BAD BUGS, NEED DRUGS

The 10 x ‘20 initiative

FIS Conference; Manchester, United Kingdom, November 18, 2011
IDSA Membership: 9,800 strong

Primary Professional Activity

- Administration: 2%
- Basic Research: 7%
- Clinical Microbiology: 5%
- Clinical Research: 8%
- Hospital Epidemiology: 3%
- Patient Care: 14%
- Public Health: 3%
- Teaching/Education: 4%
- Other: 4%

54%
Lives Devastated/Lost Due to Antibacterial-Resistant Organisms
Declining Antibacterial Approvals, U.S.

Spellberg, CID 2004, Modified
IDSA Applauds the British Society of Antimicrobial Chemotherapy’s (BSAC) new Antibiotic Action Initiative

www.antibioticaction.com
Bad Bugs, No Drugs

As Antibiotic Discovery Stagnates ...
A Public Health Crisis Brews
**IDSAs Motivation/Perspective**

**Our patients need new antibiotics to stay alive!**

- Unlike other disease areas (cancer, HIV/AIDS, etc.), there are no easily identifiable patient advocacy groups to put a push for change and to put a human face on the drug resistance problem
- IDSA decided it must step in to advocate on our patients’ behalf
- We have not taken any pharmaceutical funding to support these advocacy efforts
To Understand Market Forces & Disincentives

On-going information sharing efforts with:

- Senior pharmaceutical, biotechnology, and diagnostic company executives, anti-infective division heads, government relations and public policy staff
- Venture capitalists
Challenges in the Pathway to Antibiotic Approvals

MARKET FAILURE

- Economic/Return on Investment
- Regulatory uncertainty—FDA plus
- Scientific challenges
PEW, IDSA, PhRMA Meeting

Reviving the Pipeline of Life-Saving Antibiotics: Exploring Solutions to Spur Innovation

Antibiotics Conference Addresses Lack of New Drugs to Fight Deadly Superbugs

WASHINGTON – Leaders from government, industry, academia, medicine and science today will come together to discuss one of the most pressing health challenges we face: the rising incidence of drug-resistant bacteria and the lack of new antibiotics to fight them. The conference, “Reviving the Pipeline of Life-Saving Antibiotics: Exploring Solutions to Spur Innovation,” is organized by the Pew Health Group, the Infectious Diseases Society of America (IDSA), and the Pharmaceutical Research and Manufacturers of America (PhRMA).
Challenges in the Pathway to Antibiotic Approvals

- Antibiotics used for short duration
- Science is difficult (e.g., gram negative cell wall)
- Insufficient research support
- Lack of sufficient diagnostic tools
- Antimicrobial stewardship is essential, but affects profitability
- Pricing: generic competition is cheap
- Drugs in other markets (chronic disease, lifestyle) are more attractive
Additional IDSA Policy Reports/Continued Advocacy

Additional Reports:

• “Bad Bugs, No Drugs; No ESKAPE”; IDSA’s latest update on the antibiotic drug pipeline; Boucher et al, CID, January 1, 2009
• “The Epidemic of Antimicrobial Resistant Infections: A Call to Action to the Medical Community”, Spellberg et al, CID Jan. 2008
• Numerous position papers focused on FDA clinical trial designs (CAP; cSSSI; HAP/VAP, superiority for MDR organisms)
• The 10 x ‘20 Initiative, Global Commitment, April 15, 2010
World Health Day 2011

State of Antibiotic R&D is Dire

2009 analyses by IDSA & European Centre for Disease Prevention and Control (ECDC)/European Medicines Agency (EMA)

• Only 15-16 antibiotics are in development
• Only 8 have activity against key Gram-negative bacteria; these cause the most life-threatening infections
• Of these, NONE have activity against bacteria resistant to all currently available drugs

Boucher et al. Clinical Infectious Diseases 2009; 48:1–12
Few Antibiotics are Being Developed

Two Years Later….2011 IDSA Update

• 10 compounds active vs. resistant Gram-negative bacteria in clinical development as intravenous (IV) therapy
  • It is still the case that NONE have activity against bacteria resistant to all currently available drugs
  • No ongoing studies for the most life-threatening Gram-negative infections (hospital-associated pneumonia, aka HABP/VABP), an infection where > 20% of patients die
## Many Disincentives to Antibiotic R&D

<table>
<thead>
<tr>
<th>Therapy Area</th>
<th>NPV*</th>
<th>Development ($)</th>
<th>Development (years)</th>
<th>Price</th>
<th>Use</th>
<th>Patient pop</th>
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<tr>
<td>Musculo-skeletal</td>
<td>$1150m</td>
<td>$$$$$</td>
<td></td>
<td></td>
<td>Chronic</td>
<td>Large</td>
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<td></td>
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<td>Medium</td>
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<tr>
<td>Anti-bacterials</td>
<td>$100m</td>
<td>$$$</td>
<td></td>
<td></td>
<td>Acute</td>
<td>Small (specialist hospital antibiotics)</td>
</tr>
</tbody>
</table>

*Projan 2003

David Payne, GSK, September 2011 IDSA/Pew/PhRMA conference

*Projan 2003
**Antibiotics have high attrition rates**

<table>
<thead>
<tr>
<th>Phase</th>
<th>Leads</th>
<th>Candidates</th>
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<tbody>
<tr>
<td>DISCOVERY</td>
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<td>PRECLINICAL</td>
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<tr>
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</tbody>
</table>

*Discovery to Phase 2 attrition based on real data for 12 novel mechanism antibiotic candidates at GSK

How to Stimulate Antibiotic R&D?

**Bottom Line**

- We can’t **make** companies develop new antibiotics
- We have to make them **want** to develop new antibiotics
The 10 x ‘20 Initiative

Bad Bugs Need Drugs

10x ‘20

Ten new ANTIBIOTICS by 2020
The 10 x ‘20 Initiative

- Global Commitment to Develop 10 new systemic antibiotics by 2020 (CID; April 2010)

- Bring together essential leaders: global political, scientific, industrial, economic, intellectual property, policy, medical and philanthropic leaders to determine the right combination of incentives necessary to establish a sustainable R&D enterprise
“High-Priority” Products

• new systemic antibacterial drugs through the discovery of new drug classes as well as exploring possible new drugs from the existing classes of antibiotics (includes oral formulations)

• products that treat serious/life-threatening infections that are resistant to current antibiotics (the “ESKAPE” pathogens, e.g., emerging gram-negative bacteria, S. aureus)
Current Status of the 10 x ‘20 Initiative

Bad Bugs Need Drugs
Ten new ANTIBIOTICS by 2020

ceftaroline fosamil: Forest Laboraties, Inc.
Approved October 29, 2010
What Will Motivate Industry?

To Improve Antibiotic Return on Investment/Net Present Value (NPV)

Need a variety of types of push and pull incentives—there is no single, rate-limiting step to overcome—although economic modeling shows that push incentives likely are more helpful

**Push:** Decrease cost of development (e.g. tax credits, grants, contracts, milestone payments, public/private collaborations)

**Pull:** Increase income linked to antibiotics (e.g. market exclusivity, patent extensions, prizes), but must not promote use/increased resistance

Need to change societal/payor valuation of antibiotics—their true value is not recognized
IDSA’s actions have prompted the U.S. Congress to consider solutions

- Three antimicrobial resistance hearings held since April 2010 (IDSA testified at 2)
- We have succeeded in getting FDA and NIH leaders to publicly articulate the need for statutory incentives
- Incentives legislation is moving forward Generating Antibiotic Incentives Now (GAIN) Act, introduced 2011 (data exclusivity)
- Discussions around including incentives provision on must-pass FDA legislation in 2012
Political & Practical Realities

- Most promising approaches may not be politically feasible due to lack of support for drug industry and costs
- U.S. Congress is looking to cut health care and other costs—not to increase them
- We are seeking the best achievable solutions in this difficult fiscal environment
A Clearly Defined and Viable Regulatory Approval Pathway

- After a decade of collaborative work (FDA/IDSA/industry), no clear FDA pathway to antibiotic approval
- Several FDA issued clinical trial guidances are not feasible
- Industry sponsors are at a loss as to how to proceed
- October 2011: IDSA urged the FDA Commissioner to ask the Institute of Medicine for its opinion on the agency’s approaches
- One positive note: In 2010, FDA contacted the Foundation for the NIH (FNIH)Biomarkers Consortium to assist
  - Independent collaboration with academia, industry, IDSA, others to address endpoints in antibacterial trials
  - Initial focus skin infections and pneumonia (often the first studies of a new drug)
What Will Motivate Industry?

Finding Answers to Tough Scientific Questions and a Commitment to Share the Risk through Funding

- IDSA lobbies Congress, NIH, Biomedical Advanced Research and Development Authority (BARDA) to invest more resources
- IDSA analysis of 2009 NIH/NIAID funding found that, because of investments in other serious medical problems, NIAID's total funding commitment for antibacterial resistance research < $100 million; support for antibacterial drug discovery research < $70 million
- We have called for significant expansion of NIAID’s commitment to a total of $500 million
- We also want a central patient clinical specimen repository to support diagnostic development/validation
Recent NIAID Actions
- Since 2007 NIAID has funded numerous studies related to optimizing antibiotics’ effectiveness
- Oct 2011 awarded $150 million in grants to companies with promising antibiotics/antivirals
- Expanding Clinical Trials Infrastructure
  - Purpose
    - To do studies that industry can’t, or are not willing, to perform
    - Built upon existing infrastructure (from AIDS Trials Networks, etc.)
    - Develop clinical trials leadership group
  - Timeline
    - Earliest start date: December 2013 (FY 2014)
  - Funding
    - Initially $15-20M USD (the cost of ONE typical early study in patients) – IDSA is lobbying for more funding
Additional Research Support

Biomedical Advanced Research and Development Authority (BARDA)

• Newly created in 2006
• Contracts for advanced R&D of Gram-negative active drugs awarded to:
  • Achaogen ACHN 490
    • $27M over the 1st two years; up to $64.5M
  • GSK 2251052
    • $38.5M over the 1st two years; up to $94M
What Else is Needed?

Global Collaboration
Global Collaboration is Underway

EUROPEAN ANTIBIOTIC AWARENESS DAY

GET SMART
Know When Antibiotics Work

www.cdc.gov/getsmart
The EU-US Summit set up a Transatlantic Task Force on Antimicrobial Resistance (TATFAR), November 2009

CDC, FDA, NIH, ECDC, EMA, EFSA, EC (SANCO, RTD)

1) Appropriate therapeutic use of antibacterial drugs in the medical and veterinary communities

2) Prevention of health care - and community – associated infections

3) Strategies to improve the pipeline of new antibacterial drugs

Anna Lonnroth Sjödén  ICAAC, October 2011
The final TATFAR report issued on September 22 with 17 recommendations for strengthened EU and US cooperation in human and veterinary medicines against AMR

Harmonization of two clinical trials on off-patent antibiotics (colistin) – one funded by NIH, the other by EU

EU-US Workshop "Challenges and solutions in the development of new diagnostic tests to combat antimicrobial resistance" 28-29 September 2011, Brussels
Plan to promote, in a staged approach, unprecedented collaborative antibiotic R&D efforts

Use existing Innovative Medicines Initiative (IMI) -- a public-private scheme jointly funded by industry and the Commission

To encourage "unprecedented open sharing of knowledge" between companies at the pre-competitive research stage

Use flexibility in the current pharmaceutical legislation to give rapid approval to new antibiotics and work with governments to make sure they enjoyed "adequate market and pricing conditions."

Continued Global Collaboration is Key

IDSA Plans to Continue to Leverage the EU’s Efforts

• As we too are currently seeking:
  • a designated lead US agency to explore public private collaborations focused on early antibiotic discovery
  • Appropriate value-based reimbursement for novel antibiotics
• As well as:
  • Tax-related incentives
10 x ’20 Endorsing Organizations

33 Medical Societies including:

• American Medical Association
• American Academy of Pediatrics
• American College of Physicians
• American College of Surgeons
• American Society for Microbiology

And from the European Union:

• British Society of Antimicrobial Chemotherapy
• British Infection Society & Association of Medical Microbiologists
• European Society of Clinical Microbiology and Infectious Diseases
• International Society of Chemotherapy

WE WANT YOUR ENDORSEMENT TOO!
Prior generations gave us the gift of antibiotics.

Today, we have a moral obligation to ensure this global treasure is available for our children and future generations.

rguidos@idsociety.org