection.

Despite the clear need for innovation, antibiotic R&D faces a set of hurdles that reduce private interest for the space and discourage investment. These hurdles are four:

- Limited public and private funding for basic microbiology research; this places more, and the more risky part, of the R&D burden in the private sector
- Challenging regulatory requirements with a high bar for improvement versus the standard of care make R&D into new molecules for ‘old diseases’ difficult
- Reduced patient populations and short treatment courses result in limited commercial potential for antibiotics
- Comoditized market (low prices compared to other therapeutic areas) compounding the effect of reduced patient populations and short treatments

As a result of these hurdles it is unclear how long the large and mid-sized pharmaceutical companies that still do research and development in infectious diseases, and particularly in antibiotics, will remain in the area. To tackle this lack of incentives, a solution should:

- Encourage basic research by both academic and private sector laboratories
- De-risk private sector R&D from a financial standpoint OR increase the probability of positive financial return OR increase the size of financial return
- Engage governments and regulatory authorities to ensure the products of the R&D effort will be evaluated with a framework appropriate for antimicrobial resistance (AMR) research and not the regular novel drug regulatory paradigm
- Couple the support to R&D with mechanisms to guarantee the appropriate use of antibiotics developed through the R&D efforts, e.g.,
  - Support the co-development of rapid diagnostics to reduce empirical use
  - Limit production volumes to match epidemiological needs
  - Advocate for policies to restrict resistance-fostering practices like non-prescription sales, veterinary use, etc.
- Ensure the financial incentives for private sector R&D do not prevent drug accessibility by developing countries, e.g., like a mechanism based on overall price increases would do

A potential solution for AMR R&D

Decouple sales from R&D to separate the incentive to innovate from the incentive to sell while allowing for investor returns. Main characteristics of the proposed solution:

- An entity created to incentivize R&D through
  - Grants to academic institutions to focus in basic microbiology
— Research and drug development grants to private sector institutions to de-risk AMR research
— Funds for clinical research organizations to conduct clinical trials on the results of the AMR R&D supported or other promising candidates that could be acquired or in-licensed

■ The entity invests in promising assets in which it is able to have significant stakes in the intellectual property (IP) generated
■ The entity uses IP rights to have meaningful decision power over registration and manufacturing to
  — Ensure timely access for all countries in need
  — Limit production volumes based on epidemiological needs
  — Control pricing and quality in developing countries through manufacturing licenses

■ The entity is created as an independent company where
  — Funding parties, both public and private, buy shares of the entity
  — The entity owns a share of the IP generated through its investments but no IP is assigned to a particular funding party
  — Scientific decisions are left to an independent Board of scientific advisors
  — Funding parties participate on the Board of the entity but not on managing it
  — Management is left to a small set of professional managers incentivized to develop products, extend the active life of those products, and generate returns

■ Returns are defined for, and together with, each funding party and could take several forms depending on each party’s interests, e.g., financial returns, savings to a health system, savings to a nation, etc.

Open questions

■ How to prevent generic players to manufacture and sell large volumes of the products once IP protection expires and in countries where IP rights are not enforced?
■ Can returns be defined in a pragmatic manner to match the KPIs of the entity by selecting the right mix of funding parties?