

# ACHAOTGEN

---

**BARDA Industry Day**  
November 7-8th 2017

Lee Swem, Ph.D. Chief Scientific Officer

# Forward Looking Statements

The presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation, including statements regarding future operational and financial results and positions, business strategy, prospective products, potential market, commercial opportunity and market share, availability and potential sources of funding, clinical trial results, product approvals and regulatory pathways, research and development costs, timing (including but limited to timing of clinical development and approval), strategies for completion and likelihood of success for our business activities, our regulatory timelines and plans for future operations are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Such risks and uncertainties include, among others, those inherent in the preclinical and clinical development process; the regulatory approval process; commercialization and gaining market acceptance; conditions when bacteria will evolve resistance to plazomicin or other antibiotics; third party claims alleging infringement of patents and proprietary rights or seeking to invalidate Achaogen's patents or proprietary rights; and the risk that Achaogen's proprietary rights may be insufficient to protect its product candidates. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to our business in general, see our Annual Report on Form 10-K for the fiscal year ended December 31, 2016 filed with the Securities and Exchange Commission on March 14, 2017 and our Form 10-Q for the quarter ended June 30, 2017, filed with the Securities and Exchange Commission on August 8, 2017 and our other past and future filings with the SEC. Except as required by applicable law, we assume no obligation to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. This presentation concerns plazomicin and other product candidates of the Company, none of which have been approved for commercialization. They are currently limited to investigational use, and (except as specifically described herein) no representation is made to their safety or effectiveness for the purposes for which they are being investigated.

# Disclosures

- This presentation concerns a drug that is under clinical investigation and which has not yet been approved for marketing by any regulatory authority, including the US Food and Drug Administration (FDA)
- This drug is currently limited by law to investigational use, and no representation is made as to the safety or effectiveness for the purposes for which it is being investigated
- This project has been funded in whole or in part with Federal funds from the Biomedical Advanced Research and Development Authority (BARDA), Office of the Assistant Secretary for Preparedness and Response, Office of the Secretary, Department of Health and Human Services, under Contract No. HHSO100201000046C
- Disclosure: Full time employee of Achaogen

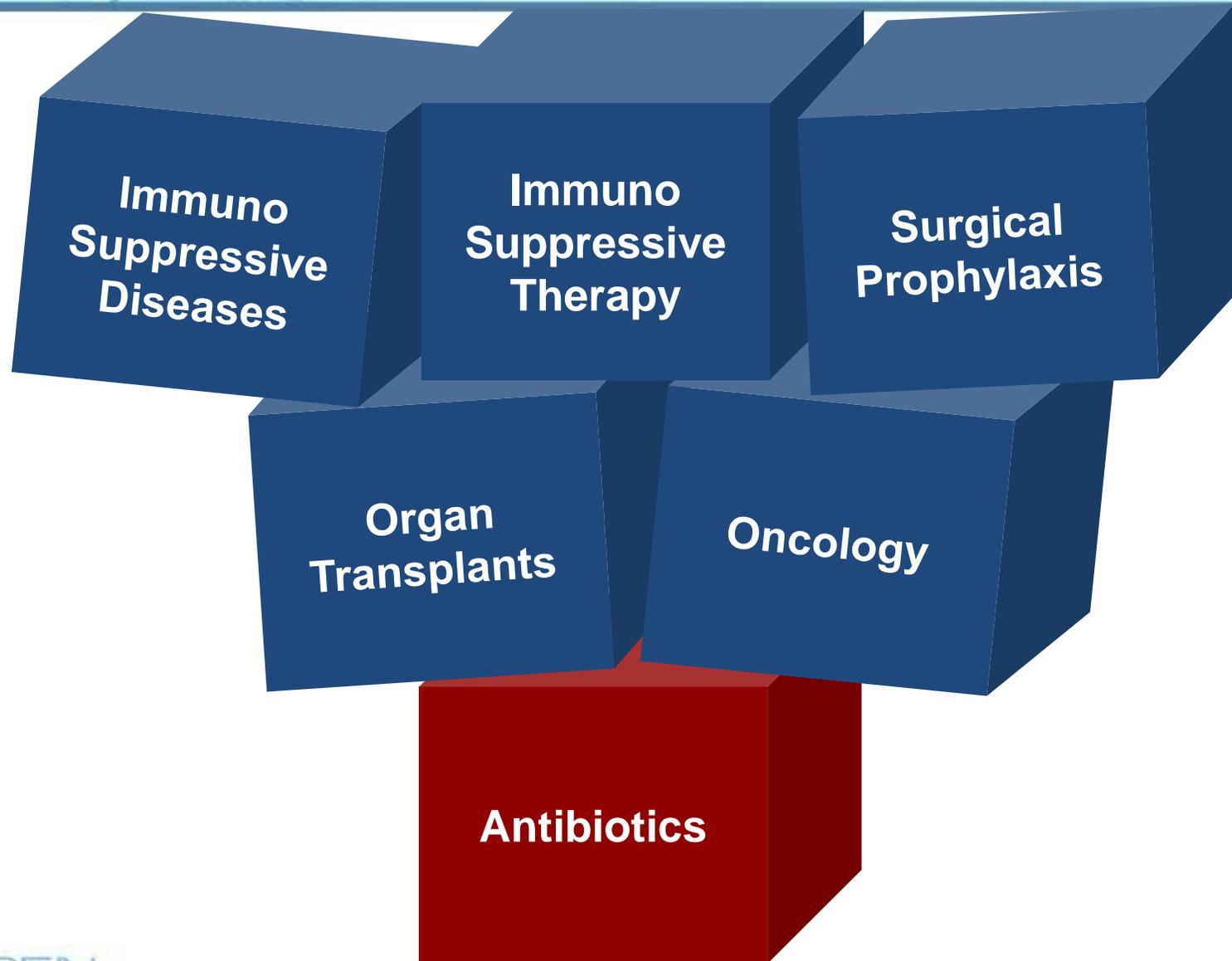
# Achaogen is Committed to the Discovery, Development and Commercialization of Potentially Life-Saving Antibiotics



South San Francisco, CA

- Began operations in 2004, now over 200 employees
- Experience with public-private partnerships
  - BARDA (plazomicin & C-Scape)
  - NIAID (LpxC and aminoglycosides)
  - DTRA, MIDRP and CARB-X (LpxC)
- Seasoned management team with experience regarding over 20 INDs and drug approvals
- Lead program is plazomicin
  - Discovered and developed internally
  - Expected to launch commercially in 2018
- World-class Scientific Advisory Board

# Antibiotics are a Cornerstone of Modern Medicine



# Achaogen's Pipeline Addresses All of the WHO Tier 1 Priority Pathogens

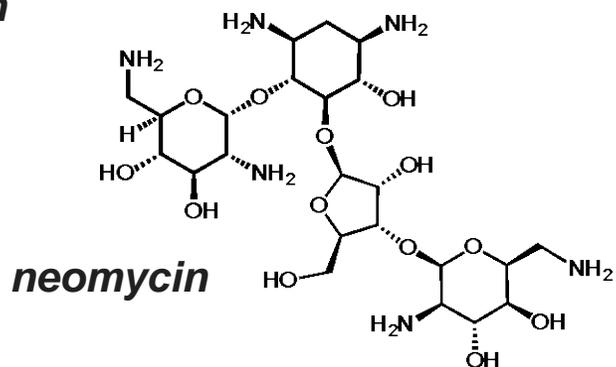
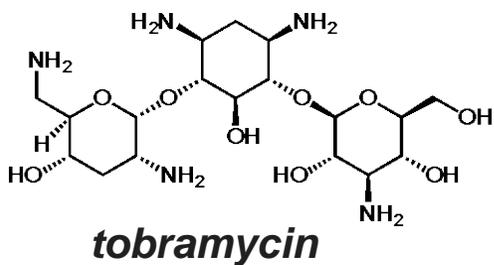
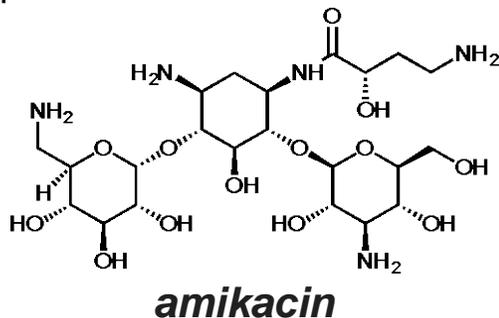
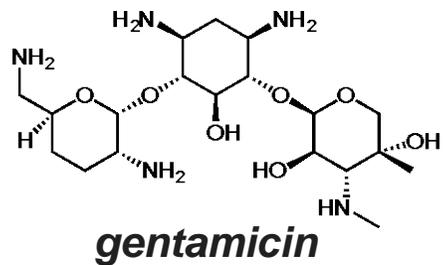
Highlighted Pipeline Programs	Stage	WHO Tier 1 Priority Pathogen
<b>Plazomicin</b> – complicated urinary tract infections	NDA Submitted	✓
<b>Plazomicin</b> – blood stream infections due to CRE	NDA Submitted	✓
<b>C-Scape</b> – ESBL+ Enterobacteriaceae (oral)	Phase 1	✓
<b>Novel Aminoglycoside</b> – Enterobacteriaceae, <i>Pseudomonas aeruginosa</i> , <i>Acinetobacter baumannii</i>	Pre-clinical	✓
<b>Bactericidal mAb</b> – <i>Acinetobacter baumannii</i>	Pre-clinical	✓

CRE: carbapenem-resistant Enterobacteriaceae, ESBL: Extended-spectrum beta-lactamase, mAb: monoclonal Antibody

- The aminoglycoside plazomicin is the first antibiotic to be granted Breakthrough Therapy Designation
- Our research on aminoglycosides has generated new insights for creating a next generation candidate

**Novel AG Project vision:** A broad-spectrum aminoglycoside capable of treating *all* the WHO Tier 1 Priority Pathogens

# Aminoglycosides are Essential Drugs in the Fight Against Gram-Negative Bacterial Infections



~70 years of clinical use

Rapidly bactericidal

Broad spectrum

Highly soluble and stable

Lack of metabolism

Predictable pharmacokinetics



# Plazomicin is Potent in Vitro Against CRE

## *In vitro* Activity vs. Clinical Isolates of CRE

Compound	Class	N	MIC <sub>90</sub> (µg/ml)
<b>Plazomicin</b>	<b>Aminoglycoside</b>	<b>983</b>	<b>2</b>
Gentamicin	Aminoglycoside	978	>64
Amikacin	Aminoglycoside	983	64
Ciprofloxacin	Fluoroquinolone	822	8
Ceftazidime	Cephalosporin	498	64
Piperacillin/tazobactam	Penicillin/Beta-lactamase inhibitor	756	>64
Tigecycline	Glycylcycline	804	4
Colistin/polymyxin B	Polymyxin	877	8

 **Susceptible**

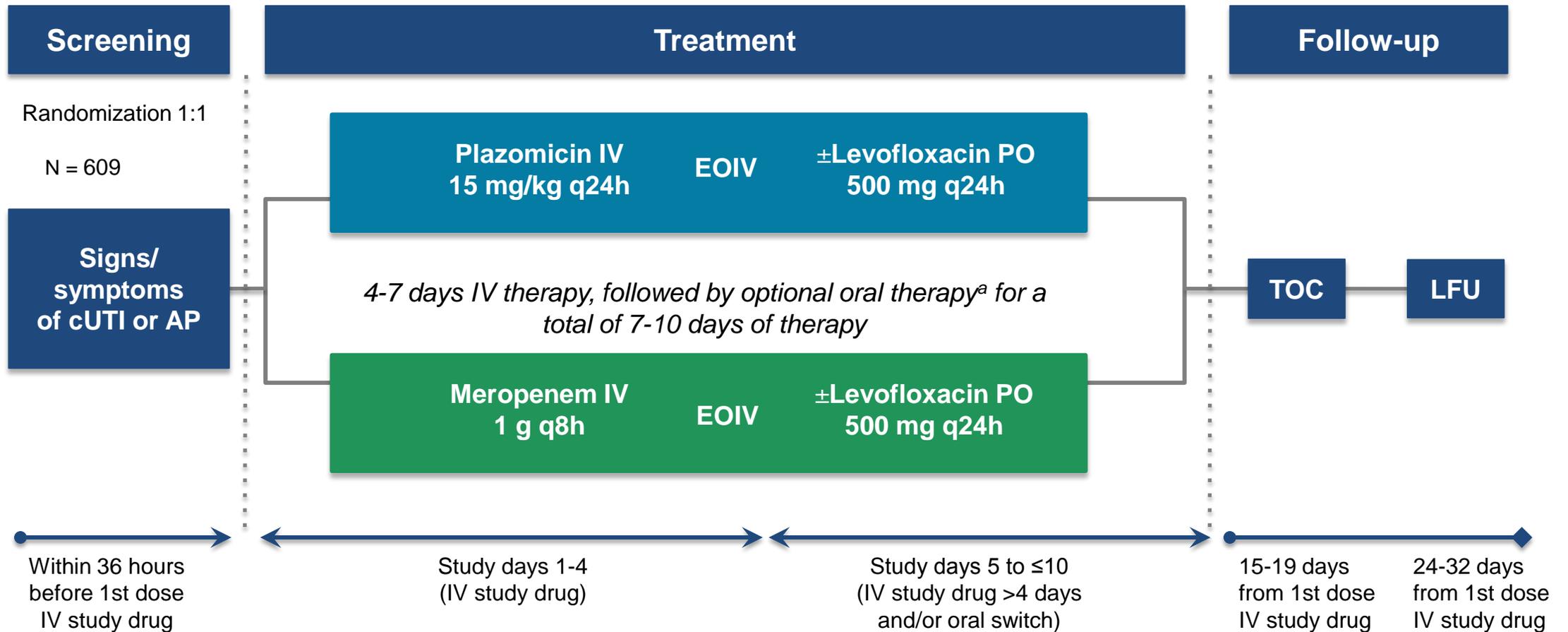
 **Non-Susceptible**

• CLSI 2012 susceptibility criteria were used except for tigecycline and colistin, for which EUCAST 2013 criteria were used because CLSI criteria were not available. Isolates selected had an MIC<sub>90</sub> ≥ 2 µg/mL for any type 2 carbapenem, a value defined as non-susceptible for this class according to CLSI.

• Data includes clinical isolates from six studies: 1) Galani *J Chemother* 2012;**24**:191-4, 2) Livermore *J Antimicrob Chemother* 2011;**66**:48-53, 3) Landman *J Antimicrob Chemother* 2010;**65**:2123-7, 4) Endimiani, *Antimicrob Agents Chemother* 2009;**53**:4504-7, 5) Oiaflisoye *IDSA* 2014:E-1168B, 6) Rodriguez-Avial *ECCMID* 2014:P1682

# EPIC cUTI Study Design

Objective: Demonstrate non-inferiority to Meropenem



<sup>a</sup>Patients could receive levofloxacin or other approved oral therapy.

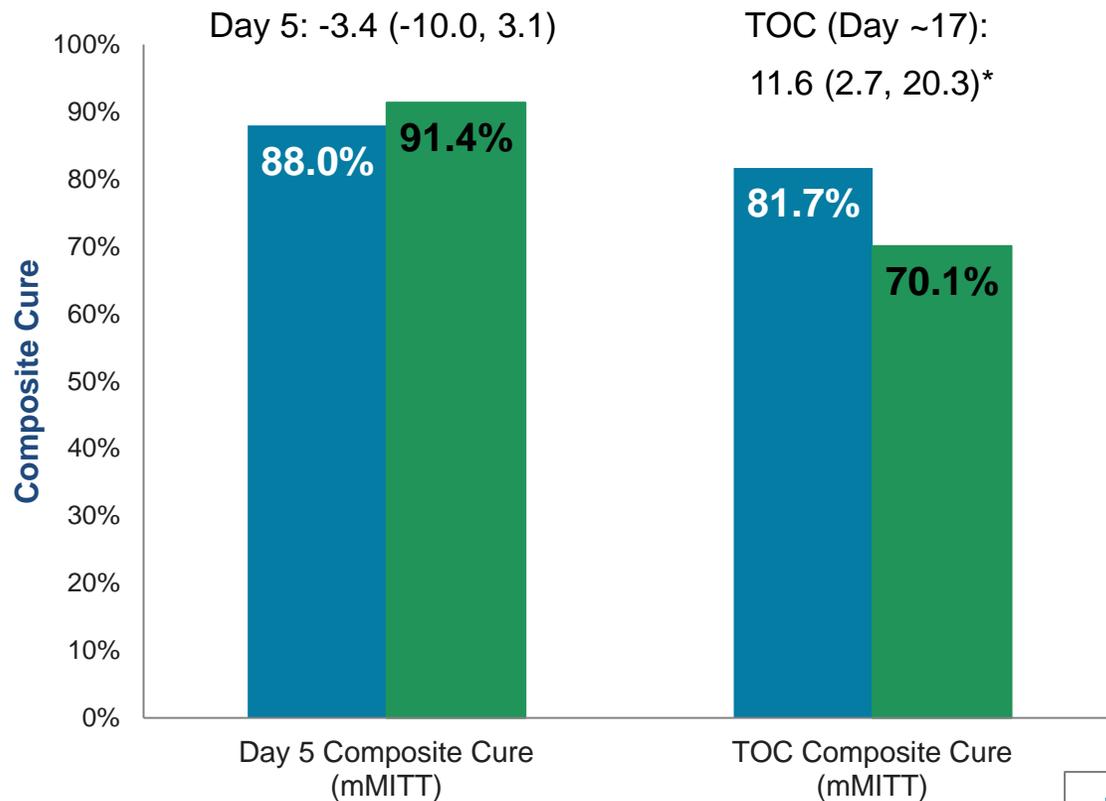
EOIV, end of intravenous therapy; LFU, late follow-up; PO, orally; q8h, every 8 hours; q24h, once every 24 hours.

# EPIC Efficacy Endpoints

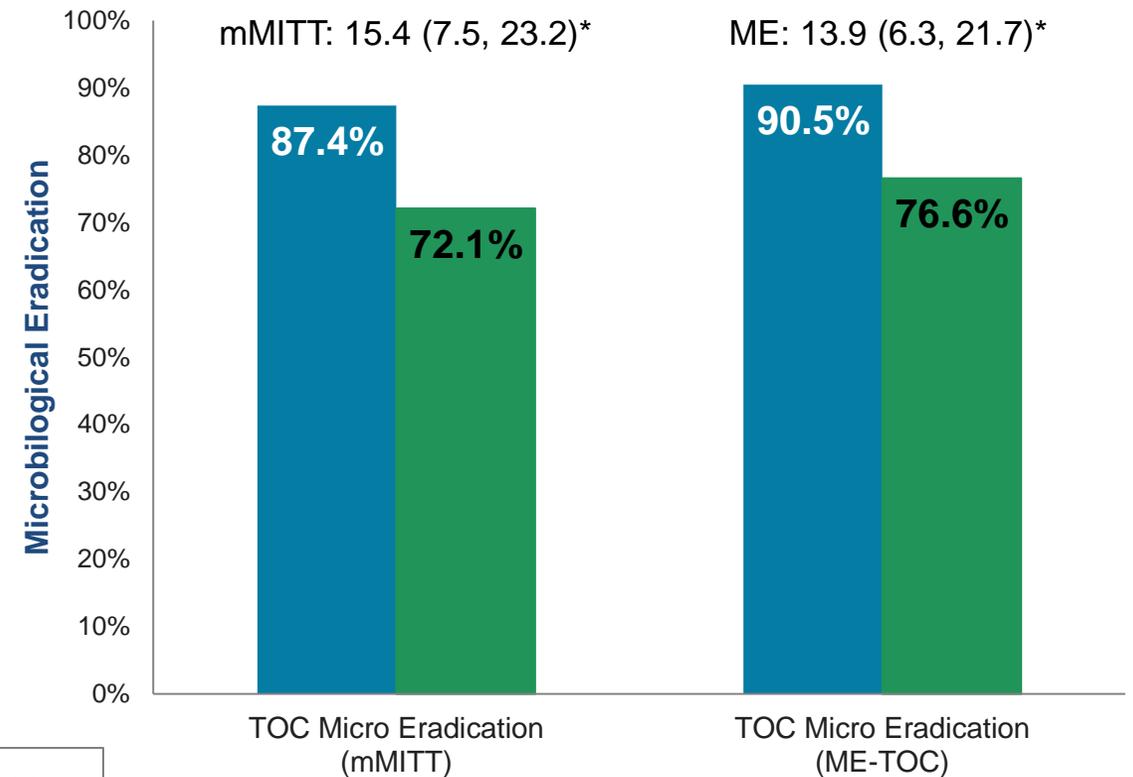
Plazomicin demonstrated non-inferiority on FDA co-primary endpoints and statistical superiority on EMA co-primary endpoints to meropenem

**% Difference [Plazomicin minus Meropenem] (95% CI)**

## FDA Endpoint



## EMA Endpoints



\*lower bound of the CI exceeds zero indicating statistical significance  
TOC: Test-of-Cure visit  
Composite Cure includes microbiological eradication and clinical cure



# EPIC Overall Summary of TEAEs and SAEs

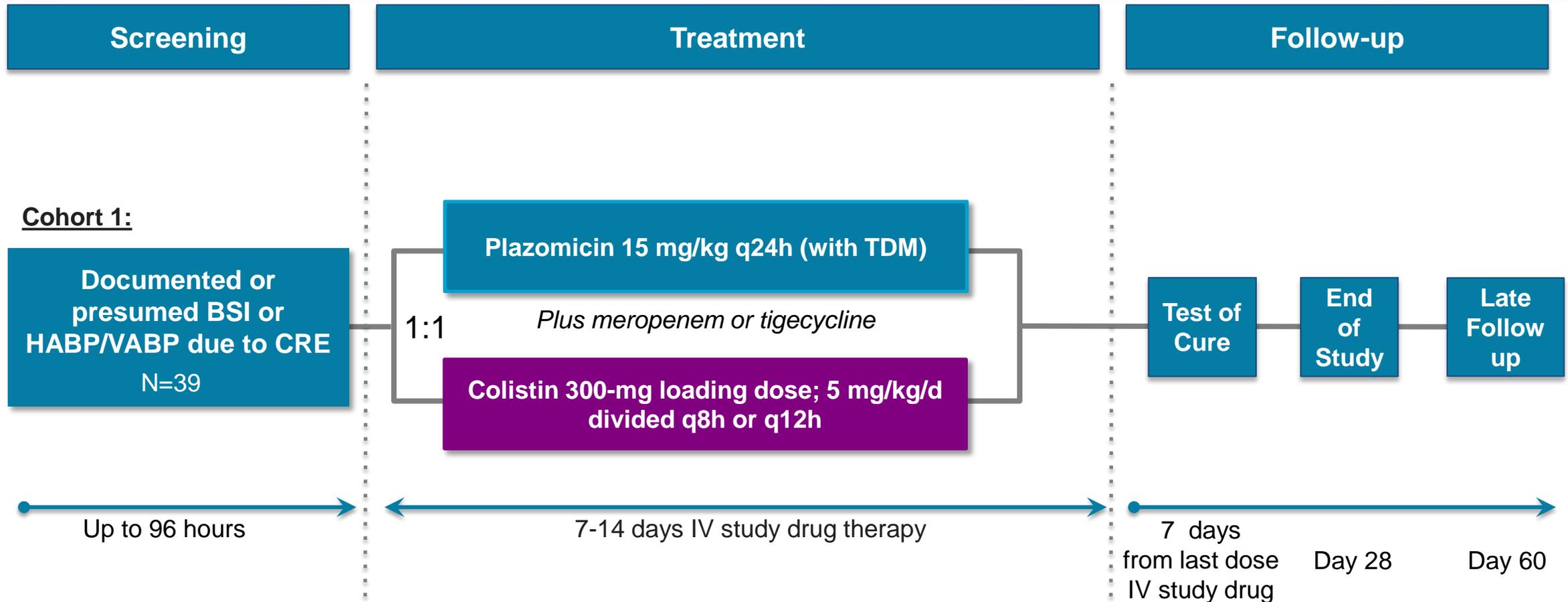
*Similar incidence across study arms*

Patients with Any of the Following: (Safety Population)	Plazomicin (N=303) n (%)	Meropenem (N=301) n (%)
<b>TEAE</b>	<b>59 (19.5)</b>	<b>65 (21.6)</b>
IV Study Drug Related	18 (5.9)	16 (5.3)
Led to Discontinuation of IV Study Drug	6 (2.0)	6 (2.0)
Pooled TEAEs Related to Renal Function	11 (3.6)	4 (1.3)
<b>SAE</b>	<b>5 (1.7)</b>	<b>5 (1.7)</b>
IV Study Drug Related	1 (0.3)	1 (0.3)
Death	1 (0.3)	0 (0.0)

TEAE: Treatment Emergent Adverse Event; SAE: Serious Adverse Event

- Most common TEAEs occurring in plazomicin-treated patients were diarrhea (2.3%), hypertension (2.3%), headache (1.3%), nausea (1.3%) and vomiting (1.3%)
- One death in the plazomicin group due to pre-existing cancer, not related to study drug
- One case of potential ototoxicity in each treatment arm; both cases mild and recovered

# CARE CRE BSI or HABP/VABP Infections Phase 3 Study Design



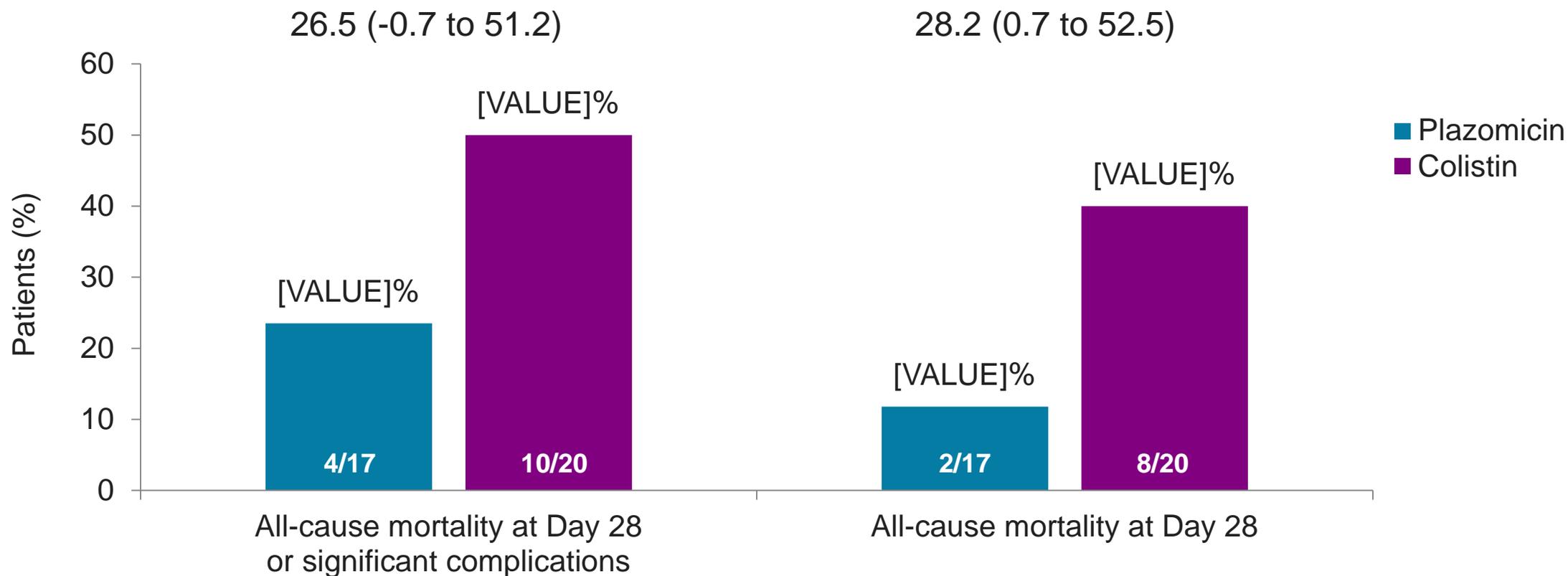
BSI, blood stream infection; CRE, carbapenem-resistant Enterobacteriaceae; HABP, hospital-acquired bacterial pneumonia; q $\times$ h, every  $\times$  hours; TDM, therapeutic drug management; VABP, ventilator-associated bacterial pneumonia.

# CARE Primary Efficacy Results (Randomized Cohort 1)

Improved outcomes at Day 28 for plazomicin versus colistin treated patients

## BSI and HABP/VABP (mMITT Population)

Difference (colistin minus plazomicin) (90% CI)



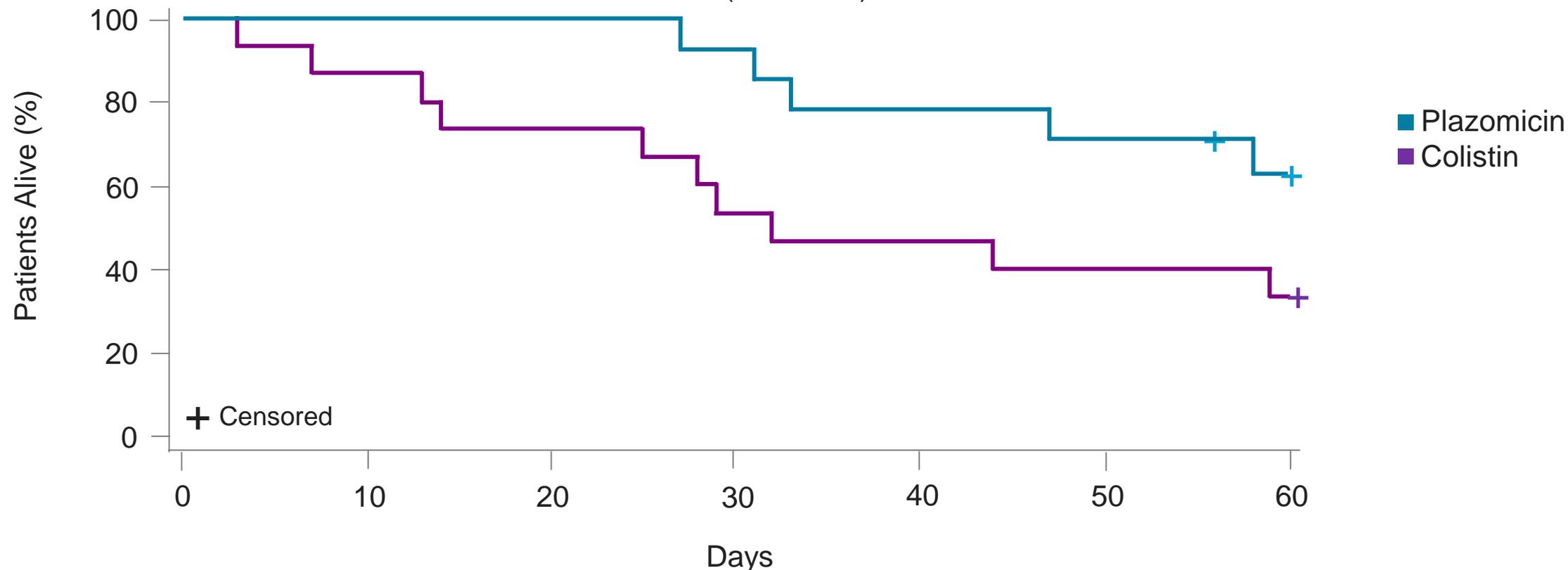
Two-sided 90% confidence interval (CI) calculated based on the unconditional exact method.

# CARE Kaplan-Meier Survival Curve

## Sustained Survival Benefit in Plazomicin-treated Patients With BSI

### 60-day Survival in BSI Subset (mMITT Population)

HR for death (plazomicin:colistin) (90% CI)  
0.37 (0.15-0.91)



Estimate of hazard ratio (HR) calculated as plazomicin:colistin based on Cox proportional hazards regression model.

# CARE Overall Summary of TEAEs and SAEs

## *Favorable Safety Profile for Plazomicin Versus Colistin*

Safety Population	Plazomicin (N=18) n (%)	Colistin (N=21) n (%)
<b>TEAE</b>	<b>16 (88.9)</b>	<b>21 (100.0)</b>
Study Drug-related	5 (27.8)	9 (42.9)
Led to Discontinuation of Study Drug	2 (11.1)	1 (4.8)
<b>SAE</b>	<b>9 (50.0)</b>	<b>17 (81.0)</b>
IV Study Drug-Related	1 (5.6)	4 (19.0)
<b>TEAEs Related to Renal Function</b>		
Overall Pooled	6 (33.3)	11 (52.4)
Study Drug Related	3 (16.7)	8 (38.1)

- Reduced drug-related AEs, SAEs, and AEs related to renal function in plazomicin arm
- No study drug-related deaths or events of ototoxicity reported

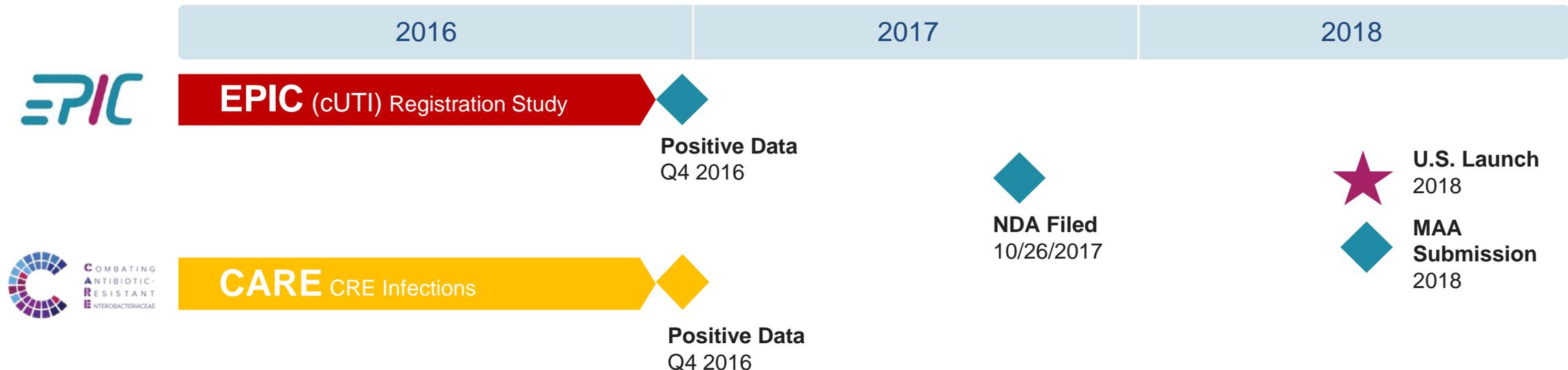
# EPIC and CARE Show a Favorable Benefit-Risk Profile in Their Respective Target Patient Populations

## • EPIC

- Significantly higher composite cure and eradication rates at test-of-cure in cUTI/AP and higher eradication rates for ESBL-producing pathogens compared to meropenem, a preferred agent for MDR Enterobacteriaceae
- Significant efficacy results combined with generally favorable safety profile provide a strong benefit-risk compared to meropenem for patients with cUTI

## • CARE

- Large reduction in mortality and improved safety profile provide a clinically compelling benefit-risk compared to colistin, a standard of care agent for CRE



# Next Generation Aminoglycosides

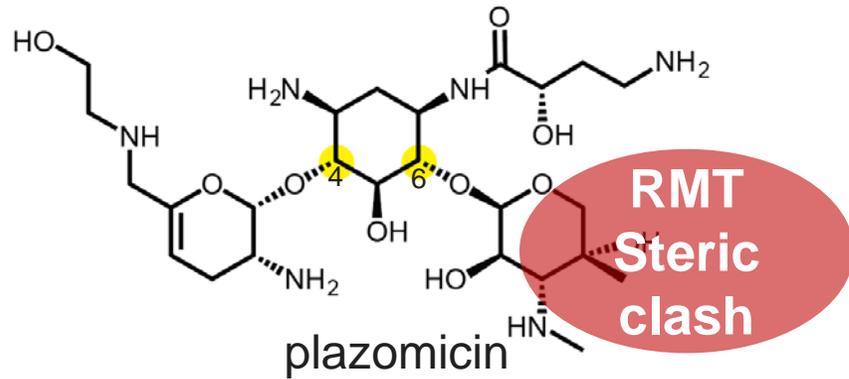
## Current Limitations

- Potential for nephrotoxicity and ototoxicity
- Spectrum limited to Enterobacteriaceae
- Resistance mediated by ribosomal methyltransferase resistance

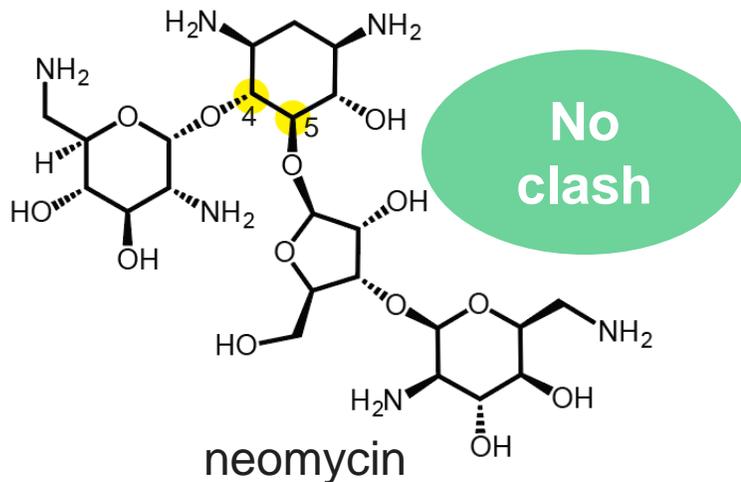
## Future Possibilities

- Widen the nephrotoxicity therapeutic window
- Expand the spectrum to target *A. baumannii* and *P. aeruginosa*
- 4,5-linked aminoglycoside to avoid ribosomal methyltransferase resistance

# ArmA-Type RMTs Prevent 4,6-Linked Aminoglycosides, but Not 4,5-Linked Aminoglycosides from Binding the Ribosome



V.S.



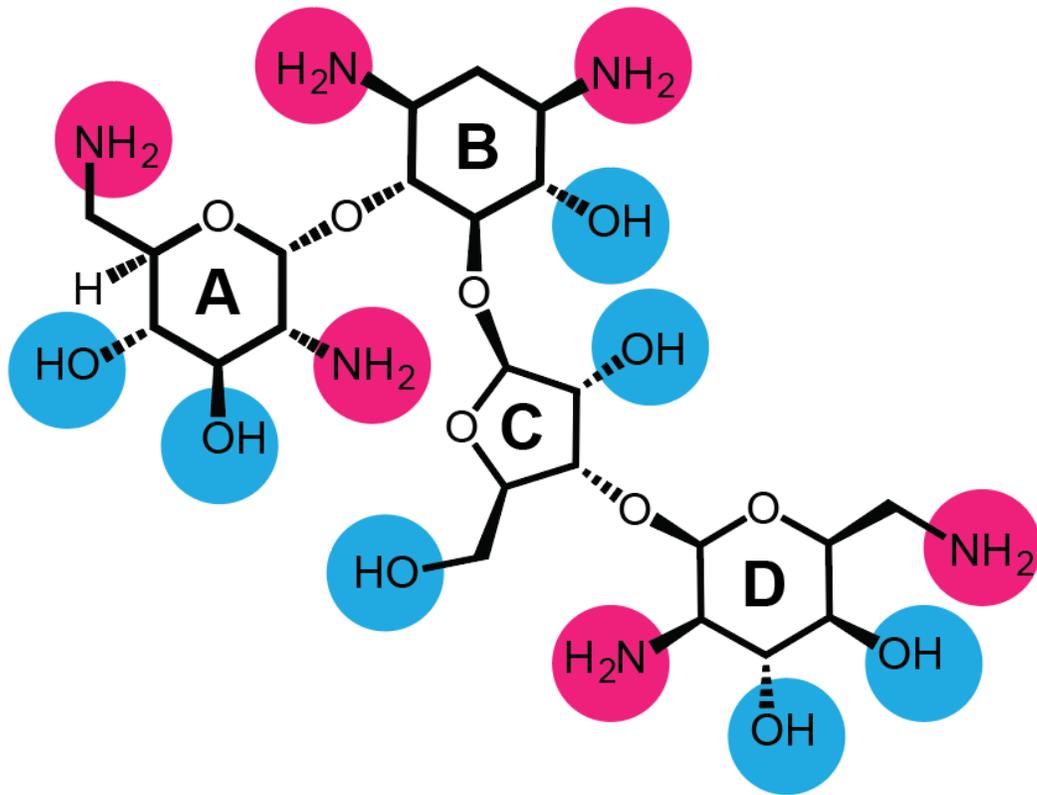
**Table.** MICs ( $\mu\text{g/mL}$ )  $\pm$ ArmA RMT in Isogenic *E. coli* strain

Scaffold	Compound	WT MIC	+ArmA MIC
4,6	gentamicin	0.5	>256
	tobramycin	0.25	>256
	plazomicin	0.5	>256
4,5	neomycin	0.5	0.5
	paromomycin	1	1
	ACHN-978*	1	1

\*Former Achaogen lead developed under NIAID contract #HHSN2722008000043C

- RMTs are currently rare in U.S. Enterobacteriaceae but reported more frequently in Asia
- 30% prevalence in contemporary *Acinetobacter* panels

# Aminoglycoside Chemistry is Challenging Due to the Extensive Array of Chemically-Reactive Groups



**Solution:** We have developed a highly innovative chemistry approach to rapidly derivative the core AG scaffold to potentially broaden the spectrum beyond Enterobacteriaceae, widen the therapeutic window and address future resistance liabilities

# Summary

- We are incredibly excited about the positive Phase 3 data for Plazomicin
- Plazomicin was the first antibiotic to ever receive breakthrough therapy designation
- We have submitted the NDA and anticipate a commercial launch in 2018, if approved
- Our new aminoglycoside program is focused on improving the safety profile and extending the spectrum to target *P. aeruginosa* and *A. baumannii*