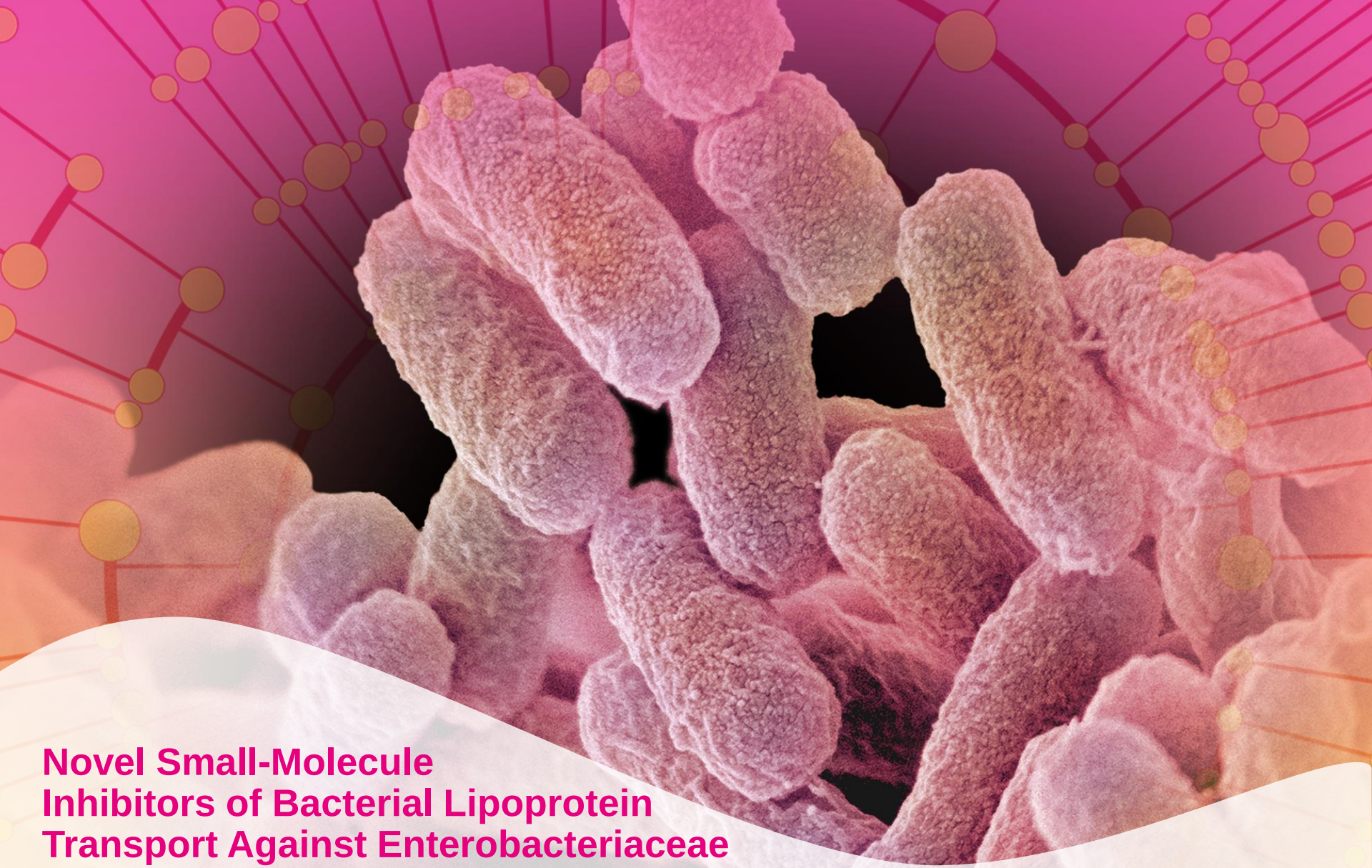

Novel Small-Molecule Inhibitors of Bacterial Lipoprotein Transport Against Enterobacteriaceae

Elena Breidenstein, PhD

20 November 2019

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Forward-Looking Statements and Disclosure

Statements in this presentation, other than statements of historical fact, constitute forward-looking statements within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements include statements regarding Summit's clinical trials supporting the safety and efficacy of its product candidates and the potential novelty of such product candidates as treatments for disease, plans and objectives for preclinical, clinical trials, product development and regulatory filings, Summit's collaboration with Eurofarma Laboratorios SA, Summit's award from BARDA and CARB-X, Summit's Discuva Platform, strategies, future performance, expectations, assumptions, financial condition, liquidity and capital resources. These forward-looking statements may be preceded by, followed by or otherwise include the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions. Actual results or events may differ materially from those expressed or implied in any forward-looking statements due to various factors, including the risks and uncertainties inherent in clinical trials and product development and commercialization, such as the uncertainty in results of preclinical studies, clinical trials for product candidates, the uncertainty of whether the preliminary results from a clinical trial will be predictive of final results of that trial or whether the results of clinical trials will be predictive of results in later stages of product development, the risk of delays or failure to obtain or maintain regulatory approval, the risk of failure of the third parties upon whom Summit relies to conduct its clinical trials and manufacture its product candidates to perform as expected, the risk that any third-party collaborator, including Eurofarma, terminates or fails to meet its obligations to Summit, the risk of the ability of BARDA or CARB-X to terminate our contract for convenience at any time, the risk that Summit's discovery and development platform may not identify new potential drug development candidates, the risk of increased cost and delays due to delays in the commencement, enrollment, completion or analysis of clinical trials or significant issues regarding the adequacy of clinical trial designs or the execution of clinical trials and the timing, cost and design of future clinical trials and research activities, the timing of expected filings with the FDA or other regulatory agencies; and the other risks and uncertainties described in Summit's public filings with the Securities and Exchange Commission.

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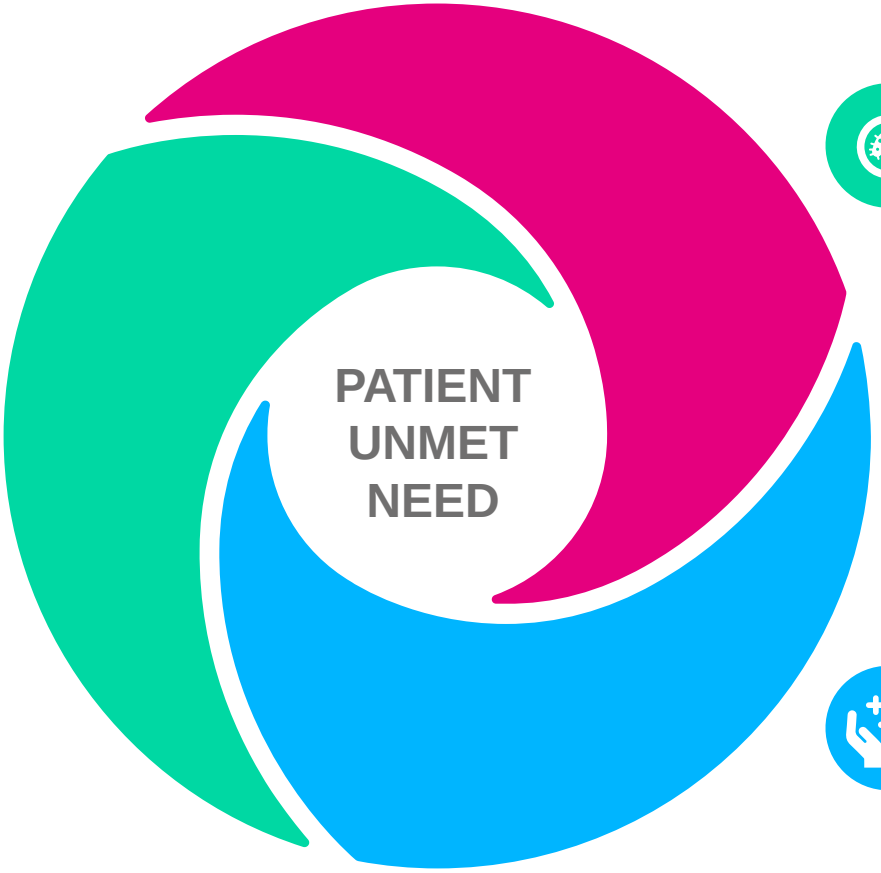
I am a full-time employee as well as a share and option holder of Summit Therapeutics

Summit's Approach: Innovation for the Patient

Translating novel science into differentiated products delivered to the patient



DISCOVER

- New classes of antibiotics
- Distinctive features and benefits
- Targeted spectrum preserves microbiomes
- Less prone to rapid resistance development

DEVELOP

- Clinical trial designs to test for unmet need
- Outcomes show superiority over standard of care
- Health economic measures demonstrate value of improved outcomes

COMMERCIALIZE

- Patients offered solution to unmet need
- Physicians have data to switch therapy
- Payors have data showing economic value
- Strong stewardship case to use new drugs

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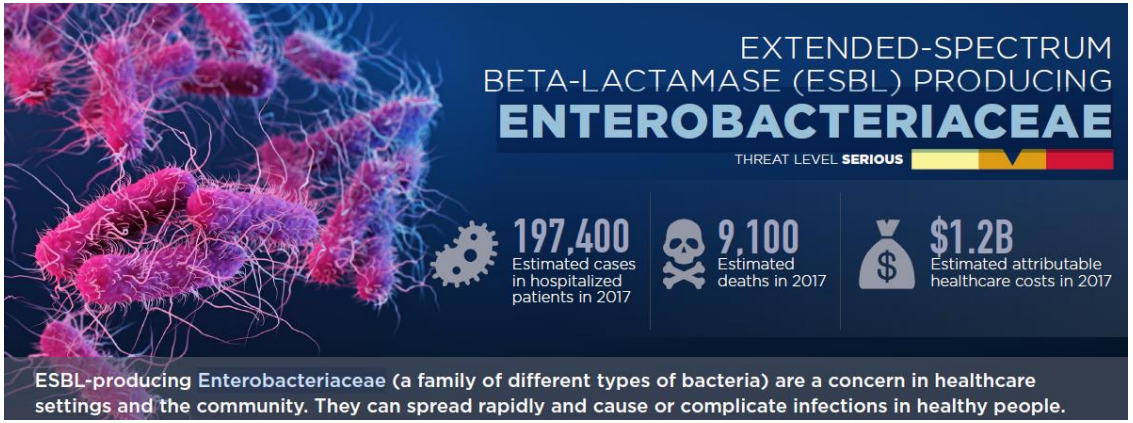
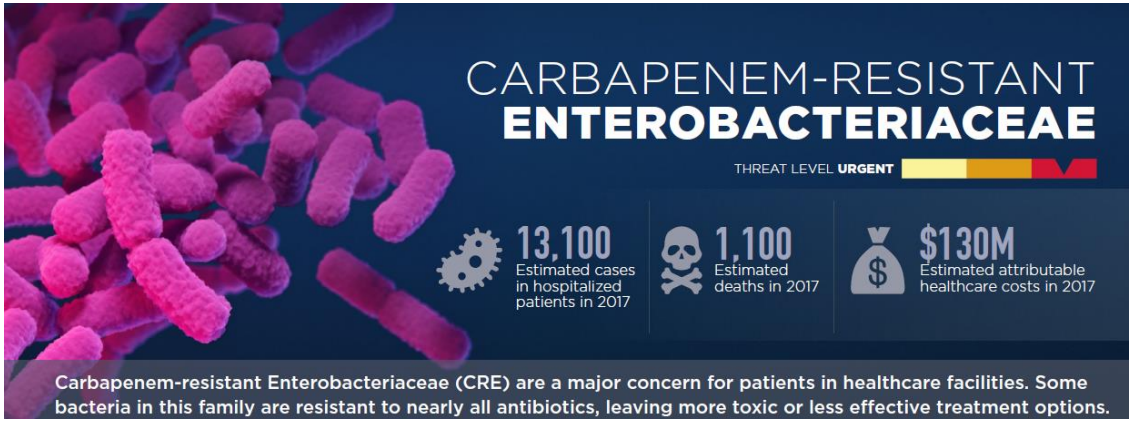
Enterobacteriaceae Infections Represent a Significant Unmet Medical Need



*

- CRE have been characterized as an urgent threat by the CDC
- Some CRE bacteria have become resistant to almost all available antibiotics

- CRE/ESBL producing Enterobacteriaceae cause a wide range of infections such as UTI/cUTI, bacteremia and HAP

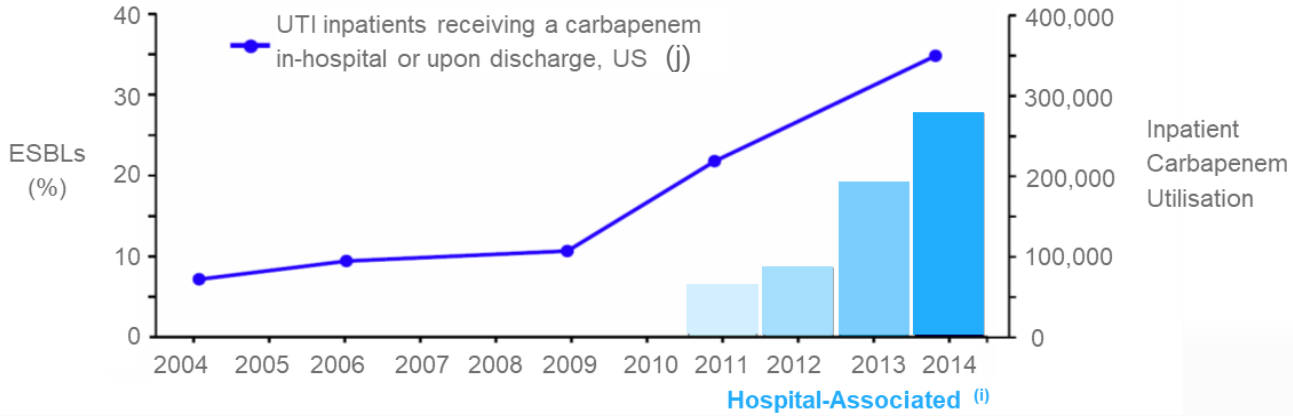


* Data from CDC 2019 Antibiotic Resistance Threats Report

Drug Resistant Enterobacteriaceae Infections Are Rising

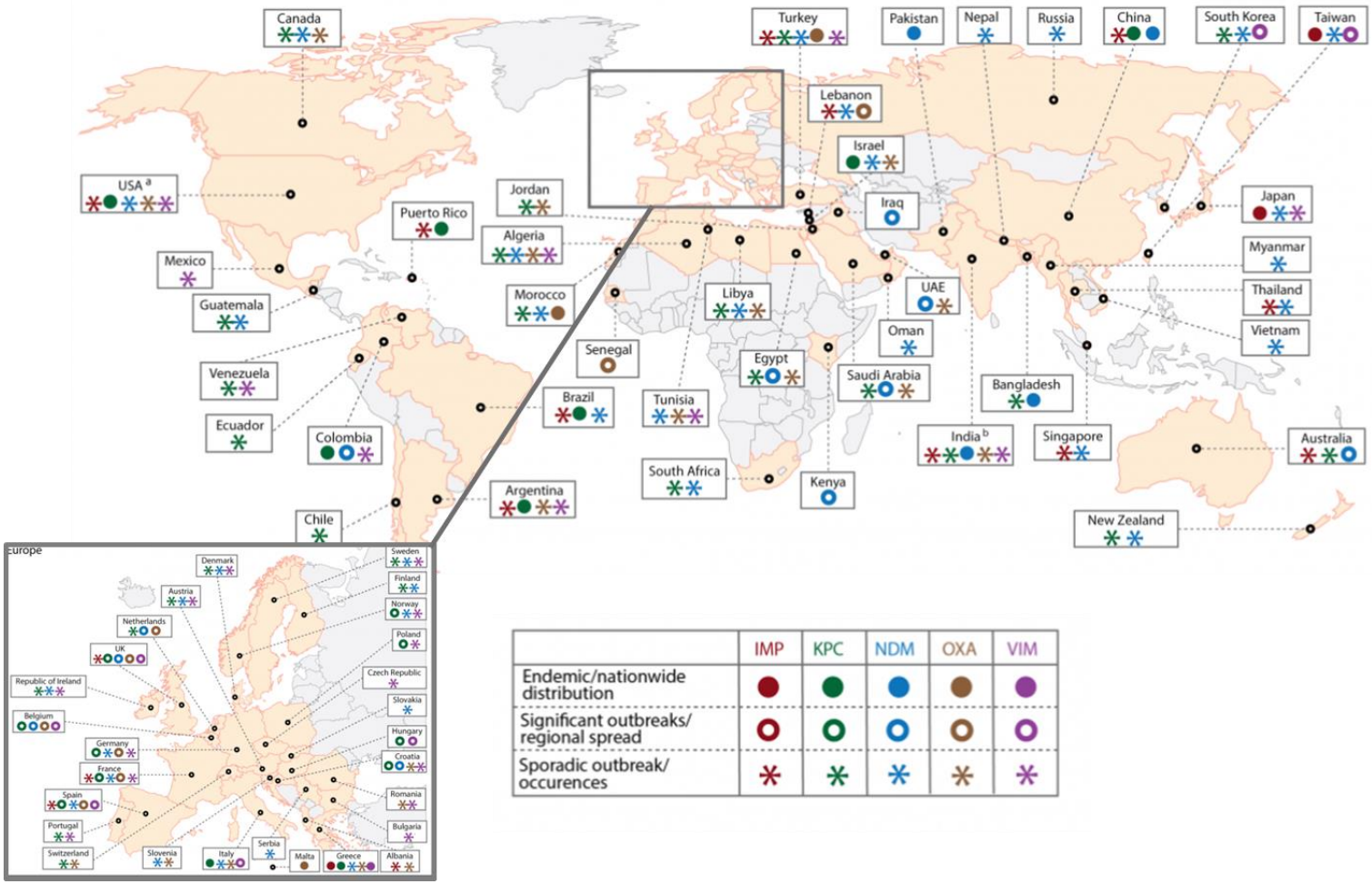
A Growing Cause of Healthcare-Associated Infections

Healthcare Associated Infection	EU incidence ('000s) †	US incidence ('000s) †	% Enterobacteriaceae
Pneumonia / Lower Respiratory Tract	861	250	27-30 [a,b]
Bloodstream	313	249	19-20 [c,d]
Urinary tract	888	562	62-75 [e-h]



† Europe incidence values from ECDC, 2011-2012, annual point estimates cited; US incidence values from Klevens, Public Health Reports, 2007.
Sources: (a) Sader et al, JAC, 2018; (b) Cilloniz et al, Int J Mol Sci, 2016; (c) NHSN 2014; (d) Magill, NEJM, 2018; (e) Flores-Mireles et al, Nat Rev Microbiol, 2015; (f) Wagenleher et al., WJU, 2012 ;(g) Magill et al, NEJM 2014; (h) Koningstein et al, PLOS One, 2014. (i) Lob et al. Diagn. Microbial Infect Dis. 2016. (j) Decision Resources AMR Hospital Antibiotic Market Guide; Data annualized from half-year datasets: 2004-H2, 2006-H2, 2009-H2, 2011-H1, 2014-H1

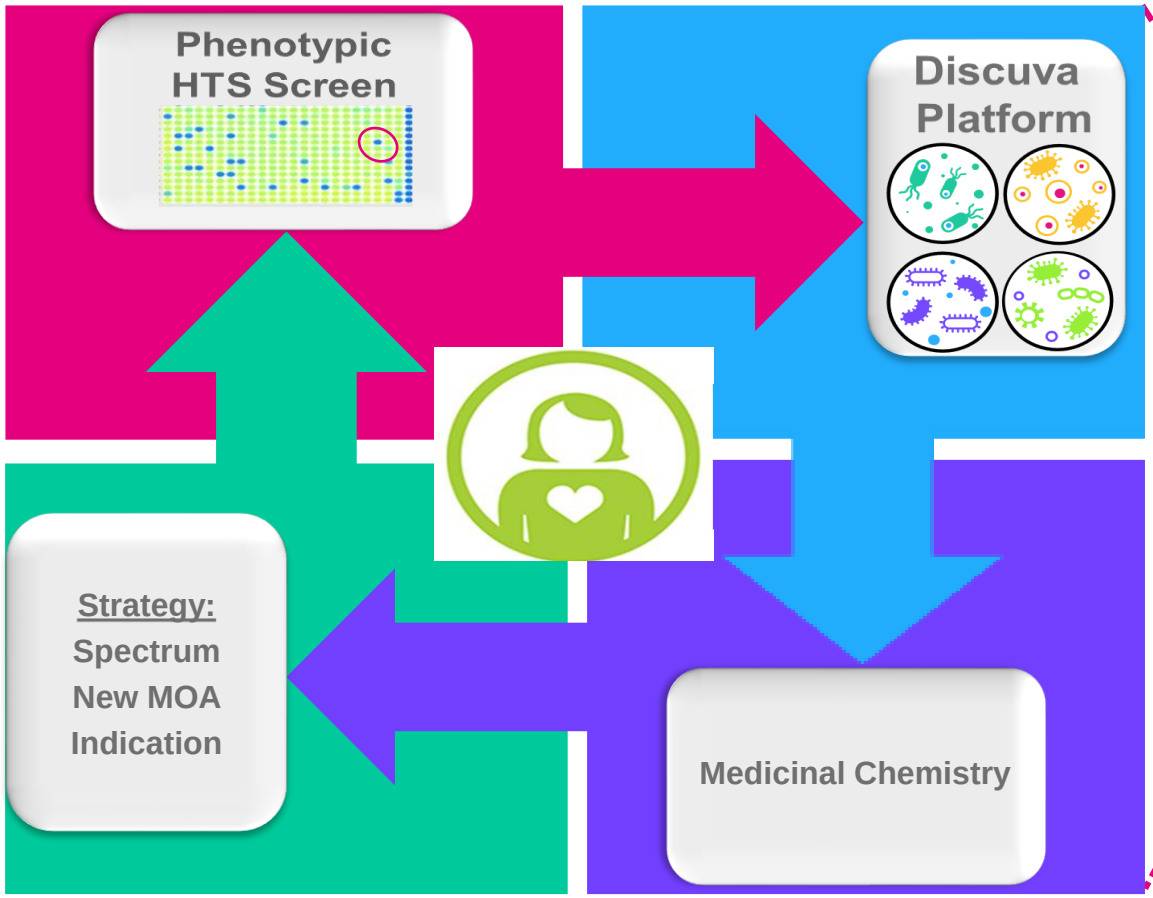
Distribution of Carbapenemases in Enterobacteriaceae Globally



Logan & Weinstein, The Journal of Infectious Diseases, Volume 215, Issue suppl_1, 15 February 2017, Pages S28-S36

Summit Discovery – Primed for New Mechanism Antibiotic Discovery

The perfect alignment of Strategy and Technology

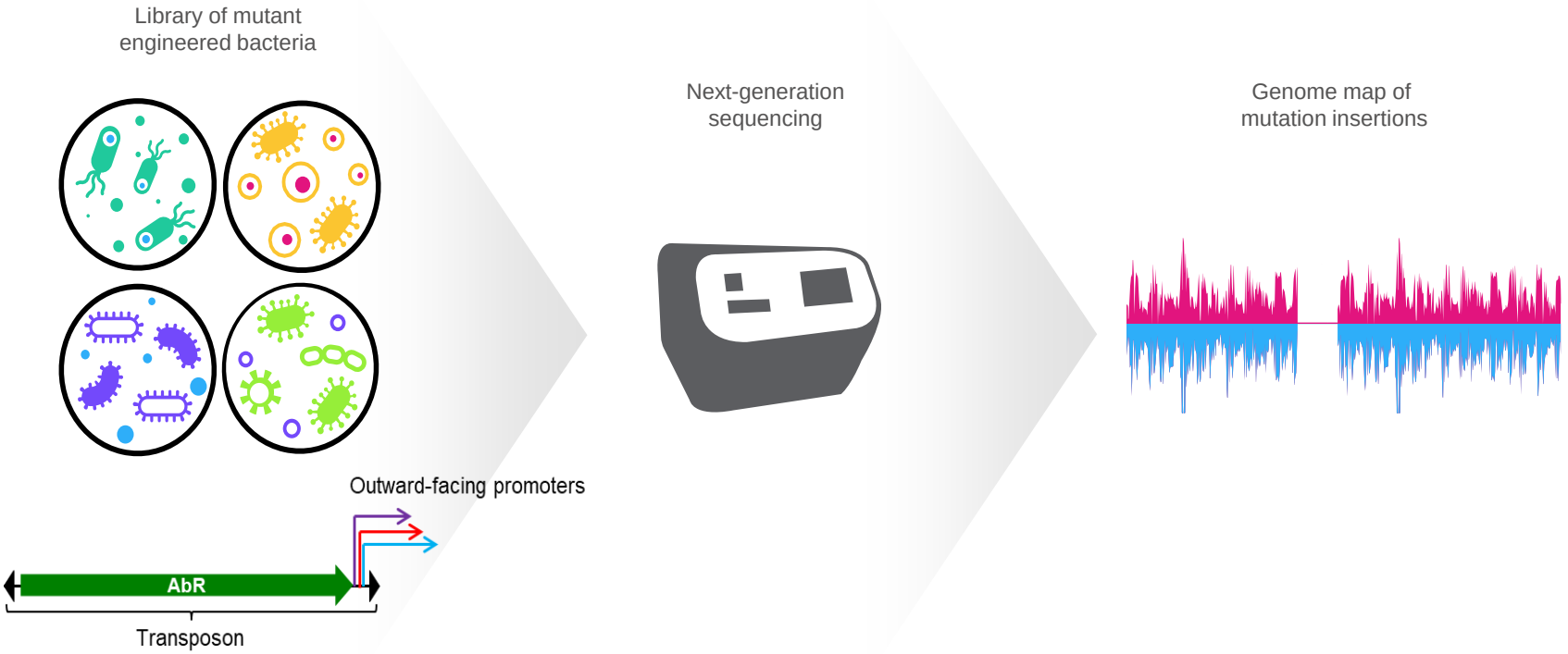


DDS-04 Series:

Enterobacteriaceae

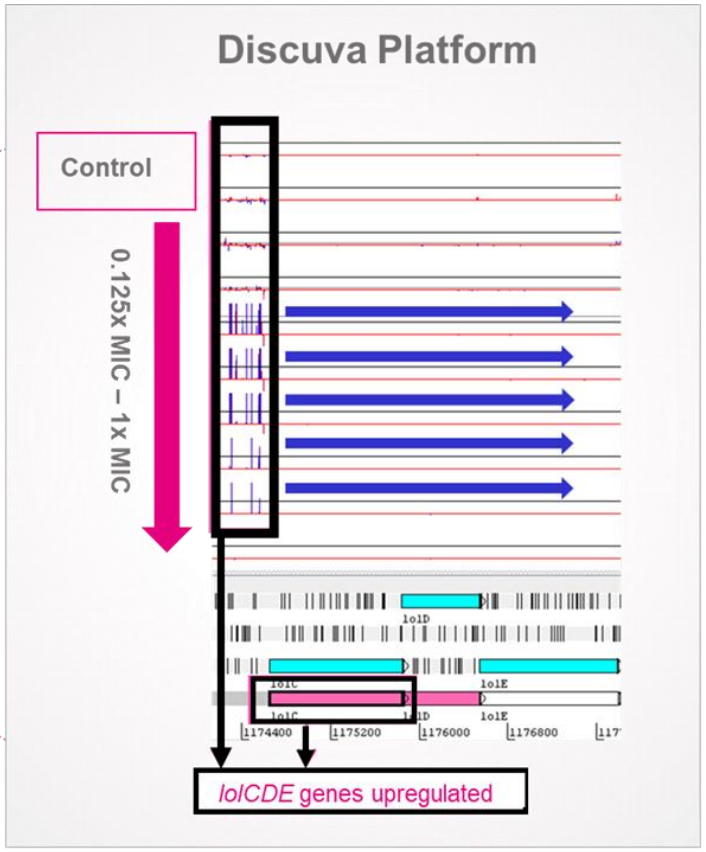
Discuva Platform

A combination of technologies and different functional expertise groups drives the Discuva Platform

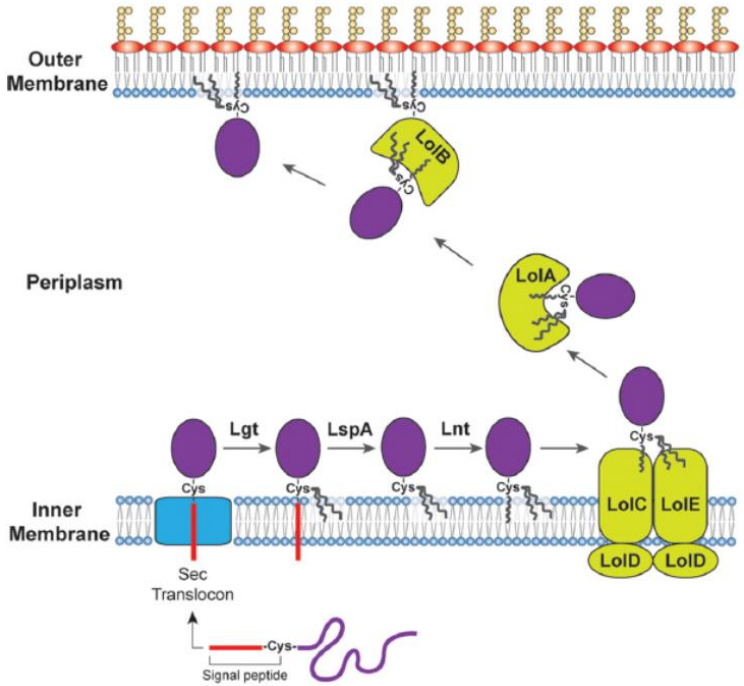


DDS-04 is a Novel LolC/E Lipoprotein Transport Inhibitor

HTS Hit



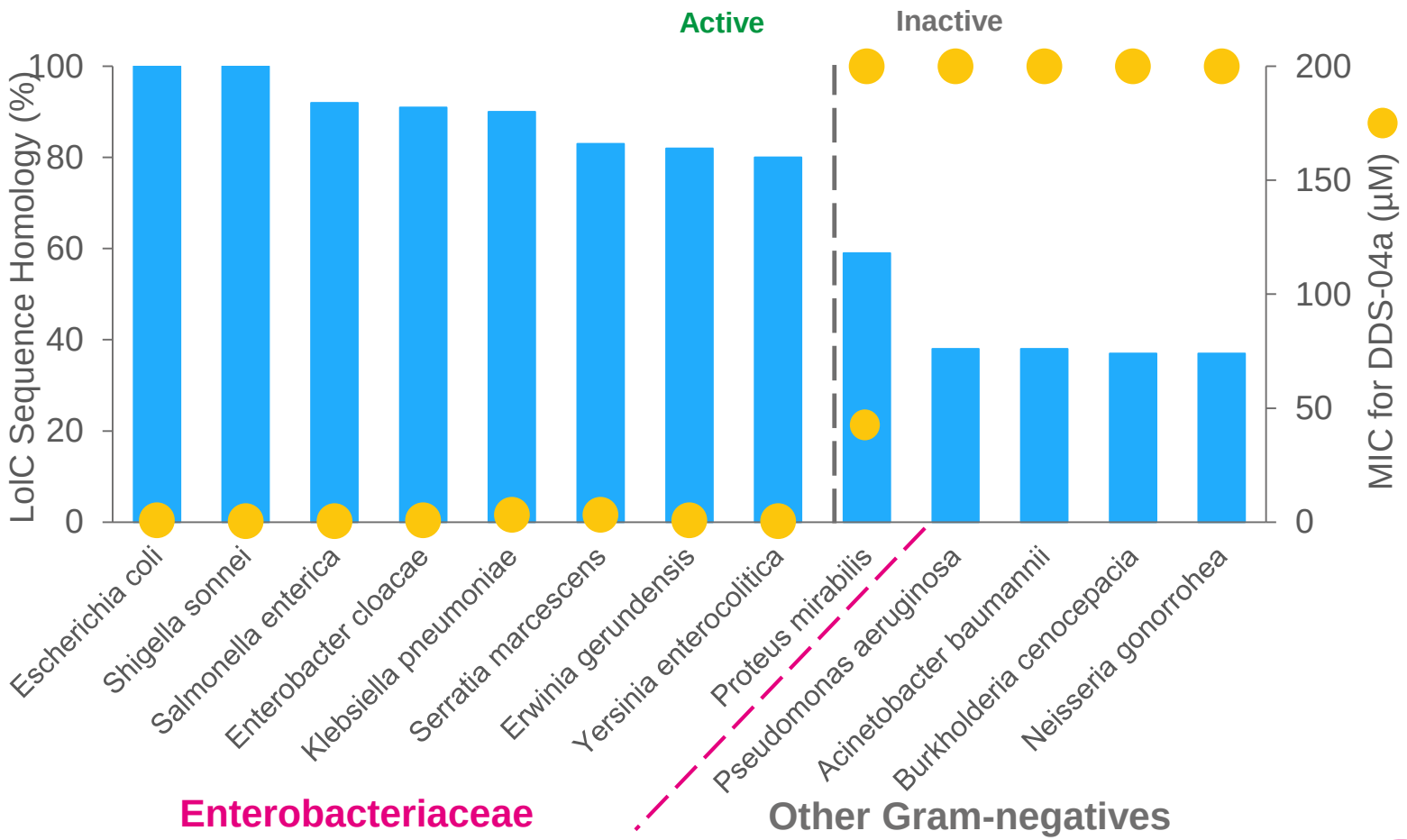
Chahales & Thanassi, 2015. J Bacteriol 197, 1702



LolCDE:

- Essential inner membrane ABC transporter in Gram negative bacteria
- Releases lipoproteins into the periplasm from the bacterial inner membrane

Sequence Homology Gives Enterobacteriaceae Specific Activity



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DDS-04 Series Exhibits Potent Activity Against a Globally Diverse Panel of Clinical Isolates

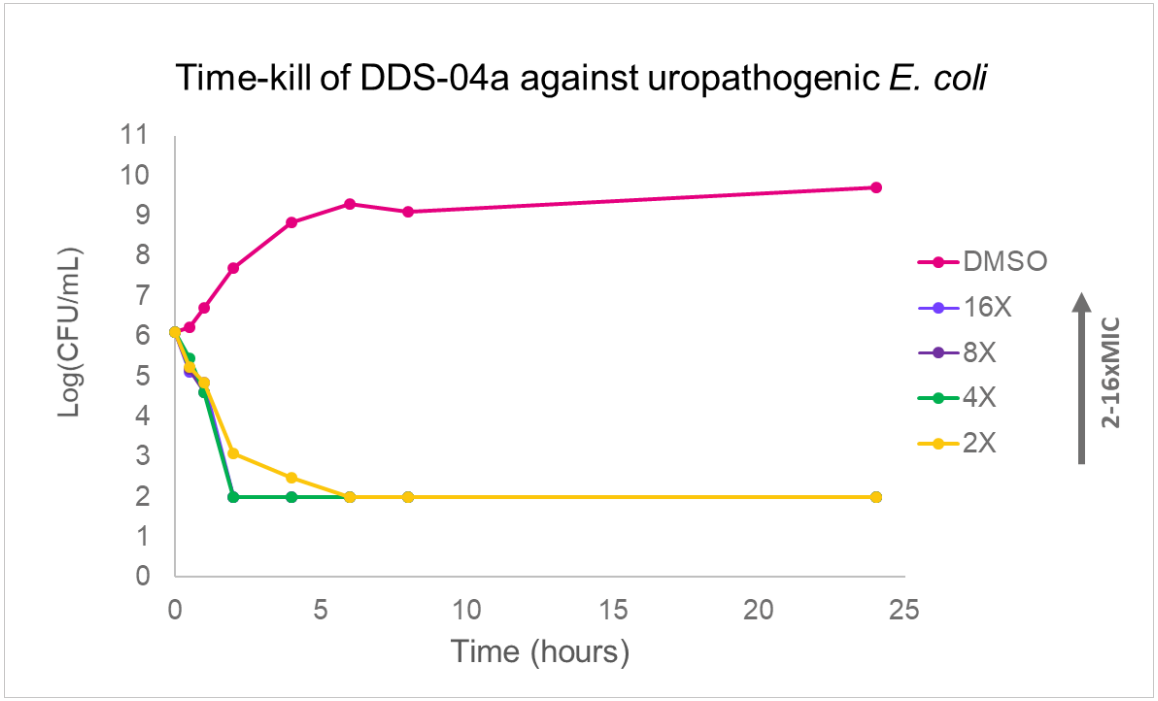
Panel of clinical *E. coli* and *K. pneumoniae* isolates

- Extended-Spectrum Beta-Lactamase (ESBL)
- Carbapenem Resistant Enterobacteriaceae (CRE)
- Fluoroquinolone Resistant (FQR)

	Range (µg/ml)		MIC_{90} (µg/ml)	
	E. coli	*K. pneumoniae*	*E. coli*	*K. pneumoniae*
DDS-04a	0.5 - 2	0.5 - 4	1	2
DDS-04b	0.5 - 1	0.5 - 2	0.5	1
DDS-04c	0.5 - 1	0.5 - 1	1	1
Nitrofurantoin	8 - 128	32 - >128	32	>128
Amoxicillin/Clavulanic Acid	2 - >32	1 - >32	>32	>32
Trimethoprim/Sulfamethoxazole	<0.5 - >16	<0.5 - >16	>8	>8
Ceftazidime/Avibactam	0.03 - >32	<0.015 - >32	1	1
Colistin	<0.06 - 4	<0.06 - >8	0.25	0.25

DDS-04 Displays Low Propensity for Resistance Development

- Frequency of resistance of 10^{-09} – 10^{-10} @ 4-16 x MIC
- Rapid bactericidal profile



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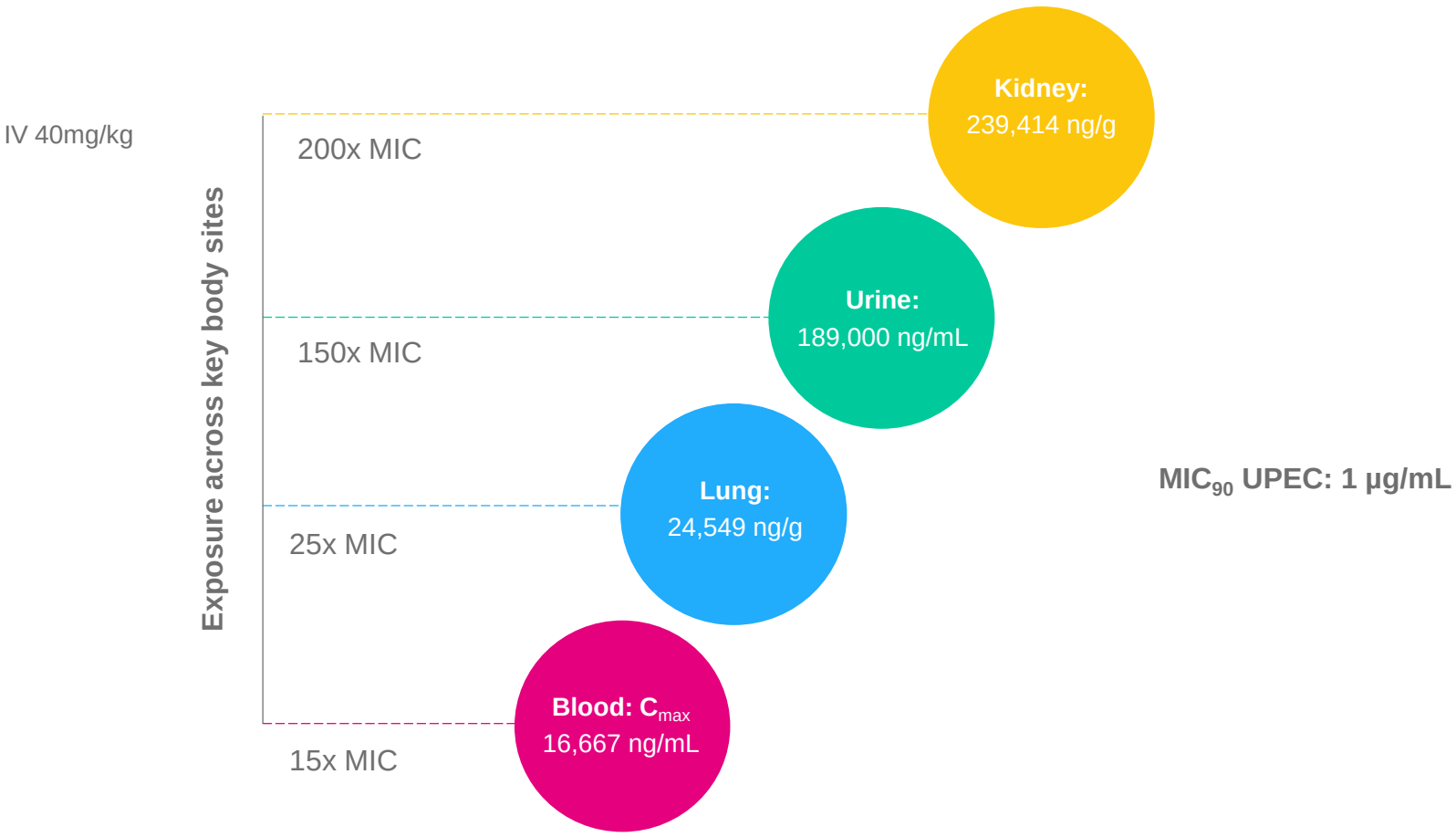
DDS-04a is Well Tolerated with Exposure at Key Infection Sites *In Vivo*

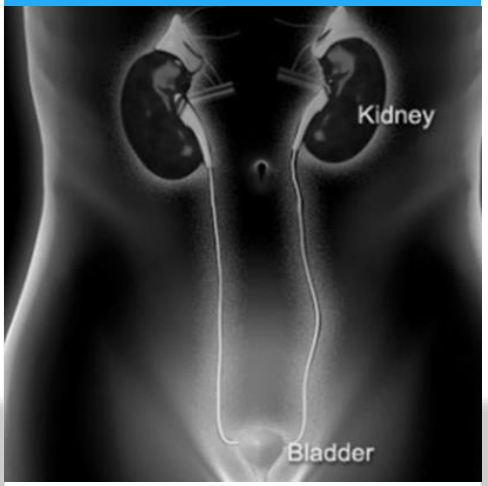


Three Potential Indications in One Drug

RESPIRATORY INFECTION PNEUMONIA

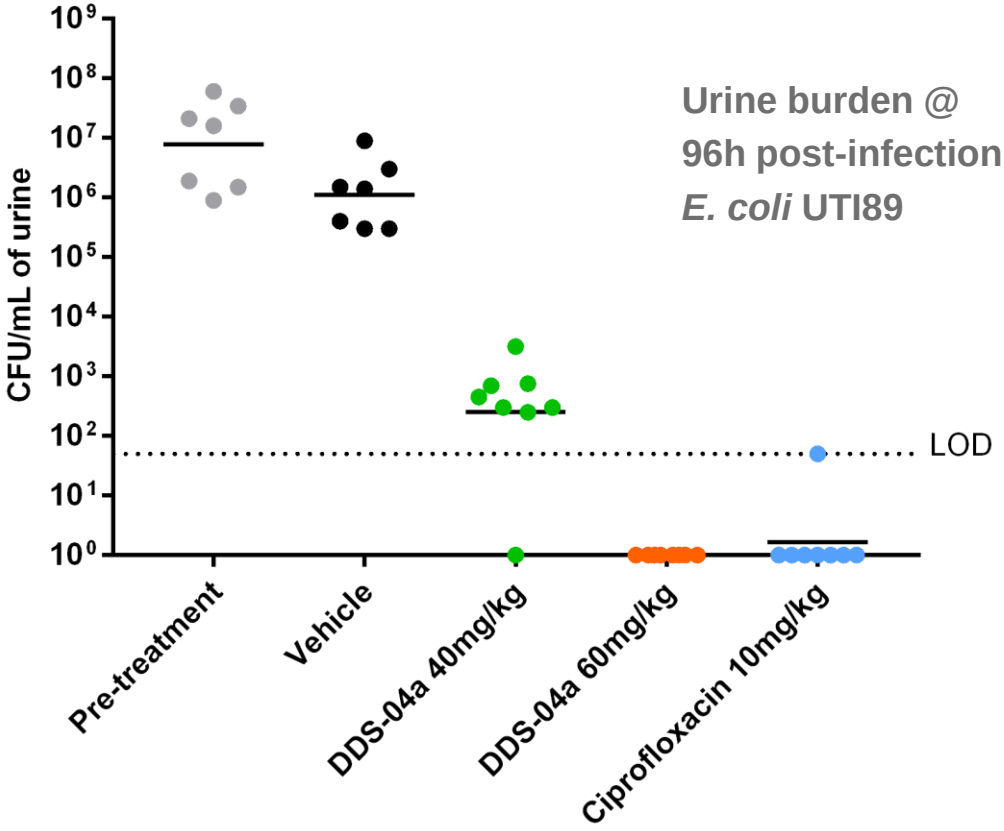
BLOOD STREAM INFECTION BACTERAEMIA/SEPSIS

URINARY TRACT INFECTION

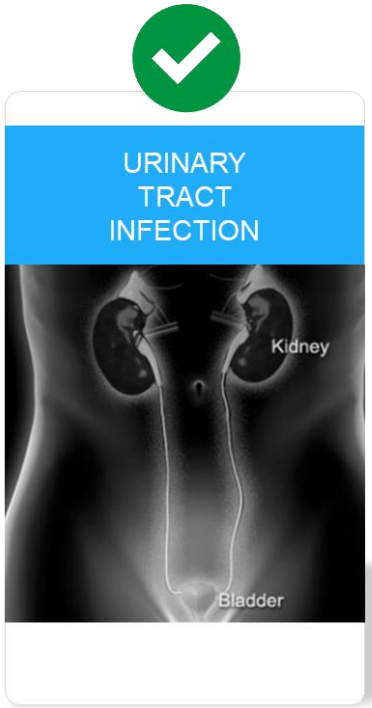


In Vivo Proof-of-Concept Achieved in a Murine UTI Model

Route/Regimen – IV TID over 3 days



Urine burden @
96h post-infection
***E. coli* UTI89**



Significant reduction in bacterial burden in the urine compared to vehicle

→ significant reduction also seen in kidney

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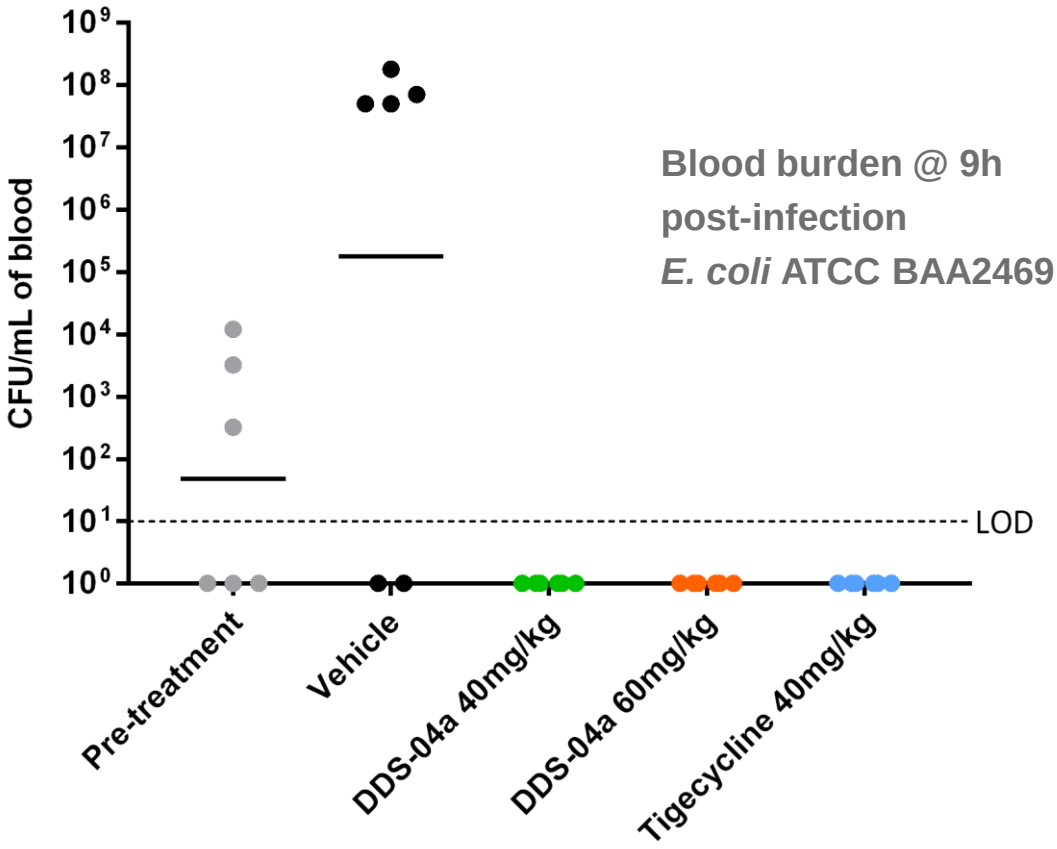
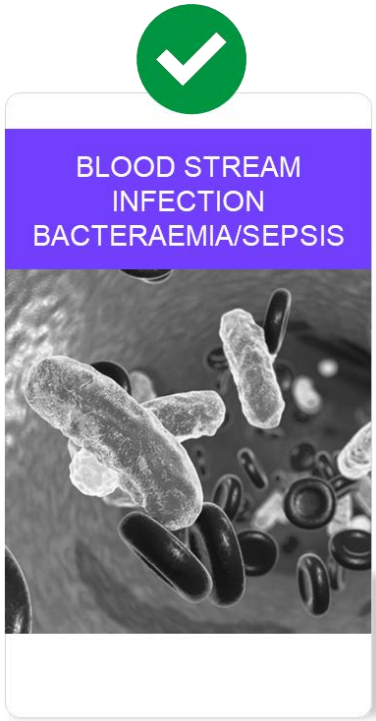
In vivo Proof-of-Concept Achieved in an Intraperitoneal Mouse Sepsis Model

Route/Regimen – IV TID over 9 hours



Blood burden @ 9h post-infection

***E. coli* ATCC BAA2469**



Significant reduction in bacterial burden in blood compared to vehicle

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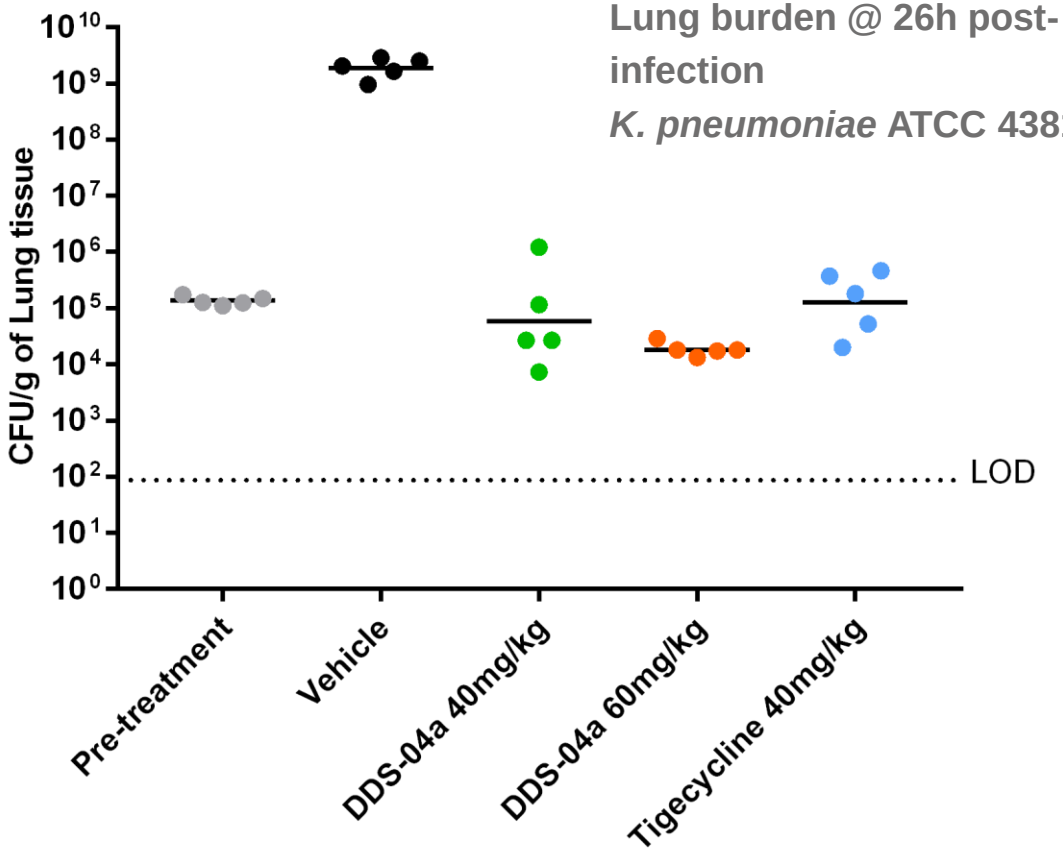
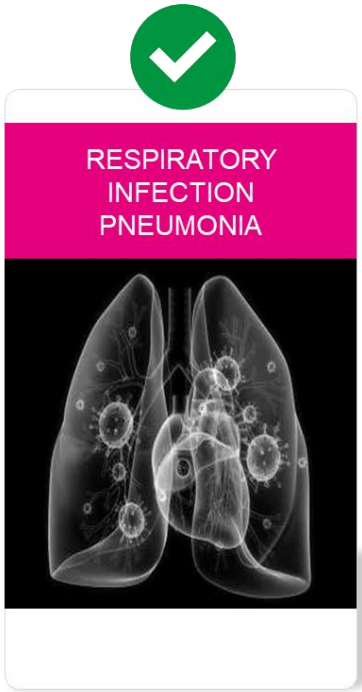
In Vivo Proof-of-Concept Achieved in a Murine Pneumonia Model

Route/Regimen – IV TID over 26 hours





Significant reduction in bacterial burden in lung tissue compared to vehicle

DDS-04: A First-in-Class Enterobacteriaceae Antibiotic Series

Programme Highlights

Novel MoA	✓	LolC/E clinically unexploited (powered by the Discuva Platform)
High Potency	✓	Potent activity against globally diverse clinical strains (Enterobacteriaceae); bactericidal profile
No Pre-Existing Resistance	✓	Very low propensity for resistance development; no cross-resistance with existing classes of antibiotics
PK Profile	✓	Drug exposure to key infection sites, including bloodstream, bladder, kidneys and lungs
Safety	✓	Pharmacological and safety properties that support advancement
Good *in vitro* / *in vivo* Correlation	✓	**Proof-of-Concept achieved in UTI, sepsis and pneumonia in *in vivo* murine models**

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