Session I: Current Landscape of Antibacterial Drug Development for Serious & Unmet Medical Need

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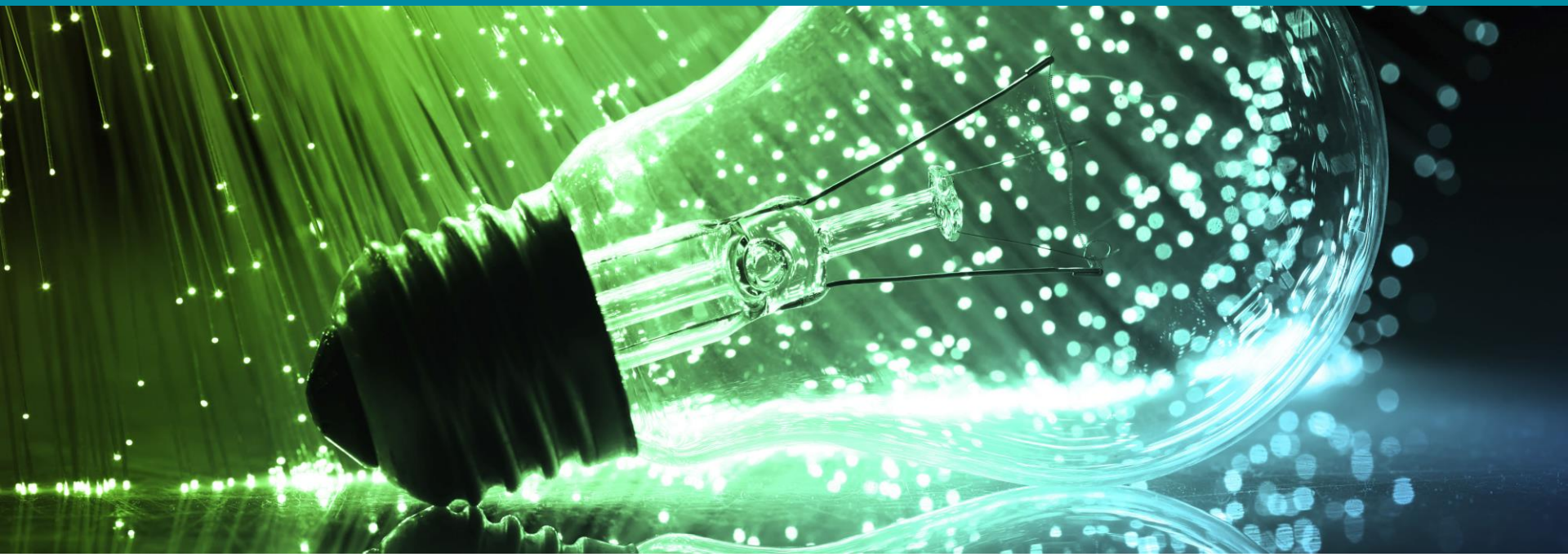
Session I Objectives

- Explore the current landscape and pipeline of antibacterial drug development
- Define and discuss streamlined development approaches



The Current Landscape and Pipeline of Antibacterial Products

Vance Fowler, MD

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The Landscape

- 2 million serious multi-drug resistant infections/year
- 23,000 deaths
- Preventing infections and improving antibiotic prescribing habits could save 37,000 lives from mdr-infections over 5 years

The Power of Antibiotics

Disease	Pre-Antibiotic Death Rate	Death With Antibiotics	Change in Death
Community Pneumonia[1]	~35%	~10%	-25%
Hospital Pneumonia[2]	~60%	~30%	-30%
Heart Infection[3]	~100%	~25%	-75%
Brain Infection[4]	>80%	<20%	-60%
Skin Infection[5]	11%	<0.5%	-10%
By comparison…treatment of heart attacks with aspirin or clot busting drugs[6]			-3%

[1]IDSA Position Paper '08 Clin Infect Dis 47(S3):S249-65;
[2]IDSA/ACCP/ATS/SCCM Position Paper '10 Clin Infect Dis In Press;
[3]Kerr AJ. Subacute Bacterial Endocarditis. Springfield IL: Charles C. Thomas, 1955 & Lancet 1935 226:383-4;0
[4]Lancet '38 231:733-4 & Waring et al. '48 Am J Med 5:402-18;
[5]Spellberg et al. '09 Clin Infect Dis 49:383-91 & Madsen '73 Infection 1:76-81;
[6]'88 Lancet 2:349-60

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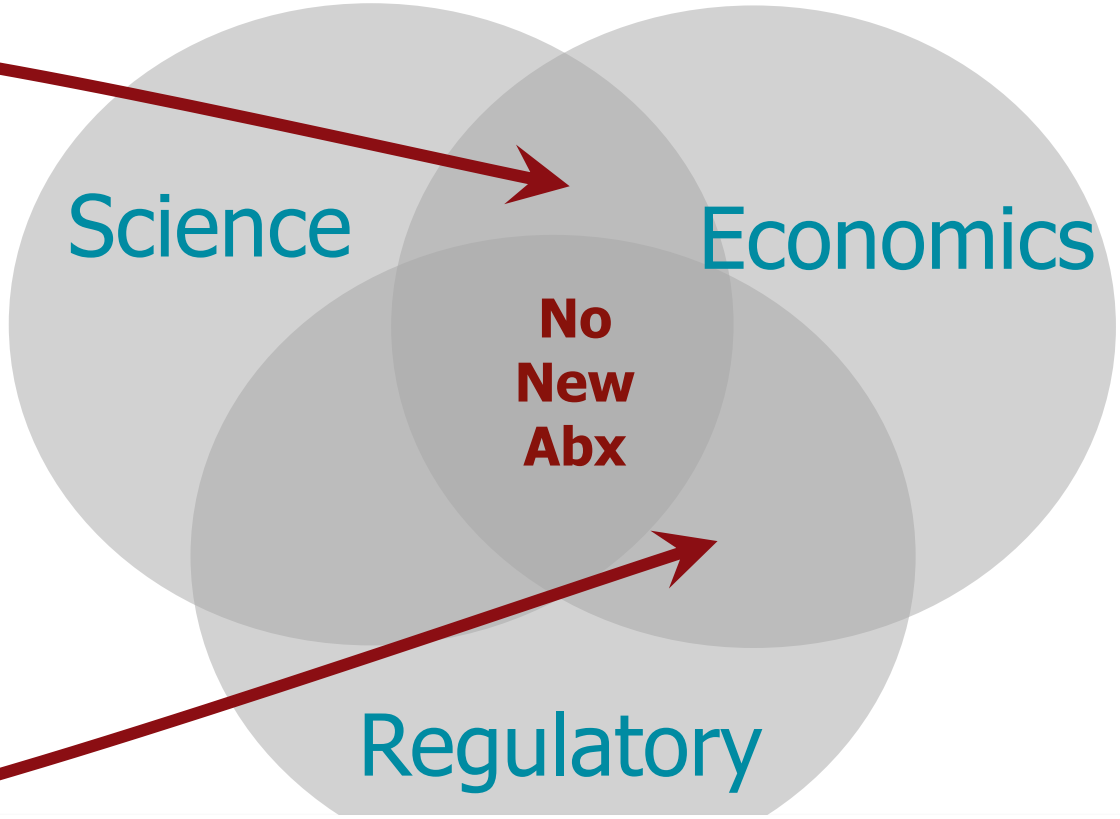
Antibiotic Market Failure: Causes

- 1. **Science**: low hanging fruit plucked
- 2. **Economics**: not a good investment
- 3. **Regulatory**: R&D too risky/expensive

Science and regulatory barriers directly impact economics by increasing cost of development and affecting return on investment

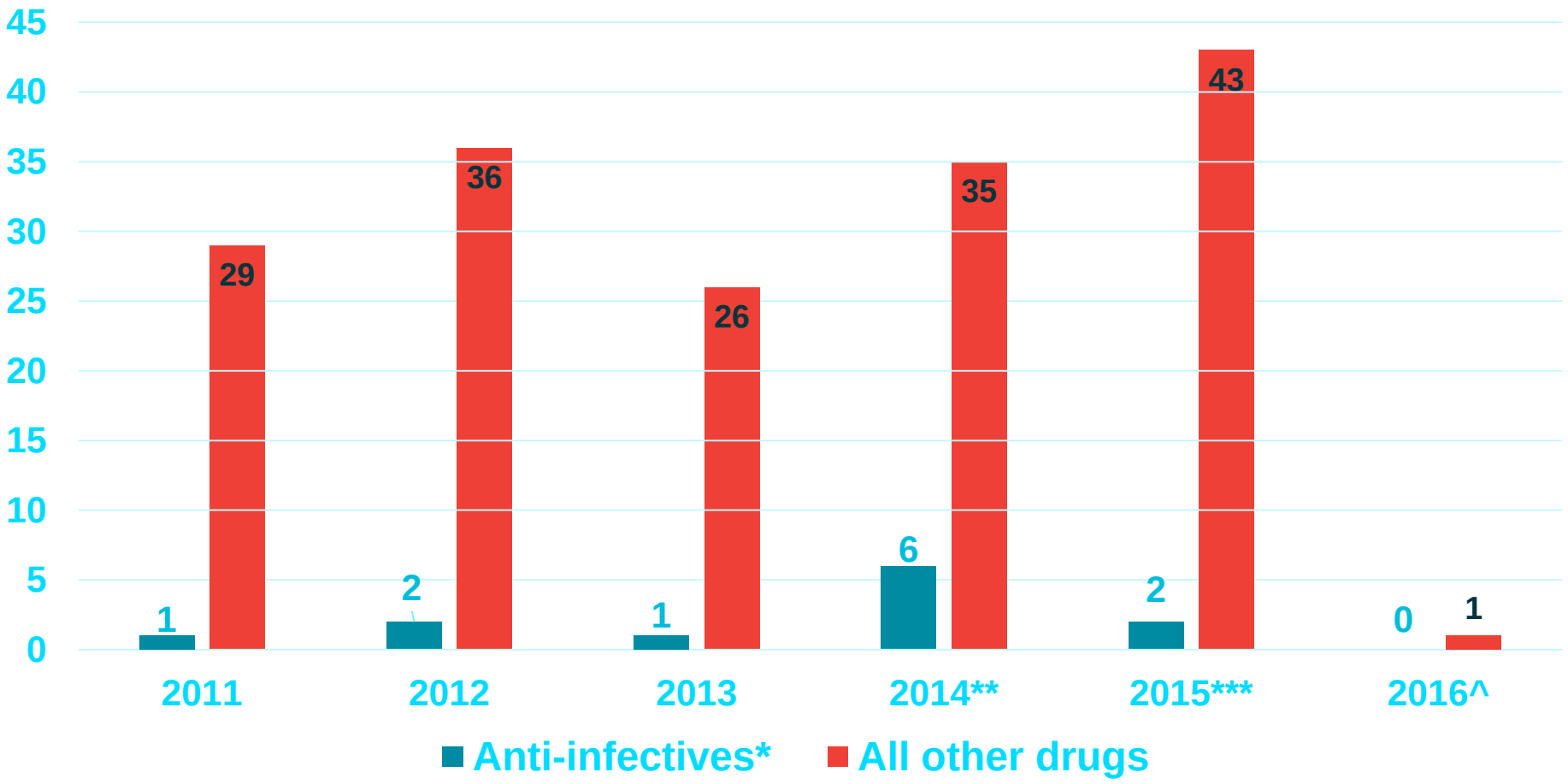


Economics: Investment Options

Neurology	**$720m**	$$$$	++++	↑↑	Chronic	Large

eNPV: expected Net Present Value

Novel Drug Approvals 2011-2016



Follow the Money

	Anti-Infectives (including anti-fungals)	All others
# of Pharma/Biotech IPOs in 2015*	**2**	**60**

*Flanagan M. 2015 in Review: Initial public offerings – is the well finally starting to run dry? 12/23/15 http://www.firstwordpharma.com/node/1341308?tsid=33#axzz40YojLdci

**Analyst: Current Crop of Biotech IPOs a Mixed Bag of Low Market Caps, Little Data. 12/3/14. http://www.biospace.com/News/analyst-current-crop-of-biotech-ipos-a-mixed-bag/356890

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The Pipeline

September 2015 Pipeline By characteristic	Phase		
	1	2	3
# new antibiotics with the potential to treat serious bacterial infections in clinical development	**10**	**17**	**12**
# new antibiotics with expected activity against CDC urgent threat pathogen	**5+**	**6+**	**7+**

ESKAPE: *Enterobacter* species,*Klebsiella pneumoniae, Acinetobacter baumanii,* or *Pseudomonas aeruginosa*

Adapted from the Pew Charitable Trust Tracking the Pipeline of Antibiotics in Development Issue Brief. Dec 2015. Accessed online at http://www.pewtrusts.org/en/multimedia/data-visualizations/2014/antibiotics-currently-in-clinical-development Accessed 2/12/2015.

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The Pipeline (cont')

September 2015 Pipeline By indication and phase	Phase		
	1	2	3
C.Diff	2	2	2
ABSSI	1	10	5
HAPB and/or VABP	1	0	7
CLABSI	0	0	1
cUTI and/or Acute Pyelo	0	2	6
cIAI	0	0	5
CABP	0	4	3
Bacteremia	1	0	1
GC (uncomplicated) and/or urethritis	0	2	1
Osteo and/or prosthetic joint infection	0	1	2
Respiratory tract infections and/or bronchiectasis	0	2	0

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In Summary

- The antibacterial pipeline remains precarious
  - Limited number of agents overall
  - Gaps for Acinetobacter, Metallo-beta-lactamase-producers, & Oral
  - Very limited diversity of mechanism

… we need a culture of cooperation between stakeholders; one that recognizes that there must be a balance between public health/clinical needs and the commercial realities of drug discovery and development.

Thank you.

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