CARB-X

Combating Antibiotic-Resistant Bacteria

BOSTON UNIVERSITY

Innovation in Solutions for AMR: the CARB-X Portfolio

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What is CARB-X?

A **global non-profit partnership** created in 2016 to support the early development of new **therapeutics, preventatives and diagnostics to** fight drug-resistant bacteria

Where Does CARB-X Funding Come From?

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

BARDA
BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY

wellcome

UKaid
from the British people

Federal Ministry of Education and Research

BILL & MELINDA GATES foundation

NIH National Institute of Allergy and Infectious Diseases

in-kind services

Key Facts about the CARB-X Portfolio

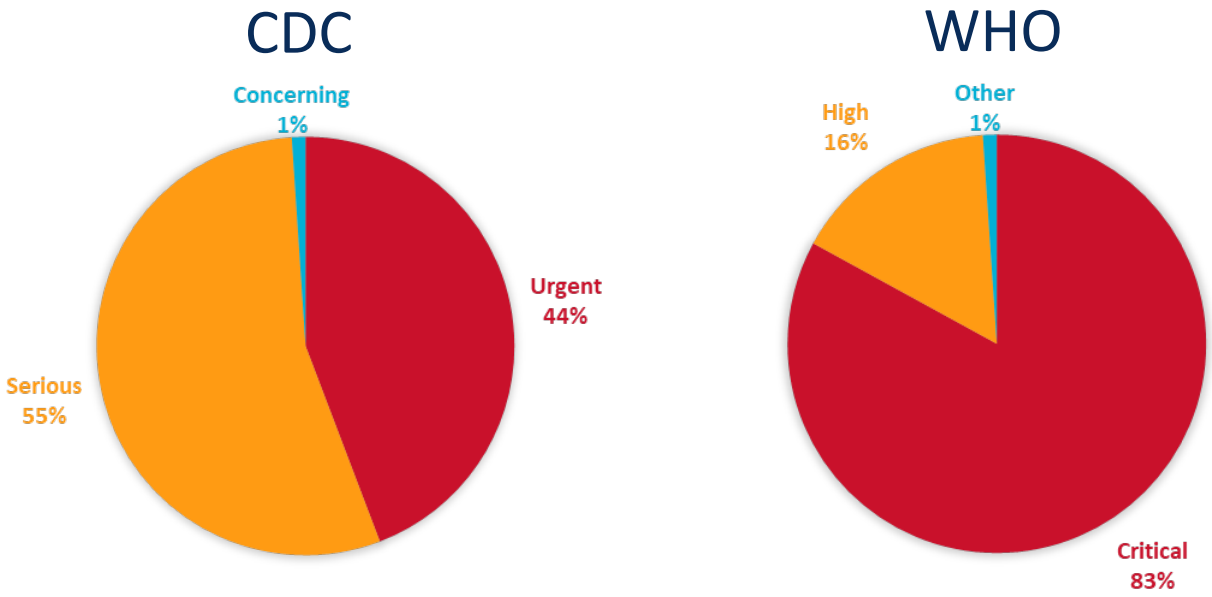
71 innovative **PROJECTS** funded since inception

45 active **PROJECTS**

10 different **COUNTRIES** Represented

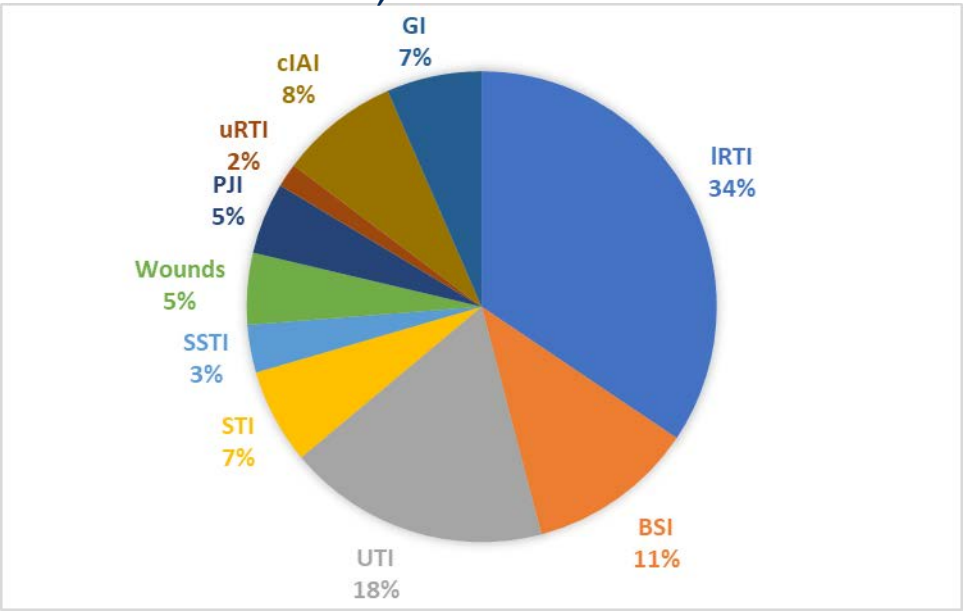
7 project **GRADUATES**

Treatment and Prevention Portfolio Targeting Priority Pathogens for US and Worldwide

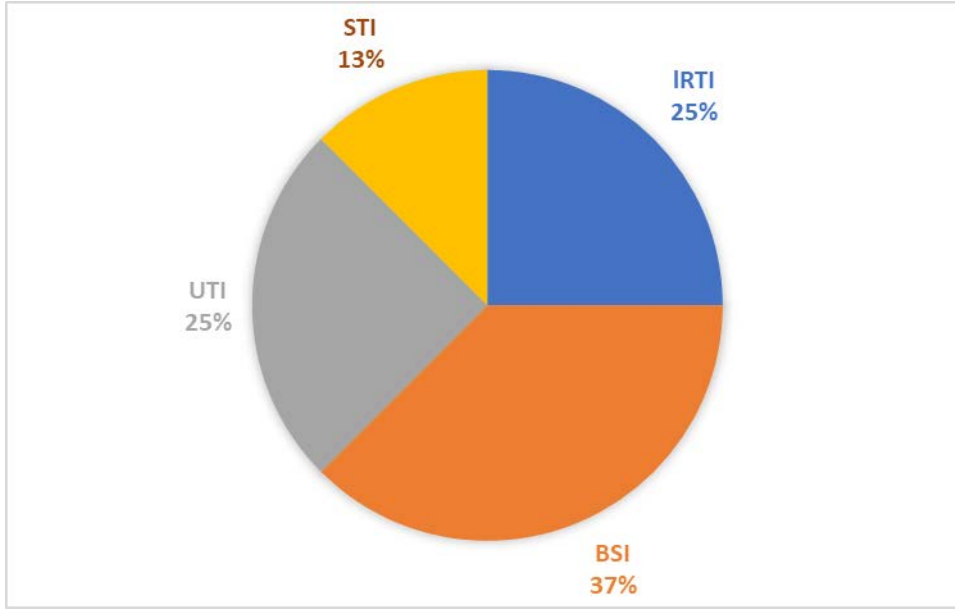


Portfolio Addresses Many Syndromes for which New Therapies are Needed

Tx, Pv Portfolio



Dx Portfolio



Critical for clinical-trial conduct and market uptake

Optimization of Performance Characteristics is Key for New Entrants to Treat a Syndrome

-- although several new antibiotics that addressed the 2000s call for new drugs to treat *S. aureus* and MRSA, dosing regimen and side-effect profiles mean there is still room for new therapies with optimized performance characteristics--

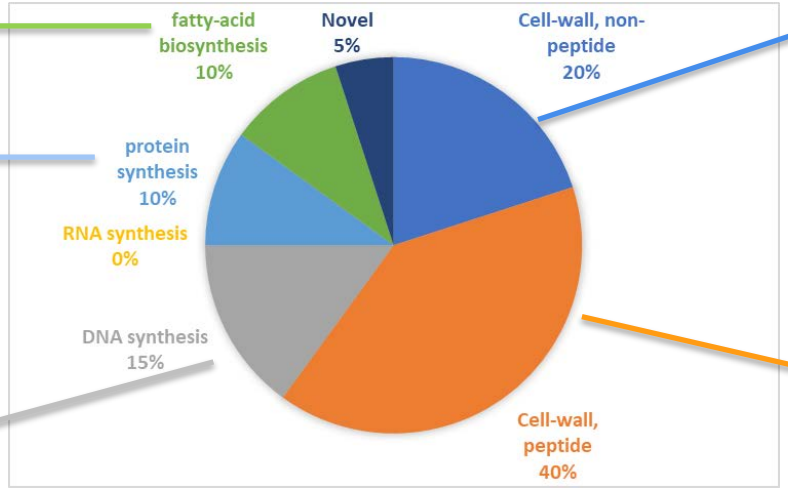
- Ceftaroline (2010) IV only
  - Anaphylaxis, drug-induced hemolytic anemia, CDAD
- Dalbavancin (2014) IV only
  - ALT elevations, infusion-related reactions, CDAD
- Tedizolid (2014) IV/PO
  - Neutropenia, CDAD
- Oritavancin (2014) IV only
  - DDI (warfarin), coagulation interference, CDAD, infusion-related reactions
- Delafloxacin (2017) IV/PO
  - Tendinitis/tendon rupture, peripheral neuropathy, CNS effects, CDAD
- Omadacycline (2018) IV/PO
  - tooth discoloration/enamel hypoplasia, inhibition of bone growth, CDAD

Therapeutics Portfolio Emphasizes Many Validated MOAs with New Chemistries and (Sometimes) New Mechanisms of Inhibition

FabI (enoyl-ACP reductase) inhibitors

aa tRNA synthetases
trans translation

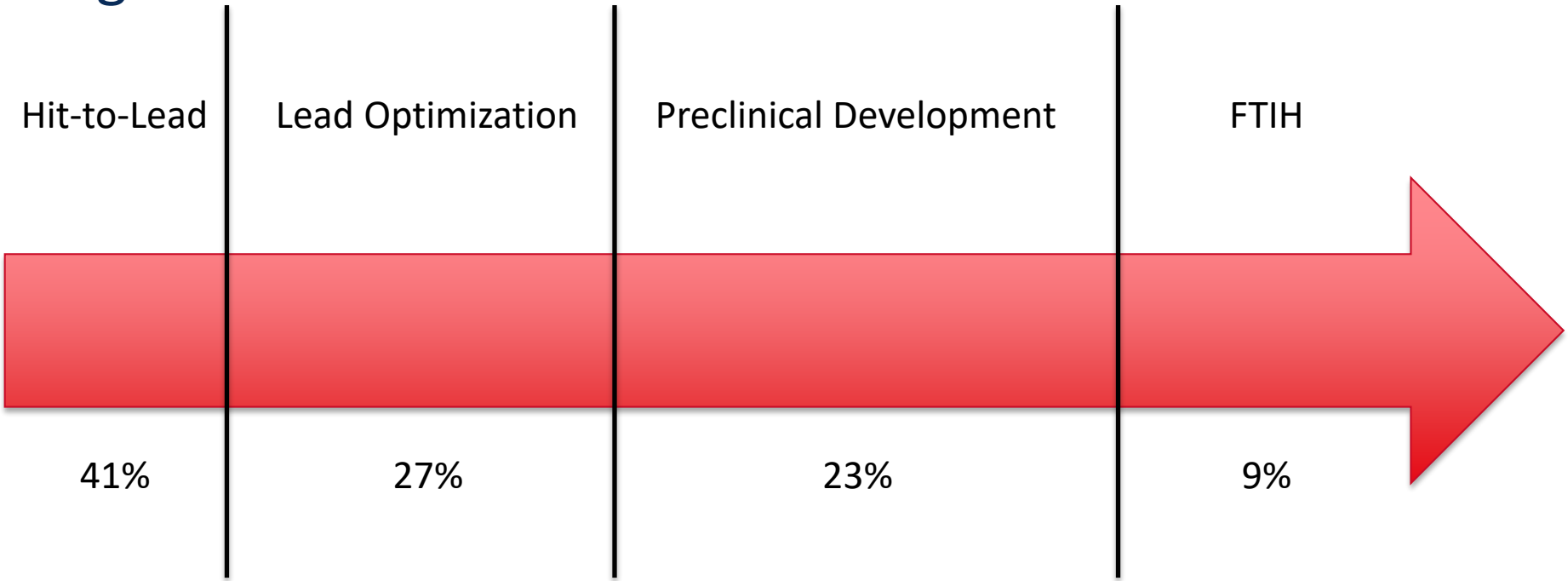
non-FQ



oral BL/BLI
novel PBPis
lpxC

polymyxin softdrug
lytic peptides
AMPs
StAMPs
OMPTAs (BamA and LptA)
octapeptins

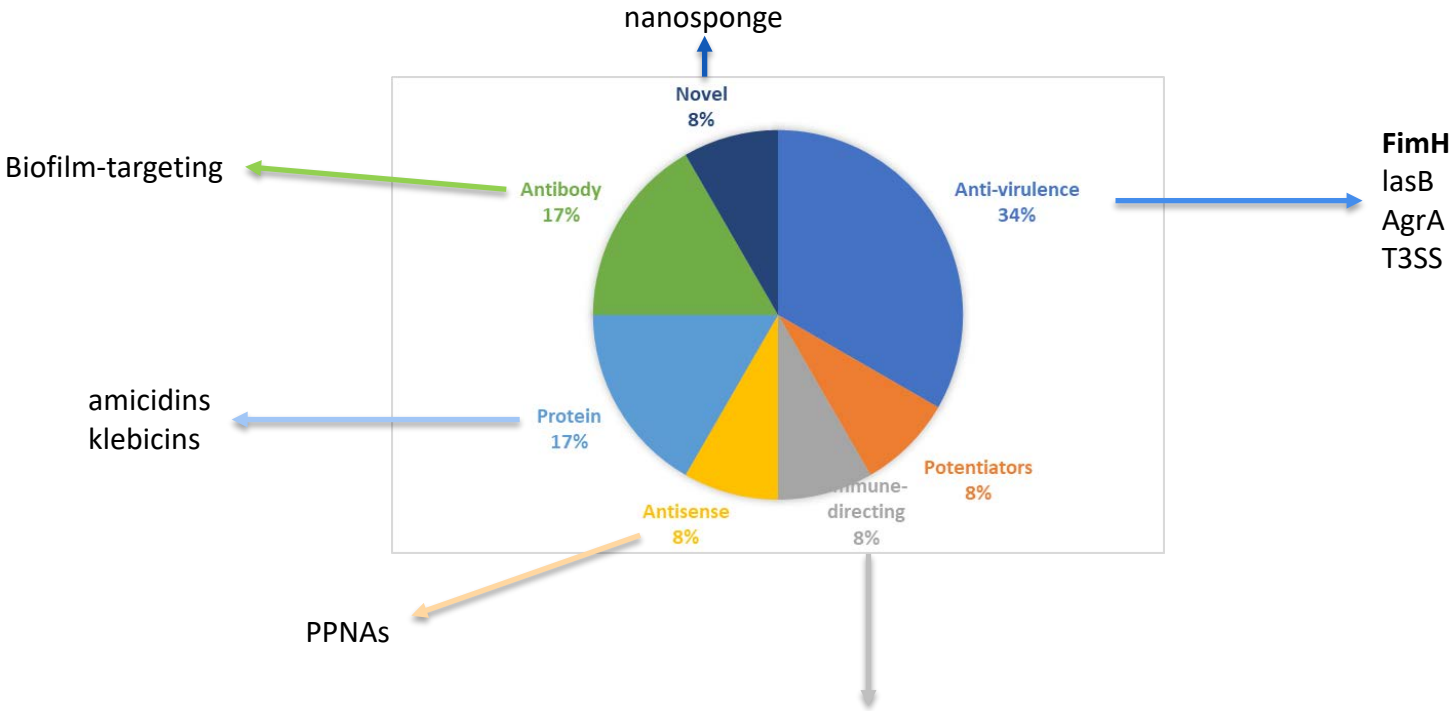
Validated Mechanism Projects Cover All Stages of Program Maturation



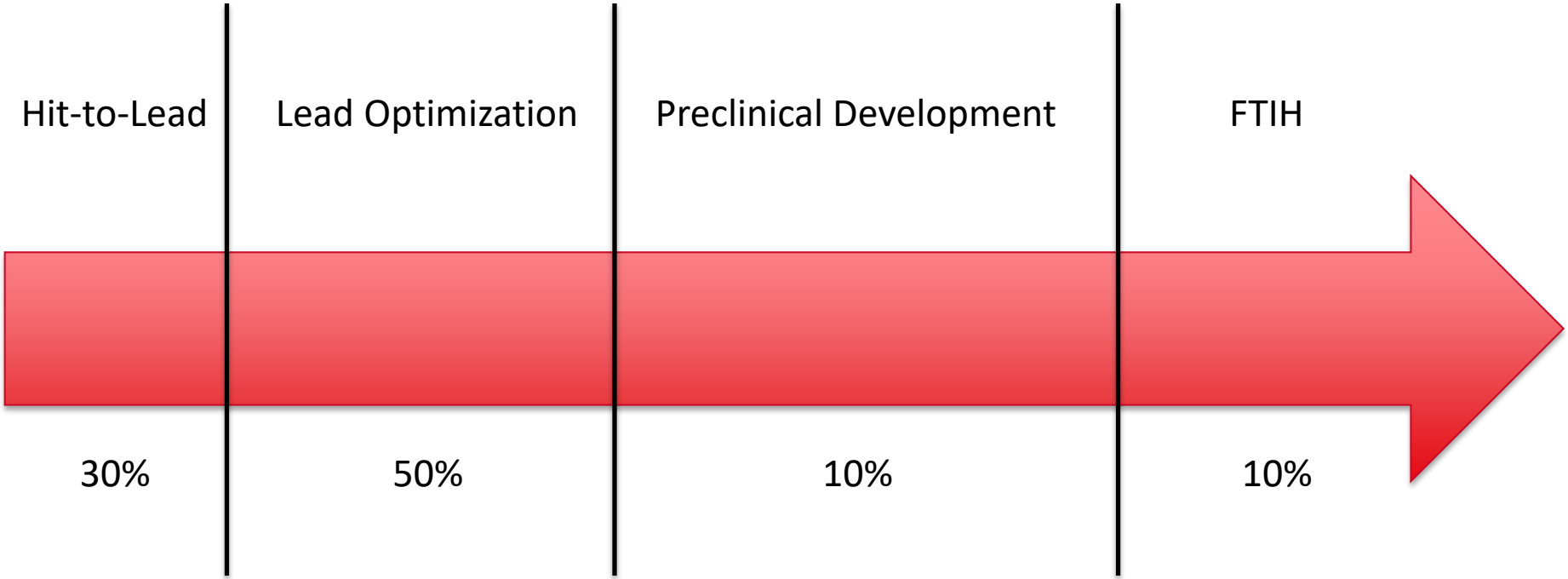
Direct-acting Tx Portfolio: Risks/Challenges

- Translation of some animal models to humans
- Toxicity and understanding of underlying mechanisms
- Existing pools of resistance (cross-project initiative to address this commenced)
- Inconsistent employment of good tools to address permeability and efflux
- Access to good bioanalytical methods development
- COVID impacts on R&D supply chain

Therapeutics Portfolio Includes Several Trailblazing Non-traditional Programs



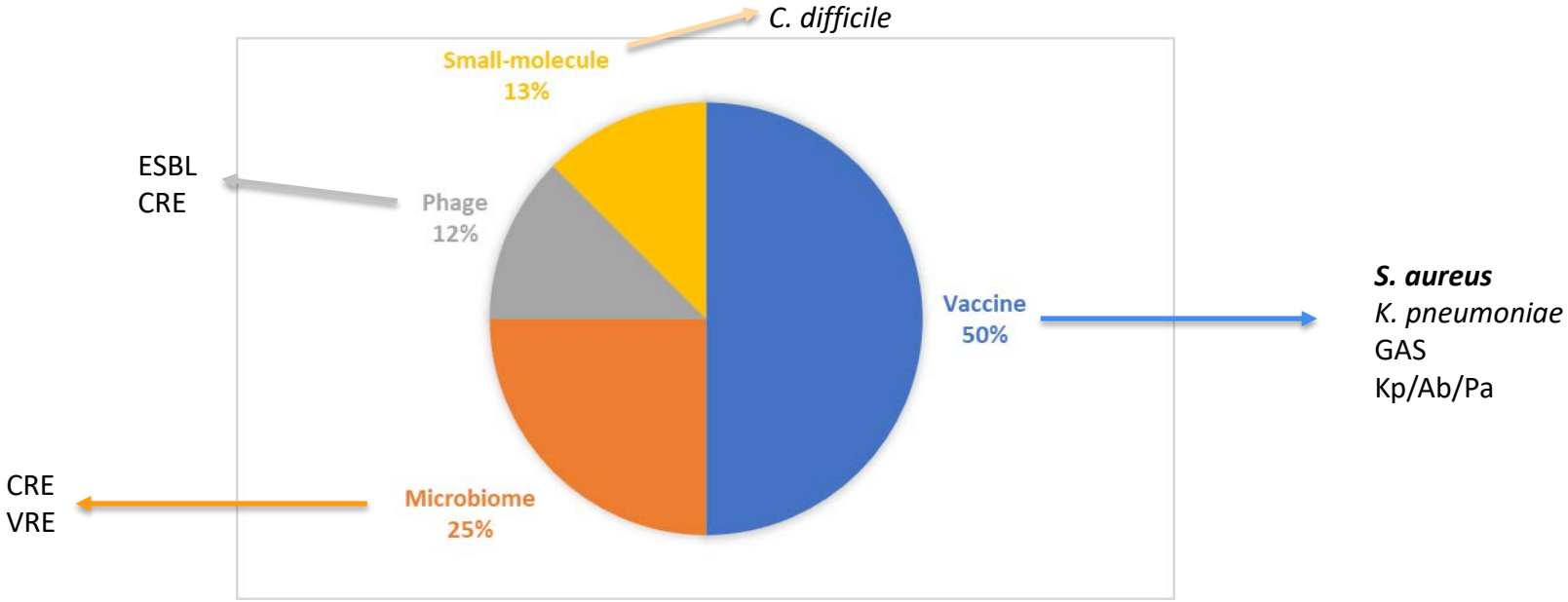
Non-traditional Programs Cover All Stages of Program Maturation



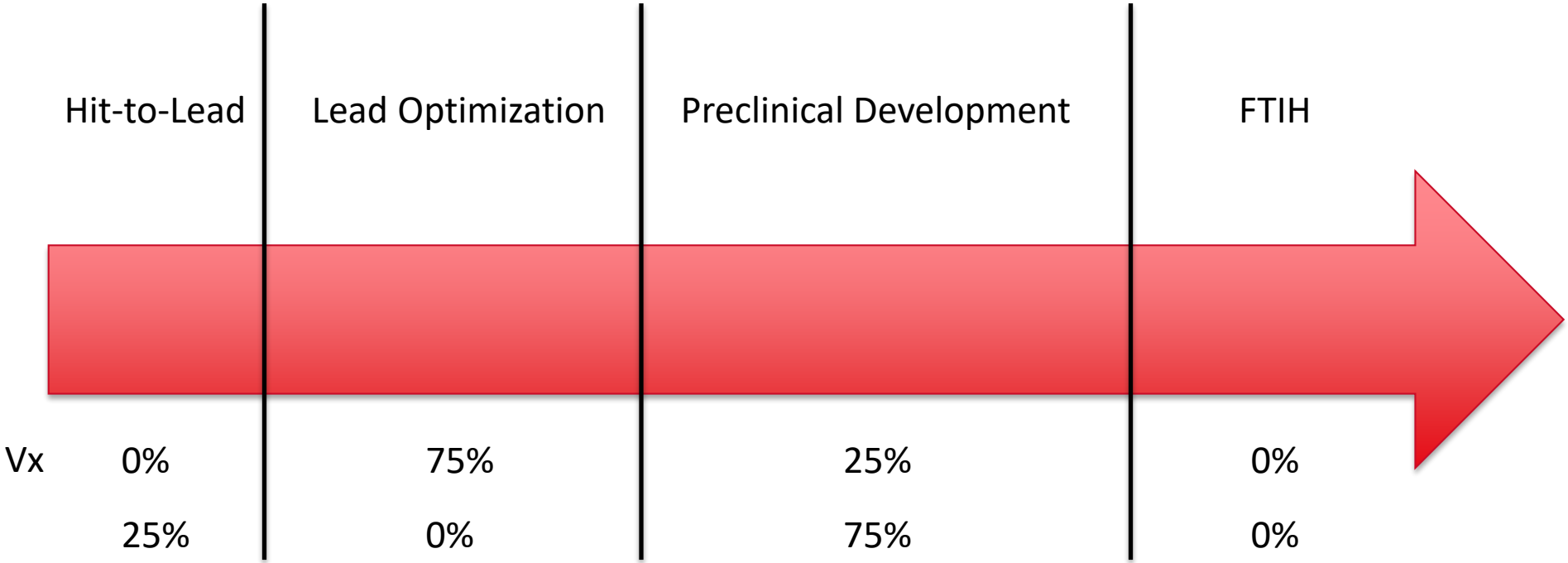
Non-traditional Tx Portfolio: Risks/Challenges

- Translation of *in vitro* activity to animal models
- Translation of animal models to humans
- Regulatory guidance/paths
- PK/PD matching
- Proof that can act as monotherapy
- Proof of additional benefit over SOC antibiotics
- For antibody-based programs
  - Humanization
  - Permeation/access to site

Prevention Portfolio



Prevention Portfolio Earlier in Development



Vx Portfolio: Risks/Challenges

- Access to adjuvants that work in humans but that are proprietary and thus not accessible for screening
- Access to human serum samples for baseline titers
- Access to genome sequence data from recent clinical isolates, particularly from LMICs, and thus to antigenic conservation data (cross-project initiative to address this has kicked-off)
- Translation of animal models to humans

Other Pv Portfolio: Risks/Challenges

- Translation of animal models to humans
- Regulatory guidance/paths
- Production of drug substance
- For microbiome-based programs specifically
  - Rationale for selecting membership in defined consortia
  - Defining dose for clinical trials
  - Impact of diet (eg HIC vs LMIC)
  - Slower onset

Summary

- CARB-X is supporting financially and scientifically many product developers, building a robust pipeline that physicians and patients need
- Push incentives in the CARB-X window are critical to ensuring a rich and robust flow of opportunities for late-stage clinical development and commercialization
- All programs begin with a laser focus on priority and emerging pathogens
- Building an important target-product profile must include a focus on the right syndromes, the right molecular characteristics
- Investing in a diagnostics portfolio matched to the treatment and prevention portfolio is key to successful conduct of clinical trials and in market uptake
- A diversity of modalities and spectrum of novelty is important for “shots-on-goal” success
- The right screening strategy, asking the key questions, is critical to delivering a product with the legs to make it through development. Cross-project initiatives can help the portfolio and broader ecosystem to tackle some of the big challenges

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Thank you!

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