Market Entry Rewards:

A framework for value

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Disclaimer

For Kevin Outterson, the views expressed are his personal views and do not necessarily represent the views of CARB-X or any CARB-X funder.

For John Rex, the views expressed are his personal views. Also note that John works widely across Industry and receives remuneration for that work.

What value new antibiotics?

- Several parallel sources have converged
  - Best known current model is from the Sertkaya et al. 2014 ERG report commissioned by ASPR (2019 update underway)
  - DRIVE-AB Final Report published March 2018
    - See also: Megiddo I et al. "Investing in antibiotics to alleviate future catastrophic outcomes: What is the value of having an effective antibiotic to mitigate pandemic influenza?" Health Economics 11 Feb 2019 doi: 10.1002/hec.3867
  - Rex-Outterson Lancet ID paper 2016
    - Proposed a thought model for debate
    - Model sought positive NPV for innovator but also to offer more NPV for products providing greater utility

It began as a thought experiment

- What creates a positive NPV for an antibiotic?
  - Sharma & Towse (2011): $500m/yr x 5yrs
  - ERG (Sertkaya 2014): $1b at registration
  - O'Neill UK AMR #3 (May 2015): $2-4b at 3rd year post registration
  - DRIVE-AB (March 2018): $1b inflection point
- *Call it $1b at a minimum – deliberately pitched at low end*
- Now, how to
  - Align with stewardship
  - Incentivize drugs of interest (Gram-negative, Oral, Novel)
  - Be transparent, predictable, and unambiguous about success measure
  - Encourage further development after initial registration
- Delinkage, of course
  - But not all antibiotics are created equal! How do we differentiate?

Model to provoke debate[1]

- Define one base payment as $200m/yr x 5yr
  - This is the global PROFIT to the developer
  - No other profit permitted; actual sales effectively at cost
- Then this scheme on a global basis…

Requirement	Step earned
FDA & EMA approval, treats a CDC 2013 threat pathogen	1x Base
Treats CDC Urgent pathogen	1x Base
Treats CDC Serious pathogen	0.5x Base
First of a novel class	1x Base
2nd, 3rd, or 4th of a novel class	0.75x, 0.5x, or 0.25x Base

Requirement	Step earned
5th or later of novel class, but offering safety, efficacy or dosing improvement	0.1x Base
Delivery of pediatric commitment	Cost recovery payment
2nd, 3rd, or 4th defined indication for a given agent	0.25x Base for each
Oral dosage form	0.25x Base

[1]Rex JH, Outterson K. Lancet ID 2016. It is possible to earn multiple payments, but each CDC pathogen category payment can only earned once. Payments need not be concurrent. Defined Indications Novel Class are broadly lumped, not finely divided – a consensus rule may be needed.

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A spectacular new oral Gram-negative agent would be well rewarded: 3.75 x base in this case

a global basis…

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Model to provoke debate (Summary)

- It's a model
  - "All models are wrong, but some are useful"[1]
- This model prioritized answering these questions
  - *What return is needed to cover the investment?*
  - *How can we align R&D with stewardship?*
  - *How can we focus R&D on things of greater value?*
  - *How do we encourage ongoing development after initial registration?*
- Estimates of value such as this will provide other approaches to this analysis
- Although this idea leaves many questions unanswered (how to do this globally, problem of free riders, etc.), it will have served its purpose if it provokes useful debate

[1]George EP Box

FAQs (1)

- Too complex?
  - Not really: clear enough to prevent gaming but also discernable targets for companies contemplating a Phase 2 investment
- Too reliant on expert committee?
  - No expert committee needed at all to trigger payments; the agency administering the program has clear standards that can be seen in the NDA and supplemental FDA filings

FAQs (2)

- Not the right amount of incentive?
  - Then just vary the Base (assumed here to be $200M/yr x 5 yr, but could be higher or lower)
- Need to cap the total amount of expenditures for CBO?
  - Then adjust the Base to meet expectations
- How much will this cost?
  - We need to model this against inbound clinical pipeline

FAQs (3)

- Why pay anything for less spectacular antibiotics?
  - Takes years of use to really understand what we have
  - Costs of registration, Phase 4 studies, supply chain
  - DRIVE-AB's 4th recommendation (often overlooked) called for payments to support the supply chain

A less-complex two-tier model

Here's one way to make it simpler

- Upper Tier for extremely high quality new antibiotics (assume 5/decade)
  - $200M/year for 10 years for each Upper Tier drug
- Lower Tier for QIDP + (assume 10/decade)
  - $50M/year for 5 years for each Lower Tier drug
- Total cost per decade:
  - Upper Tier: $10B
  - Lower Tier: $2.5B