



# *BARDA'S ROLE IN COMBATING ANTIMICROBIAL RESISTANCE*

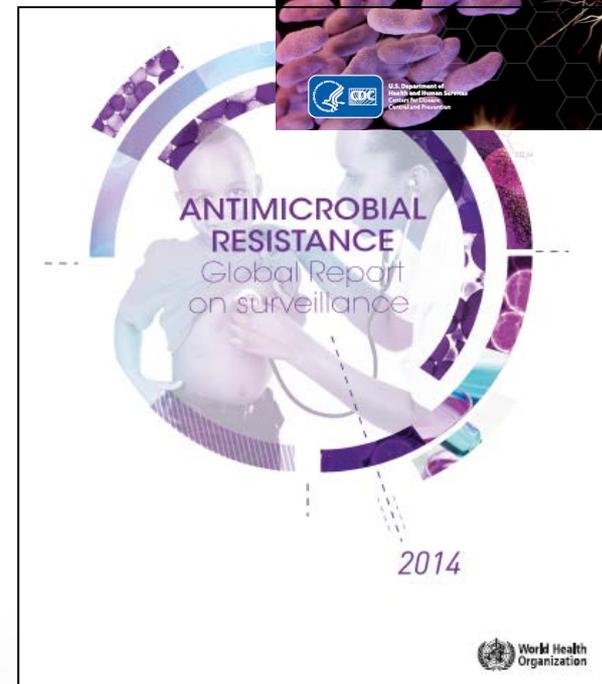
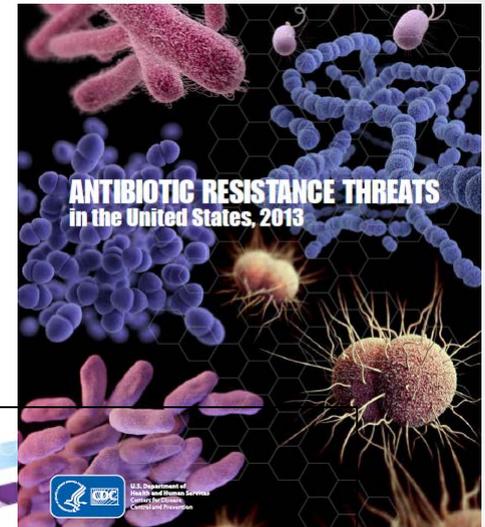
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Medical Countermeasures

October, 2015

*Resilient People. Healthy Communities. A Nation Prepared.*

# Antimicrobial Resistance Threat

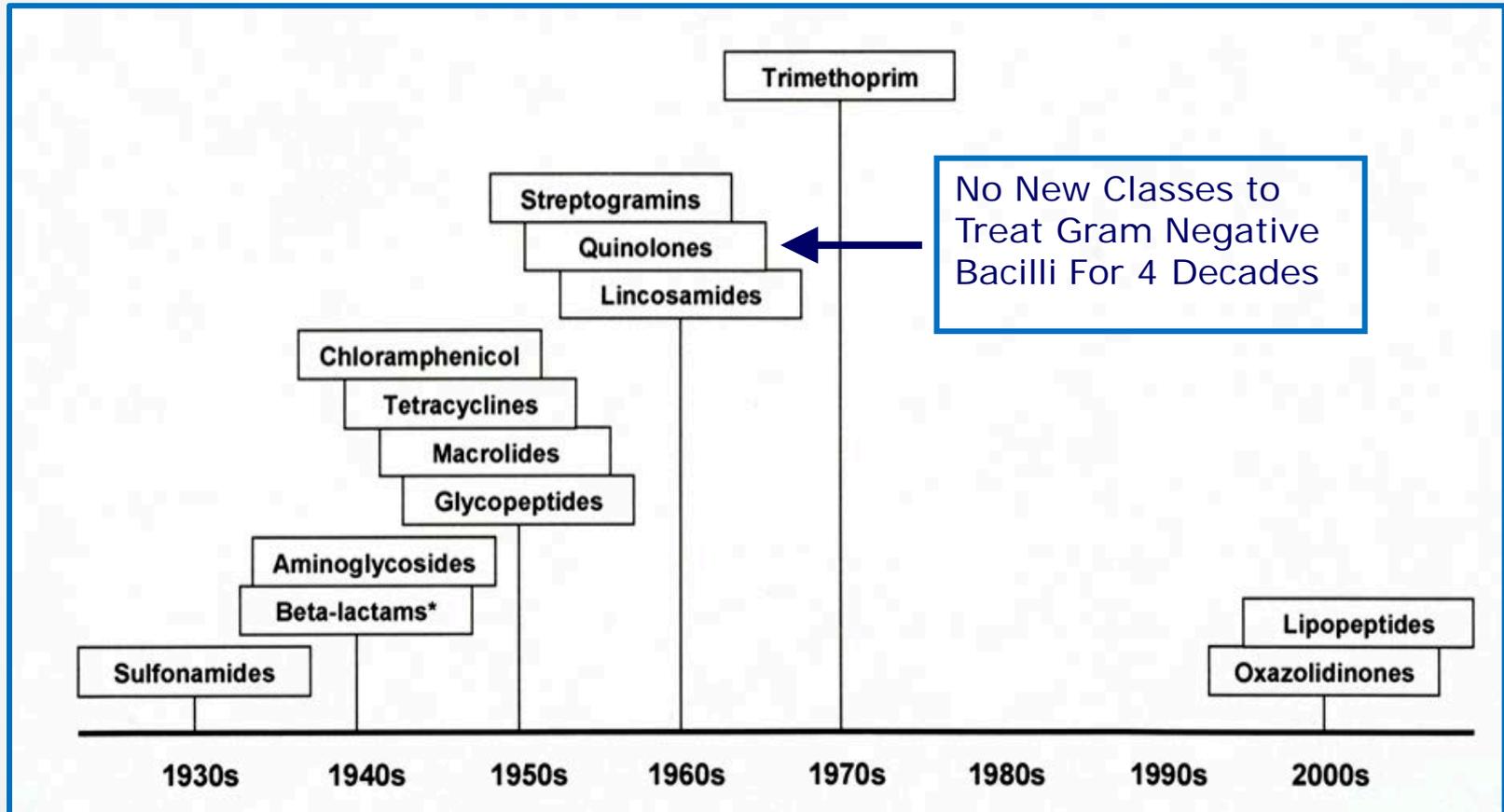
- 2M infections per year caused by AMR pathogens
- 23,000 deaths annually in US
- Estimated economic burden of \$20-35B annually
- Categorizes AMR pathogens in terms of public health threat: Urgent, Serious, or Concerning
- FQ resistance in *E. coli* now greater than 50%, untreatable GC now detected in 11 countries.



**SPR**

ASSISTANT SECRETARY FOR  
PREPAREDNESS AND RESPONSE

# The Antibiotic Development Gap



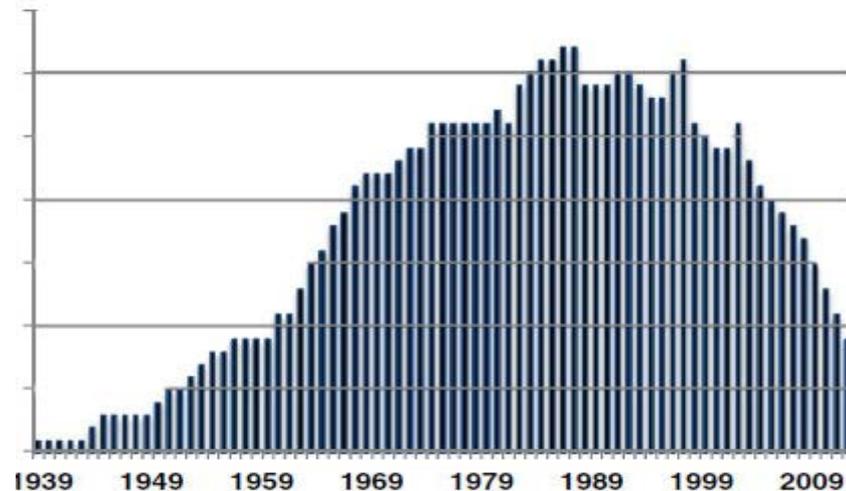
# Industry Engagement in New

## Antibiotic Development

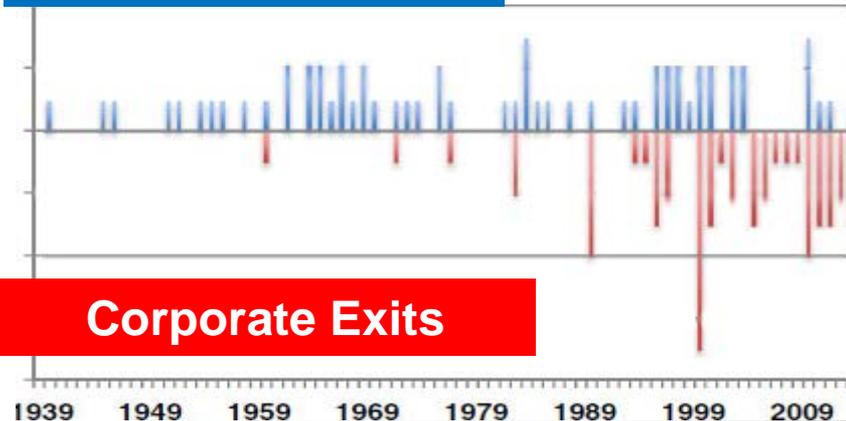
*Over the past 15 years  
(1998-2013)*

- 14 entries
- 36 exits
- New companies emerging in 2015, but we have a lot of ground to reclaim

# of companies



Corporate Entries



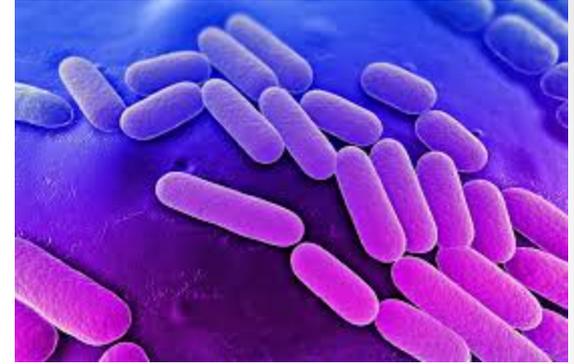
Corporate Exits

Adapted from Rex, JH

Graphic adapted from Kinch MS et al. Drug Discovery Today, July 2014.



# The BARDA Model



- The BARDA model works to address market failures
  - 21 Products FDA approved/cleared for biothreats and pandemic influenza
  - 12 Products stockpiled for emergency use
- This model is being successfully applied to antimicrobial resistance
  - Utilization of novel public:private partnerships to incentivize antibiotic research and development
  - 4 products in Phase III clinical development

# BSA Funding Priorities

## Drug Class

- **Unprecedented**
  - Novel Target
  - Novel Chemistry
- **Precedented**
  - Reduced AR
- **Nontraditional Therapies**
  - mAbs, phage
- **Infection prevention/interdiction**
  - Vaccines
  - Microbiome

## Antibiotic Resistance

- *C. difficile*
- CRE
- *N. gonorrhoea*
- *Acinetobacter*
- ESBLs
- VRE
- *Pseudomonas*
- MRSA
- *Strep pneumo*
- VRSA
- *Streptococcus*

## Biothreat

- *B. pseudomallei*
- *B. mallei*
- *F. tularensis*
- *Y. pestis*
- *B. anthracis*



# BARDA's Antimicrobial Portfolio

## BARDA's BSA Supported Product Pipeline

Sponsor	Compound	Development				
		Preclinical	Phase I	Phase II	Phase III	
Antibiotics	Achaogen	Next-generation aminoglycoside: Broad Spectrum plague, tularemia and carbapenem resistant Enterobacteriaceae (CRE)				
	CUBRC/ Tetrphase	A novel fully synthetic tetracycline: Broad Spectrum plague, tularemia, complicated intra-abdominal and urinary tract infections (cIAI, cUTI)				
	Cempra	Next-generation fluoroketolide: Broad Spectrum anthrax, tularemia, gonorrhea and community-acquired bacterial pneumonia (CABP)				
	Rempex	Carbapenem/ $\beta$ -lactamase inhibitor: Broad Spectrum CRE, cUTI, hospital-acquired pneumonia /ventilator-associated pneumonia (HAP)/(VAP), melioidosis, glanders				
	GSK	A portfolio approach	Broad Spectrum Antibiotic Portfolio A partnership to fund multiple compounds to combat antibiotic resistance at various stages of development			
	Astra Zeneca	A portfolio approach	Broad Spectrum Antibiotic Portfolio A partnership to fund multiple compounds to combat antibiotic resistance at various stages of development			

Disclaimer: The above projects are supported by BARDA's BSA Program utilizing non-dilutive funding via a contract and/or agreement. The stage of development is approximate as of July 2015 (please refer to the sponsors site for updated information). The table represents the compounds most advanced commercial indication being pursued by the developer.



# BARDA's Portfolio Partnership for Antibacterial Drug Development



- Established 5 year \$200M public:private partnership in May 2013
- Utilizes HHS's first use of Other Transactional Authority
- Supports the development of multiple antibiotic candidates
- Allows for activities and resources to be adjusted fluidly to adapt to technical risk and programmatic priorities
- Governance is through a BARDA:GSK Joint Oversight Committee



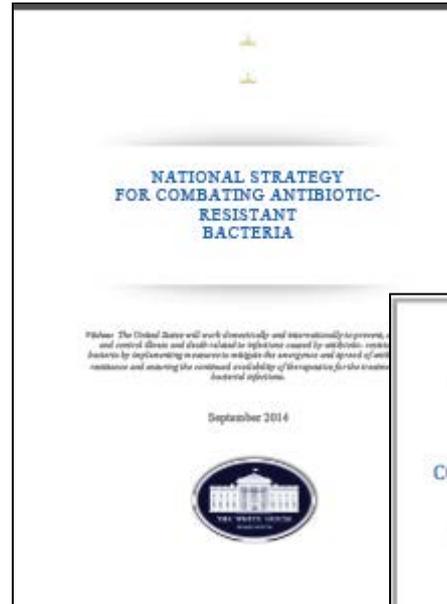
# Combating Antibiotic Resistant Bacteria (CARB) Initiative

- In February 2014 OSTP/NSC initiated the President's Initiative on Combating Antibiotic Resistant Bacteria
- BARDA was asked to lead the government working group that developed the National Strategy for Research and Development of new antimicrobial therapies
- BARDA was also asked to lead a government working group that would provide recommendations on economic incentives that could be implemented to spur innovation/investment in this field

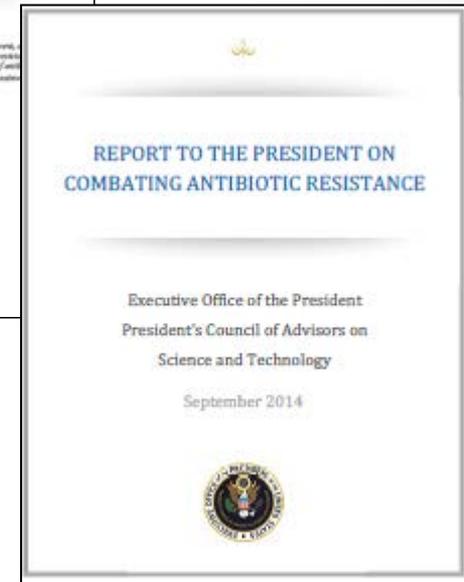


# White House Initiative on AMR

CARB Working Groups



PCAST



Executive Order -- Combating Antibiotic-Resistant Bacteria

EXECUTIVE ORDER



# BARDA Receives Expanded Authority

## **Executive Order -- Combating Antibiotic-Resistant Bacteria**

EXECUTIVE ORDER

Sec. 8. Promoting New and Next Generation Antibiotics and Diagnostics. (a) As part of the Action Plan, the Task Force shall describe steps that agencies can take to encourage the development of new and next-generation antibacterial drugs, diagnostics, vaccines, and novel therapeutics for both the public and agricultural sectors, including steps to develop infrastructure for clinical trials and options for attracting greater private investment in the development of new antibiotics and rapid point-of-care diagnostics. Task Force agency efforts shall focus on addressing areas of unmet medical need for individuals, including those antibiotic-resistant bacteria CDC has identified as public and agricultural health threats.

(b) Together with the countermeasures it develops for biodefense threats, the Biomedical Advanced Research Development

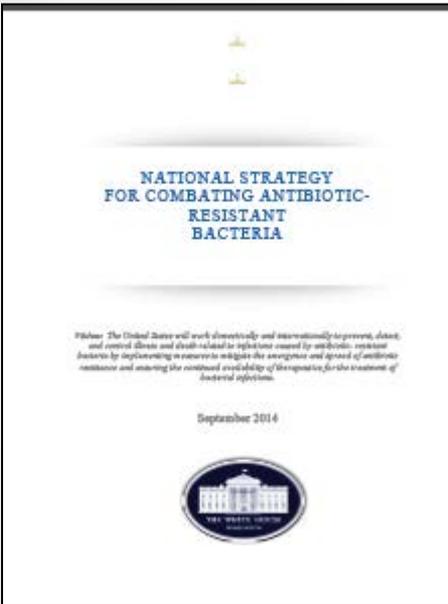
Authority in HHS shall develop new and next-generation countermeasures that target antibiotic-resistant bacteria that present a serious or urgent threat to public health.

(c) The Public Health Emergency Medical Countermeasures Enterprise in HHS shall, as appropriate, coordinate with Task Force agencies' efforts to promote new and next-generation countermeasures to target antibiotic-resistant bacteria that present a serious or urgent threat to public health.



# National Strategy

- GOAL 3: Advanced Development and Use of Rapid and Innovative Diagnostic Tests for Identification and Characterization of Resistant Bacteria



3.1 Develop and approve new diagnostics, including tests that rapidly distinguish between viral and bacterial pathogens and tests that detect antibiotic resistance that can be implemented in a wide range of settings.

3.2 Expand the availability and use of diagnostics to improve treatment of antibiotic resistant bacteria, enhance infection control, and facilitate outbreak detection and response in healthcare and community settings.

BARDA is working with NIH to co-sponsor a \$20M prize for AMR diagnostic development

# National Strategy

- GOAL 4: Accelerate Basic and Applied Research and Development for New Antibiotics, Other Therapeutics, and Vaccines

- 4.1 Conduct research to enhance understanding of environmental factors that facilitate the development of antibiotic resistance and the spread of resistance genes that are common to animals and humans.
- 4.2 Increase research focused on understanding the nature of microbial communities, how antibiotics affect them, and how they can be harnessed to prevent disease.
- 4.3 Intensify research and development of new therapeutics and vaccines, first-in-class drugs, and new combination therapies for treatment of bacterial infections.
- 4.4 Develop non-traditional therapeutics and innovative strategies to minimize outbreaks caused by resistant bacteria in human and animal populations.
- 4.5 Expand ongoing efforts to provide key data and materials to support the development of promising antibacterial drug candidates.
- 4.6 Enhance opportunities for public-private partnerships to accelerate research on new antibiotics and other tools to combat resistant bacteria.
- 4.7 Create a biopharmaceutical incubator—a consortium of academic, biotechnology and pharmaceutical industry partners—to promote innovation and increase the number of antibiotics in the drug-development pipeline.



# Action Plan Metrics

- Within one year:

## Status

BARDA will create at least one additional portfolio partnership with a pharmaceutical or biotechnology company to accelerate development of antibacterial drugs.



Program Initiated

BARDA and NIH will work to develop a strategy for establishing the Antibiotic Resistance Biopharmaceutical Incubator (ARBI).



Plan developed, no funding to initiate program

Economic WG will provide an analysis of economic incentives and provide recommendations for implementation



Recommendations provided to OSTP in March 2015

# Key Features of the AZ Partnership



- HHS's 2nd ever use of Other Transaction Authority
- Partnership will support a portfolio of antibacterial candidates, the lead of which is aztreonam-avibactam (ATM-AVI)
- Strategic decisions will be made by a BARDA-AZ Joint Oversight Committee
- Fulfills requirement in CARB National Plan that ASPR/BARDA create at least one additional portfolio partnership with a pharmaceutical or biotechnology company by March 2016 to accelerate development of new antibacterial drugs
- Establishes international collaboration between BARDA and the EU's Innovative Medicines Initiative (IMI)
  - Both entities will provide support for ATM-AVI pivotal trials



# We see press releases like this every week....why

## is the pipeline so incomplete?

- Is there a sufficient system in place to ensure AMR product innovation is accelerated and nurtured through “proof of concept”?

MEDICAL

### "Smart bomb" puts antibiotic resistant bacteria in its sights

By [Darren Quick](#)  
January 30, 2014

3 Comments



A new approach targets bad bacteria, such as Salmonella (pictured), while leaving good bacteria untouched (Image: [Shutterstock](#))

BUSINESS | BIOTECH

### UCSD scientists invent antibiotic discovery method

By [Bradley J. Fikes](#) 5:29 P.M. JAN. 24, 2014

PRINT SAVE COMMENTS 0

Scientists at UC San Diego's Scripps Institution of Oceanography have invented a way to **more efficiently discover potential drugs from ocean bacteria.**

The scientists, headed by [Bradley S. Moore](#), developed what they

---

28 JANUARY 2014

### New antibiotic could overcome drug-resistant TB

*St. Jude Children's Research Hospital scientists have discovered a promising new class of antibiotics that could aid efforts to overcome drug-resistance in tuberculosis.*

0 Recommend 10k G+1 0 Print Tweet Facebook Share

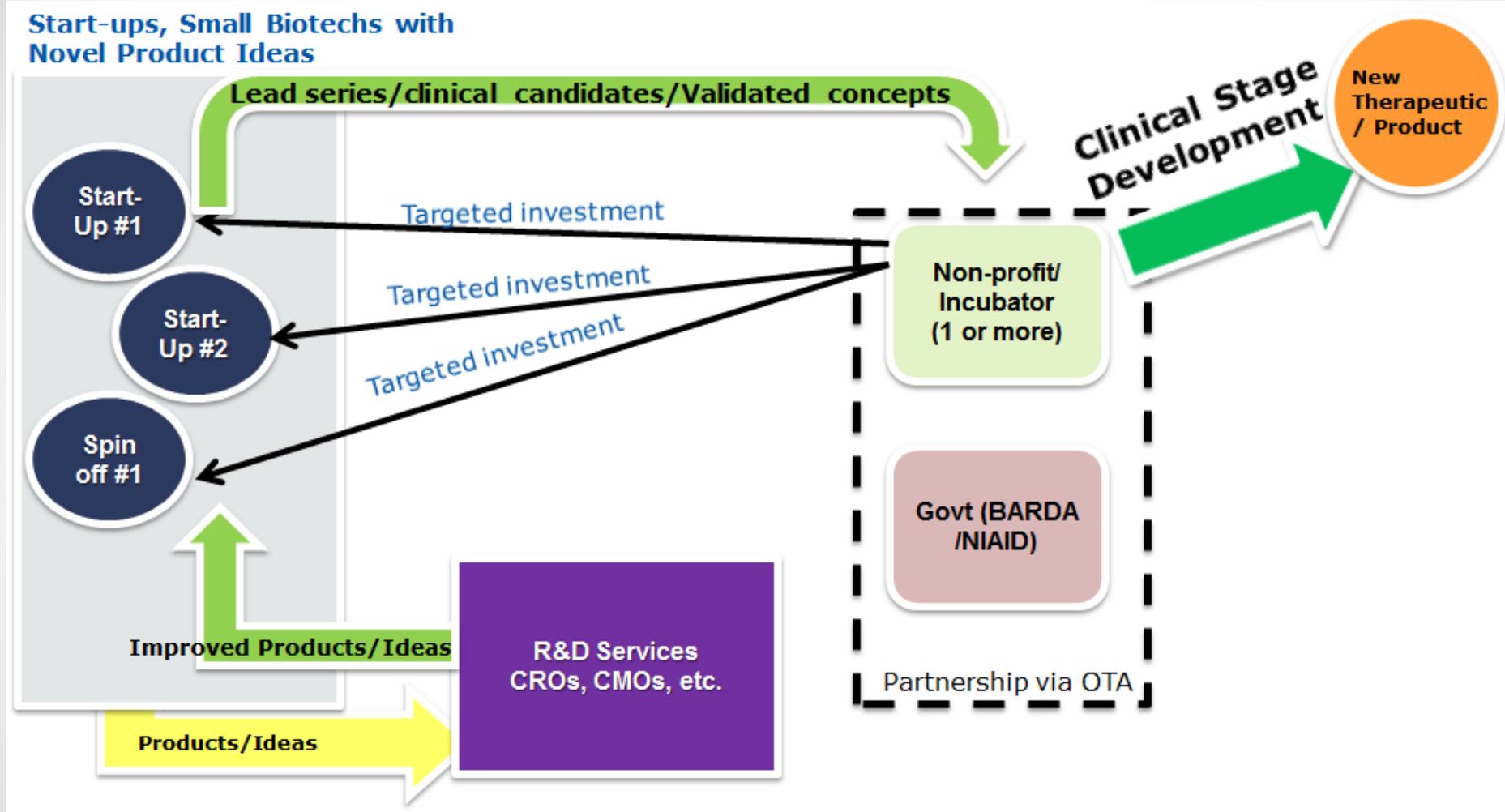


# Incubator

- A robust early stage R&D pipeline of antimicrobial products is needed to counter the increasing threat of antimicrobial resistant infections
  - There is a need to create an environment to rapidly develop and commercialize new antimicrobial products
- NIAID and BARDA will collaborate to establish a new program using other transactional authority (OTA) to fund a Biopharmaceutical Incubator(s) to identify, assemble, and accelerate a portfolio of innovative early antibacterial products
- BARDA/NIAID have been conducting market research and have identified models that currently exist to support the Incubator concept



# Proposed Incubator Process (Notional)



# Incubator Models

***Any of the following models could support the Incubator concept:***

- Evergreen Life Science Funds
  - Leverage existing experience and funding streams
  
- State-run Incubators
  - States have tax credits and direct funding that the Incubator could leverage
  
- Non-profits
  - Could leverage and share resources to maximize Incubator's scope/impact

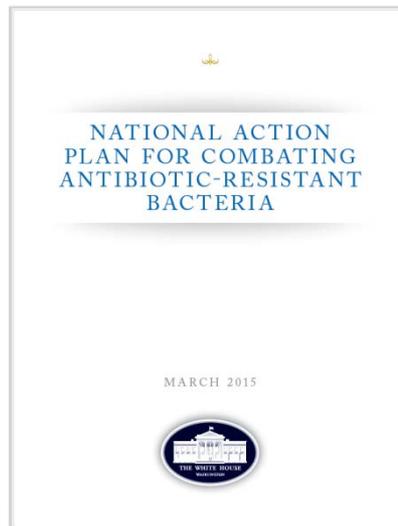


# CARB Economic Working Group

## CARB Economic Incentives Working Group

Economic incentives for product development are critical to ensuring diverse and robust pipeline of antibiotics. The PCAST report provides several key recommendations on economic incentives

In response to these recommendations, the Office of Science and Technology Policy (OSTP) and National Security Council (NSC) staff of the Executive Office of the President convened a working group to conduct an analysis of these potential economic incentives. Efforts to attract more private investment will reflect the recommendations of the CARB Economic Incentives Working Group.



# CARB and Product Development

- BARDA has requested additional funding in FY16 to form additional public: private partnerships for antibacterial drug development
- It is unclear whether the proposed increase in push incentives will be sufficient to incentivize industry to remain committed to antibacterial drug development
  - 2014 CARB PCAST report suggests more incentives are needed



# BARDA's Antimicrobial Program

- Summary:
  - BARDA's antimicrobial program will continue to support the development of novel antimicrobials and diagnostics to address the growing public health threat of antimicrobial resistance and biothreat pathogens
  - Additional funding would expand our portfolio of partnerships
  - BARDA is actively conducting outreach to relevant stakeholders to communicate our plans to implement the CARB National Strategy



# Interfacing with BARDA

- [www.phe.gov](http://www.phe.gov)
  - Program description, information, news, announcements
- [www.medicalcountermeasures.gov](http://www.medicalcountermeasures.gov)
  - Portal to BARDA
  - Register, request a meeting 
  - Tech Watch
- [www.fedbizopps.gov](http://www.fedbizopps.gov)
  - Official announcements and detailed information about all government contract solicitations. Open CBRN BAA:
    - [BAA-13-100-SOL-00013](https://www.fedbizopps.gov/contract/BAA-13-100-SOL-00013)

Technical POC for Research Area #3: Antimicrobial Drugs:

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