Session V: Sustainability and Maintenance of Business Models to Ensure Rapid and Nimble Response to Emerging Threats of National Security Concern

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The opinions expressed herein are my own.

Slides happily shared – just drop me a note.
Theme for this session

• Discuss the *business* of developing MCMs
  – Opportunities for companies to *collaborate* in pre-competitive areas
  – Use of *public-private partnerships* (PPPs)
  – Next steps to coordinate a rapid response
    • Look for common elements across threats
    • Discuss *sustainability* of business models
Five speakers

• Rex: Pharma antibacterial developer
• Larsen: US Government (BARDA)
• Garry: University-based consortium
• Majorowski: Re-imagining social change
• Hanna: PPP model from the TB world
Antibacterials as a parallel

• The efficacy of antibacterials is threatened by a rising tide of antimicrobial resistance (AMR)
  – 23,000 deaths/yr in the US (one jumbo jet/week)\(^1\)

• An empty pipeline
  – # of active companies in 2013 = # in 1960\(^2\)

• Why?
  – Hard to discover
  – Hard to develop
  – Economics are poor (despite dual MCM use!)

What motivates companies?

• We can’t *make* companies do this work ... we have to make them *want* to do this work¹

• We must address several basic tensions
  – We want to minimize use of *all* antibiotics
  – We want to have new(er) antibiotics available on demand
  – We want those antibiotics developed before the epidemic

• How can we do this?
  – Noting that “All models are wrong, but some are useful”²...
  – ... let’s now look at a model that may be instructive

The cost of creating an antibiotic

An EU-based analysis

- The typical antibiotic lifecycle can be modeled from start to finish\(^1\)
- The model allows for failed drugs
- Spend and revenue by year are based on industry average data
- Note the Phase 3 bump in spend
- And then a sales curve: \(~10\) years of protected sales and then \(~10\) years of declining sales

- Approximate total spend (years 1-13): $600m
- Approximate total sales (next 20 years): $2,500m
- But, we’ve forgotten about NPV!

Sidebar: NPV (Net Present Value)
How much is an investment worth in today’s terms?

- Cash today is worth more than a promise of cash tomorrow (or in ten years)
- Based on cost of capital, risk, etc., it is typical to discount 10% per year
- The math is the inverse of interest on a loan:
  - $100 today = $100; $100 in a year = $90; $100 in two years = $81, etc.

At 10% per year discount, $100 in 10yrs time is only worth $39 today

- A project’s NPV is calculated by
  - Computing sales less costs for each year (Annual Net Cash Flow)
  - Each future year’s Cash Flow is discounted to today
  - The total across all years is the Net Present Value

- Any NPV > 0 means you’ve created (at least some) value

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a. Actually, I’ve simplified a bit here – the actual values are $91, $83 … but this simpler way of thinking about it is close enough for illustrative purposes
Now, consider this in NPV terms

From the standpoint of year 0 (the day you decide to start discovery), the graph below shows spend & revenue discounted 10%/year

The line below is the cumulative NPV

But in NPV terms, it totals to a loss of around $50m

And think about the capital at risk and the timeline to the return. Even at +$50m, this would be unattractive
Recent US-based analysis: same result

• Comprehensive model for drugs for 6 key indications (ABOM, ABSSSI, CAP, cIAI, cUTI, HAP-VAP)\(^1\)
• NPV of the new drug always \(<\$40\text{ million}\)
  – All 90% confidence intervals on estimate went below zero
• Value to the patient was MUCH higher
  – Just based on the value of days of work and life restored, the value to society ranged from $500m to $12\text{ billion}\)
• Thus, these EU- and US-based models show that
  – Starting antibacterial R&D is not financially rational, at least not with traditional R&D costs and approaches
  – We (society) undervalue these drugs

That’s a problem we must solve

• To restore vitality to the pipeline and ensure we have the life-saving drugs we will need in the future,

• We have to move these models back into consistently positive territory

And, we’re trying now to do just that...
Global Leadership: A partial list

2003 et seq: IDSA: “Bad Bugs, No Drugs”

17 Sep 2009: (EU) Swedish presidency
  • “Innovative Incentives for Effective Antibacterials”

7 April 2011: WHO World Health day on AMR
  • “No action today, no cure tomorrow”

17 Nov 2011: (EU) ND4BB program
  • PPP for Discovery & Development

2011 forward: (US & EU) FDA & EMA
  • A steady stream of new guidances

2012: (US) GAIN Act (see subsequent slide)

3-4 Oct 2013: (EU) Chatham House Conference
  • “Antimicrobial resistance: Incentivizing Change Towards a Global Solution”

2014: (US) PCAST Report
The Innovative Medicines Initiative

- A collaboration between EC and the EFPIA\(^1\) companies
- Each provides €1b
  - EC: Contributes cash
  - EFPIA: Contributes effort
- Projects are
  - Proposed by EFPIA
  - Approved by consensus
  - And come alive as a group of academics, SMEs, and EFPIA companies
- All work is open & shared

\(^1\)EFPIA is the trade organization for EU-based pharmaceutical companies. PhRMA is the equivalent organization in the US. IFPMA is the equivalent organization outside the EU and the US.
Under IMI, we created ND4BB (New Drugs For Bad Bugs)

ND4BB cross topic collaboration and dissemination

**Topic 1: COMBACTE**
- a) Enabling Clinical Collaboration and refining clinical trial design
- b) Clinical Development of GSK1322322
- c) Clinical Development of MEDI4893

**Topic 2: TRANSLOCATION**
- Research penetration and efflux Gram-negatives Data Hub and Learning from R&D experience

**Topic 3: ENABLE**
- Discovery & development of new drugs combating Gram-negative infections

**Topic 4:**
- Driving re-investment in R&D and Responsible use of Antibiotics

**Topic 5:**
- Clinical development of antibacterial agents for Gram-negative antibiotic resistant pathogens

**Topic 6:**
- Systemic molecules against HAIs due to clinically challenging Gram-negative pathogens

**Topic 7:**
- Inhaled Antibacterials in CF and non-CF BE

**ND4BB Information Centre**
All data generated is submitted and is accessible to all consortium partners

IMI = Innovative Medicines Initiative

Rex JH - 2015-01-08 A view on the challenge of antibiotics
In the EU: IMI’s ND4BB program (New Drugs For Bad Bugs)

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And in the EU...

**ND4BB Topic 4: The DRIVE-AB Project**

- **Launch meeting:** 6 Oct 2014
  - “Driving re-investment in R&D and Responsible use of antibiotics”
- **Aim:** Address the tension between economics & stewardship
  - Create a multi-disciplinary, multi-stakeholder community (16 public partners and 7 private partners from 12 countries) with an in-depth comprehension of challenges of antibiotic development
  - Develop evidence-based measures for responsible antibiotic use
  - Create implementable options for new commercial models that address the needs of multiple stakeholders
  - Validate options through modelling
- **We expect DRIVE-AB to explore a broad range of approaches**
  - In particular, we hope to see ways to separate (delink) usage from reward to the innovator. That is, reward should not be sales-based
  - Let’s look at two possible tools...
Two intriguing economic ideas

• (Push) Refundable tax credits
  – For some percentage (e.g., 50%) of qualified expenses, the company either gets a tax credit (if the company has income) or receives a payment of that amount
  – Has immediate impact on NPV while also ensuring the company has “skin in the game” that ensures delivery

• (Pull) Insurance-based approaches
  – National acquisition at a fixed, predictable rate (e.g., US buys $100m/year of a new antibiotic for 5 years)
  – Annual fee guarantees availability of a certain number of courses of therapy, whether used or not
  – We should be pleased to buy but not use the drug, just as we are pleased when our life insurance does not pay off
Questions for speakers

• How do we create business models that are resilient despite the uncertainty of MCM markets?
• What policies (regulatory or other) are needed?
• Do other industry offer relevant business models?
• How can we sustain
  – A discovery apparatus?
  – Registered products?
• How do we value new products?
  – How do we consider value to society?