



United States Department of

Health & Human Services

Office of the Assistant Secretary for Preparedness and Response



Broad Spectrum Antimicrobials (BSA) Program

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BARDA Industry Day
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BSA Program Objective



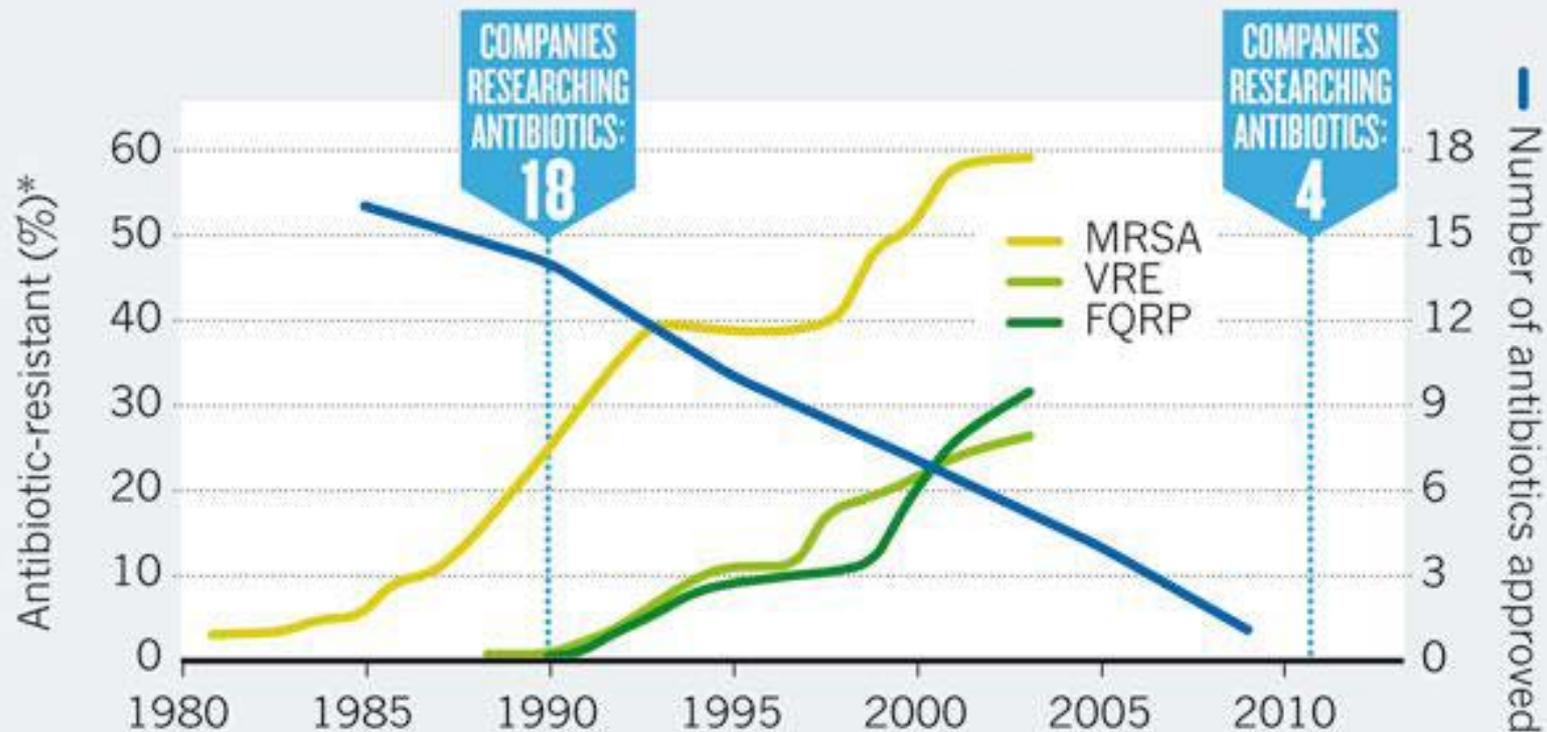
To help revitalize the antimicrobial pipeline by forming innovative public-private partnerships with companies engaged in antimicrobial therapy development



Pharma Companies Have Abandoned Antibiotic Development

A PERFECT STORM

As bacterial infections grow more resistant to antibiotics, companies are pulling out of antibiotics research and fewer new antibiotics are being approved.

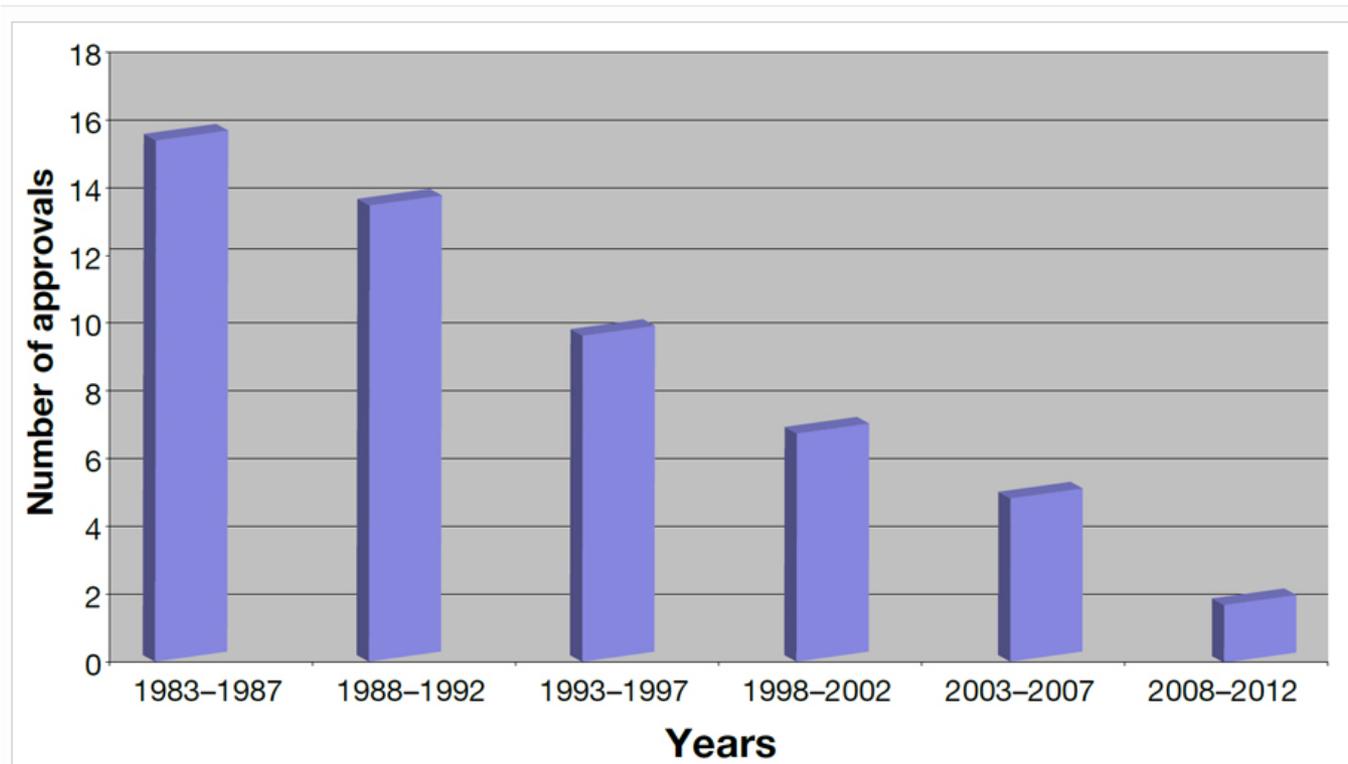


*Proportion of clinical isolates that are resistant to antibiotic. MRSA, methicillin-resistant *Staphylococcus aureus*. VRE, vancomycin-resistant *Enterococcus*. FQRP, fluoroquinolone-resistant *Pseudomonas aeruginosa*.



Fewer Antibacterial Drugs are Being Approved

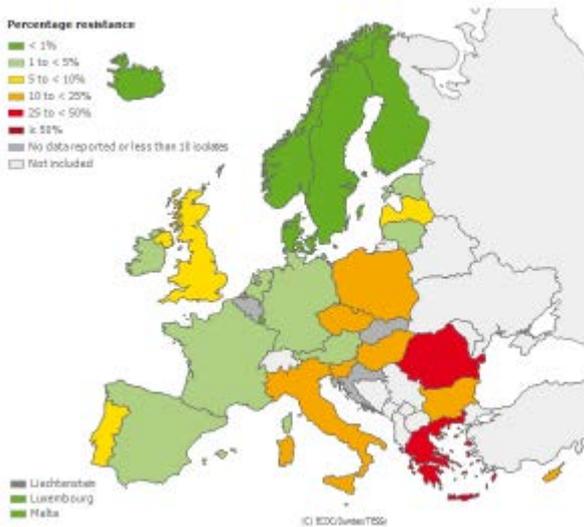
- Antibiotic approvals over the past three decades in five year increments



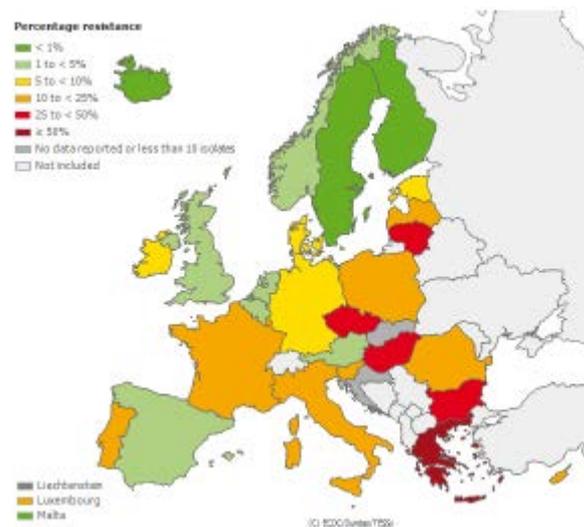
Source: Spellberg et al.; BCIQ: BioCentury Online Intelligence

Antimicrobial Resistance Rates are Rising

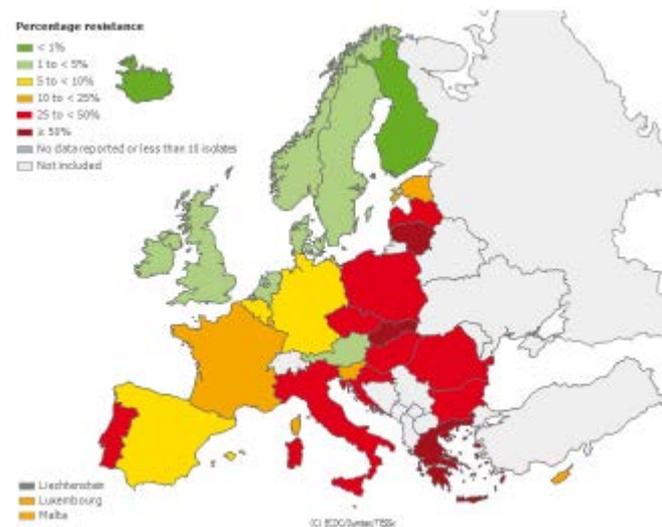
- Multi-drug resistant *Klebsiella pneumonia* isolates in participating countries (resistant to 3rd generation cephalosporins, fluoroquinolones, and aminoglycosides)



2006



2009



2012

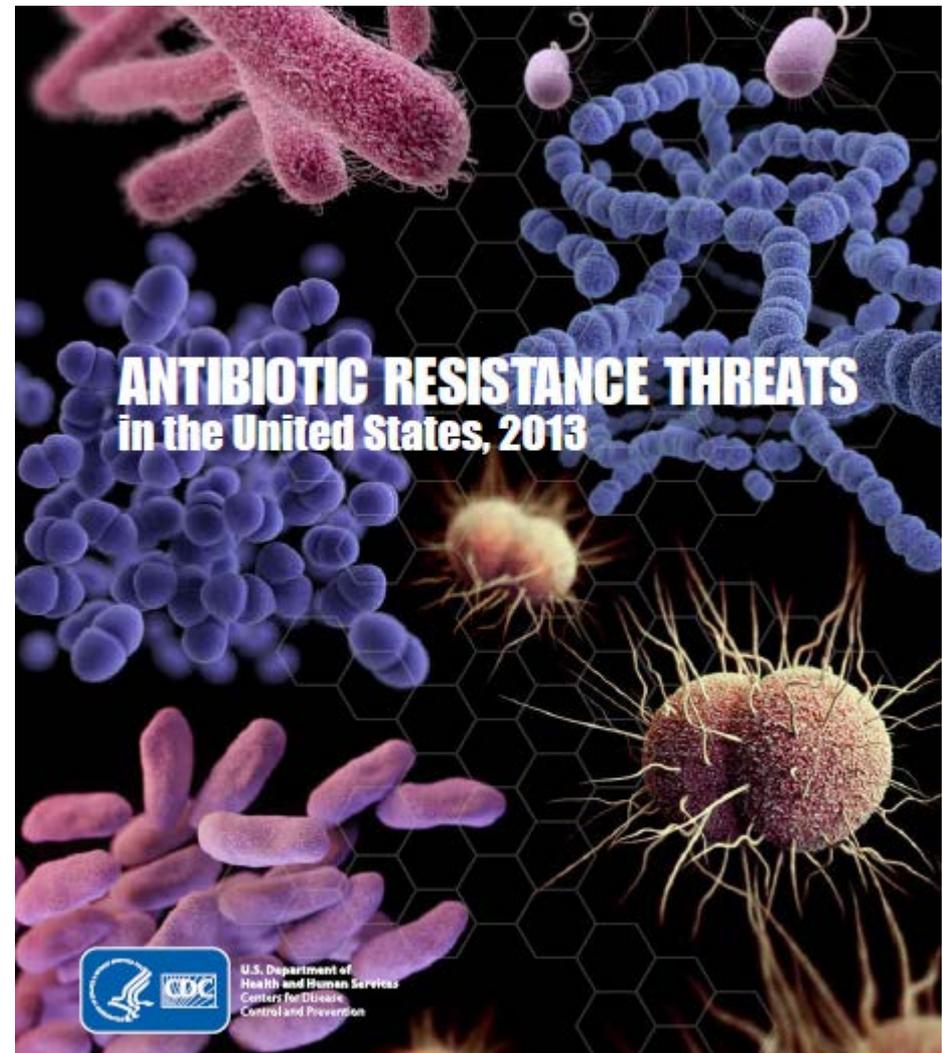
Source: European Antimicrobial Resistance Surveillance Network (EARS-Net)
<http://www.ecdc.europa.eu/en/activities/surveillance/EARS-Net/Pages/index.aspx>



Antimicrobial Resistance Poses a Threat to Public Health and National Security



- 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

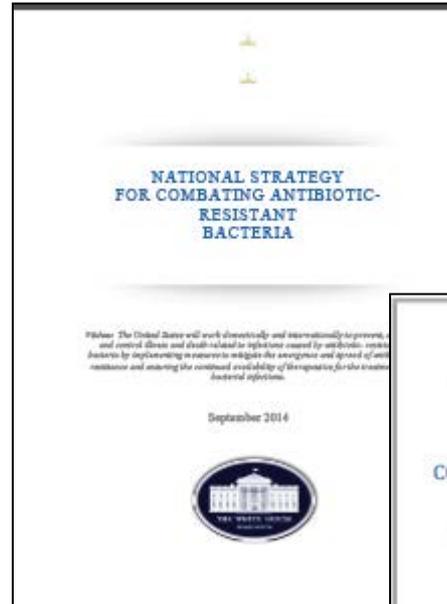




White House Initiative on AMR



CARB Working Groups



PCAST



Executive Order -- Combating Antibiotic-Resistant Bacteria





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.

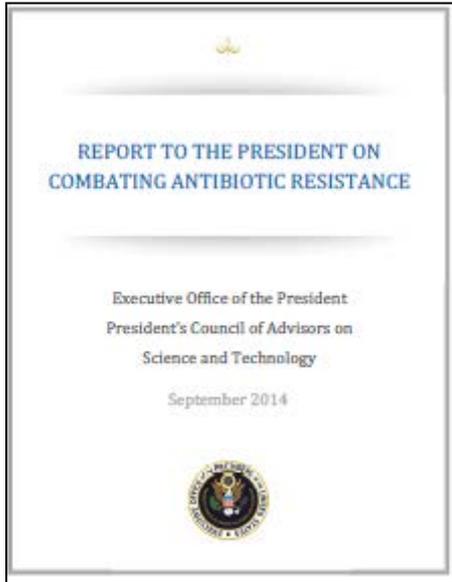
(b) Together with the countermeasures it develops for biodefense threats, the Biomedical Advanced Research Development

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.



PCAST Recommendations



5.2 'Push' mechanisms: Direct Federal partnership in antibiotic development

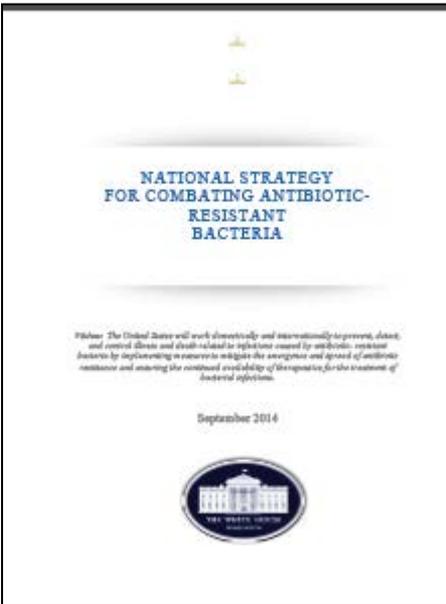
PCAST feels strongly that BARDA's antibiotic development program should be expanded beyond projects justified by security/bioterrorism considerations to include antibiotics that meet urgent public health priorities that are not traditionally defined as material threat agents. With funding of \$400M per year for such projects, BARDA's program might yield 0.5 successful antibiotic drugs per year.

5.3 'Pull' mechanisms: Economic rewards for drug developers

BARDA could create an Antibiotic Incentive Fund (AIF) to provide advance market commitments (AMC) and milestone payments as incentives for bringing a new antibiotic to market. The At one advanced drug candidate per year, this would correspond to average annual funding of \$400M – although an AIF would ideally be structured with no-year advance appropriation (e.g., \$4B over ten years) to allow flexibility in when funds are spent.

• 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.





Current BSA Program Investments



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/ Tetraphase	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)			
	Basilea	A novel surfactant: Broad Spectrum MDR Gram negative infections, melioidosis, glanders			
	Rempex	Carbapenem/ β -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			

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 2014 (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 Current Antibacterial Investments





Achaogen – Plazomicin (ACHN-490) for treatment of Plague, Tularemia and CRE



- Plazomicin is a novel aminoglycoside antibiotic
- Overcomes resistance to aminoglycoside modifying enzymes, remains susceptible to RNA methylase and efflux based resistance mechanisms
- Currently in Phase III clinical development for the treatment of Carbapenem-Resistance Enterobacteriaceae infections
- Global study, projecting ~75 clinical sites in countries with increased prevalence of CRE
- BARDA funding has been used to support Phase III clinical development, CMC activities, non-clinical studies



Rempex Pharmaceuticals Inc. – Advanced Development of Carbavance™ (meropenem/RPX7009)



- Carbavance™ is a novel carbapenem/ β -lactamase inhibitor (BLI) combination
- RPX7009 is a novel first in-class boron based BLI with activity against Class A, C and some D β -lactamases
- Currently in Phase 3; Indications being sought are for the treatment of complicated urinary tract infections, carbapenem resistant *Enterobacteriaceae* (CRE) infections, and hospital acquired/ventilator associated pneumonia
- Program aims to provide a possible treatment option for CRE infections
- Carbavance is expected to be safe for use in pediatrics and pregnant adults



Portfolio Partnership for Antibacterial Drug Development



- Established 5 year \$200M public-private partnership in May 2013
- Supports the development of multiple antimicrobial 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
- Allows for external partnerships through co-development or in-licensing agreements



CUBRC/Tetraphase – Development of Eravacycline



TETRAPHASE
PHARMACEUTICALS



- Next generation tetracycline that overcomes known tetracycline resistance mechanisms.
- Complicated intra-abdominal infections (cIAI) and complicated urinary tract infections (cUTI) are proposed indications
- Currently in Phase III clinical development for cIAI and cUTI
- Protective efficacy demonstrated in treatment models of anthrax and tularemia, plague data pending
- Program has supported clinical and non-clinical studies, CMC, toxicology studies



Basilea Pharmaceutica – Development of BAL30072



- BAL30072 is a novel surfactam antibiotic to be used in combination with a carbapenem
- Planned development is for hospital acquired ventilator associated pneumonia, pathogen specific indications for MDR Gram negative pathogens
- Pursuing biothreat data on *Burkholderia pseudomallei* and *Burkholderia mallei*
- Program is supporting clinical development, CMC, non-clinical studies
- Animal models for *Burkholderia* are being developed through BARDA Non-clinical development network



Cempra Pharmaceuticals – Pediatric Formulation of Solithromycin



- Solithromycin is a novel fluoroketolide antibiotic
- Ongoing Phase III studies: oral CABP in adults, oral to IV step-down CABP in adults, MDR-GC study (100% efficacy in Ph2 MDR-GC)
- Demonstrated therapeutic efficacy for the treatment of inhalational tularemia in a non-human primate model; Biothreat data will be generated for anthrax
- Program seeks to address gap in medical countermeasures for pediatric populations
- Current program supports development of a pediatric formulation, clinical studies to assess PK, safety, and efficacy in pediatric populations
- Initial NDA for treatment of CABP in adults (2015)



Long Term Priorities and Goals



- Near-Term Priorities & Strategic Goals (1-2 years)
 - a. Support novel therapies to treat Gram negative infections
 - b. Maintain and expand portfolio of precedented and unprecedented classes of antimicrobial therapies
 - c. Continue utilizing innovative public-private partnering mechanisms to stimulate therapeutic pipeline
 - d. NDA Submission
- Mid-Term Priorities & Strategic Goals (3-5 years)
 - a. BARDA-funded programs begin to reach NDA stage
 - b. Expand focus to include approaches that can interdict/prevent infection upon entry into the health care setting
 - c. Expand portfolio to include non-traditional therapies (mAbs, probiotics, host targets, etc.)
- Long-Term Priorities & Strategic Goals (5-10 years)
 - a. Develop novel classes antimicrobial therapies
 - b. Work closely with other Govt agencies and private partners to establish and implement policies/practices to ensure pipeline is sustainable

