



**Novel Small-Molecule
Inhibitors of Bacterial Lipoprotein
Transport with Potent Antimicrobial
Activity against Enterobacteriaceae**

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Forward-Looking Statements and Disclosure

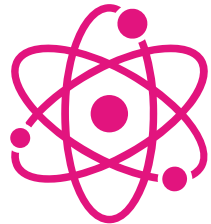
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I am a full-time employee as well as a share and option holder of Summit Therapeutics

Summit's Strategy: Innovation in Antibiotics

NEW SCIENCE



Using new science to discover
new mechanism antibiotics

Targeting a pathogen or an
infection

NEW PHILOSOPHY



Identify an unmet need

Aim to improve patient
outcomes and become the
standard

Designing clinical trials for
compelling datasets

NEW OPPORTUNITY



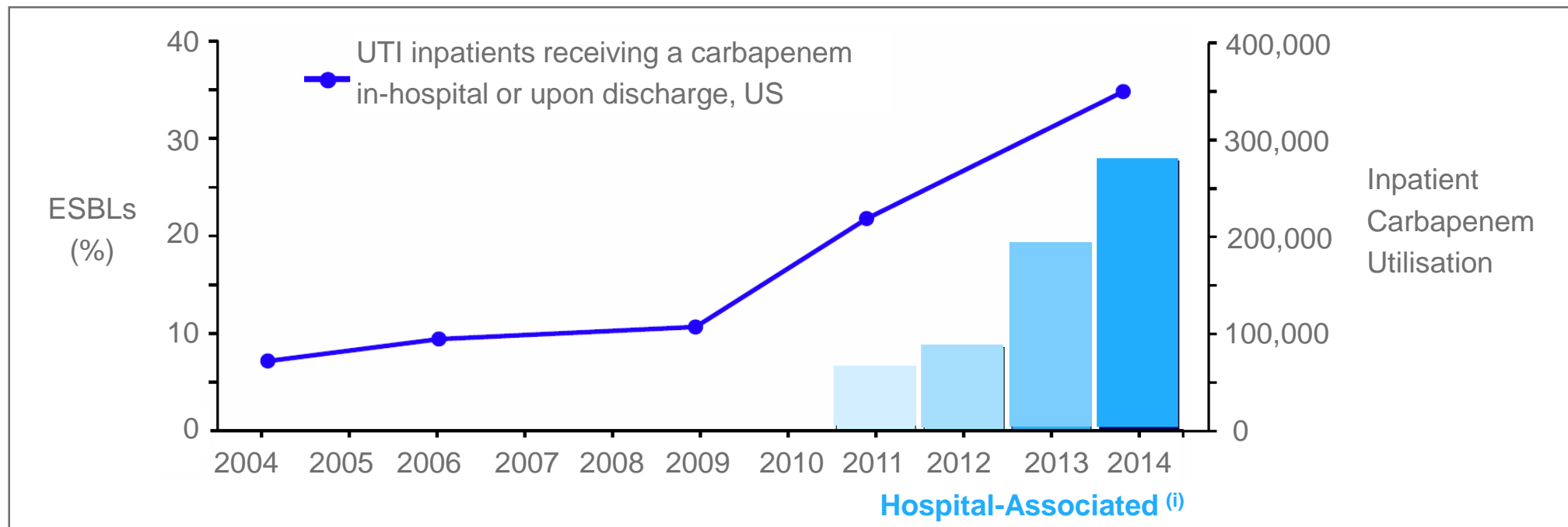
Delivering clinical and
economic data to support use

Support antimicrobial
stewardship

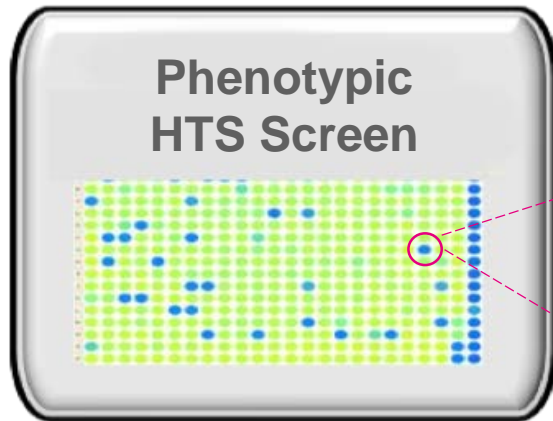
Enterobacteriaceae Infections

A Significant Cause of Healthcare-Associated Infections

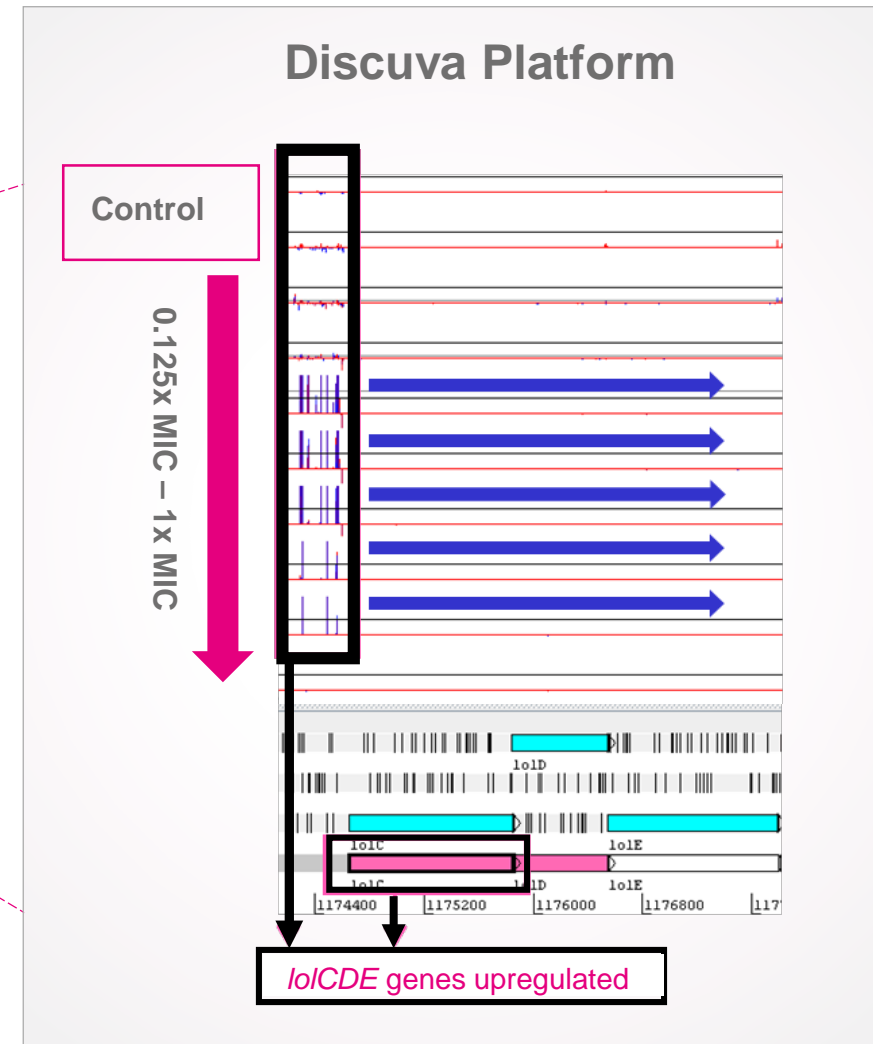
Healthcare Associated Infection	EU incidence ('000s) †	US incidence ('000s) †	% Enterobacteriaceae
Pneumonia / Lower Respiratory Tract	861	250	27-30 ^{a,b}
Bloodstream	313	249	19-20 ^{c,d}
Urinary tract	888	562	62-75 ^{e-h}



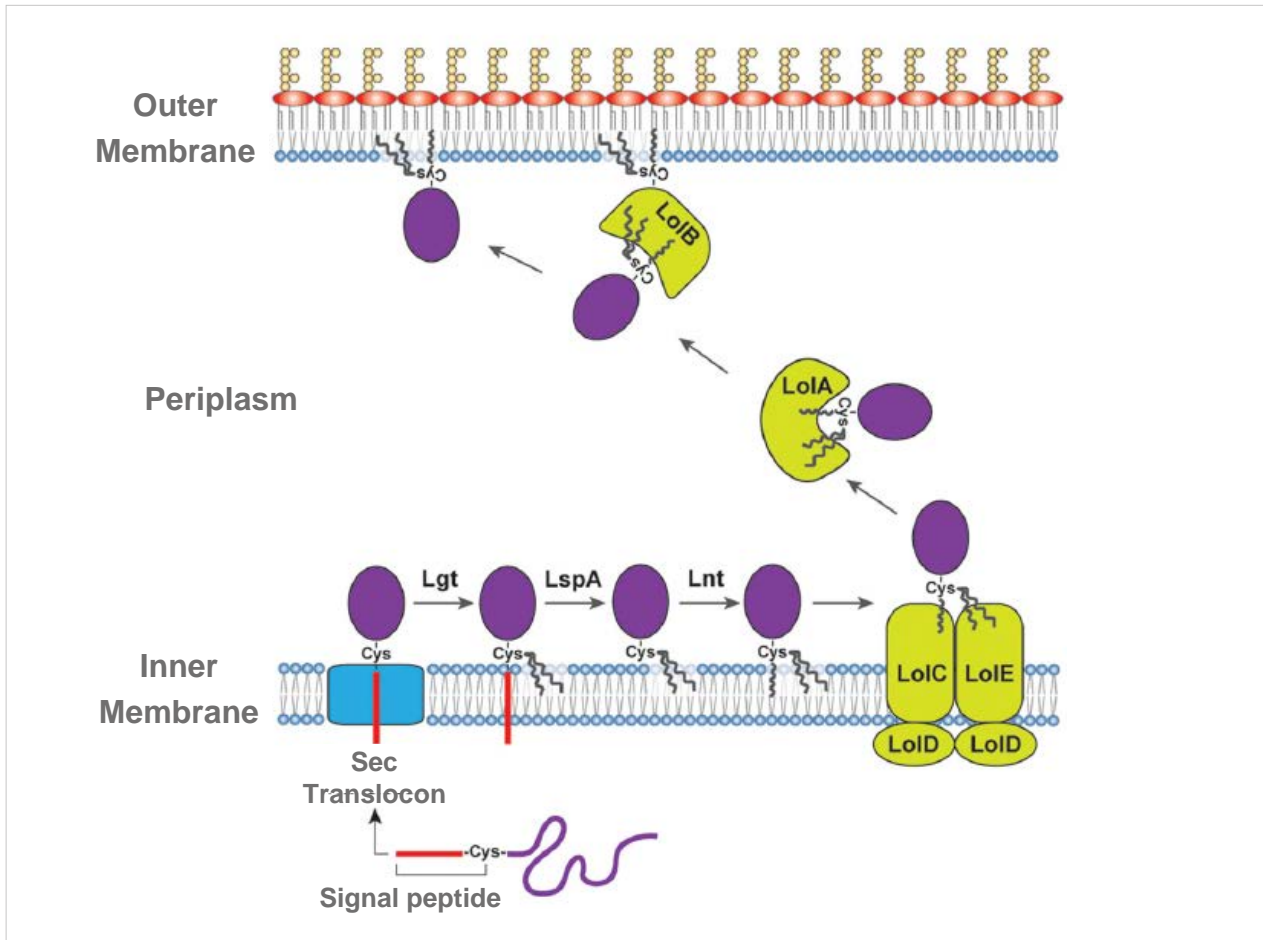
DDS-04: Novel Series with New Mechanism of Action



- Enterobacteriaceae specific
- Novel series with a new mechanism
- Powered by the Discuva Platform



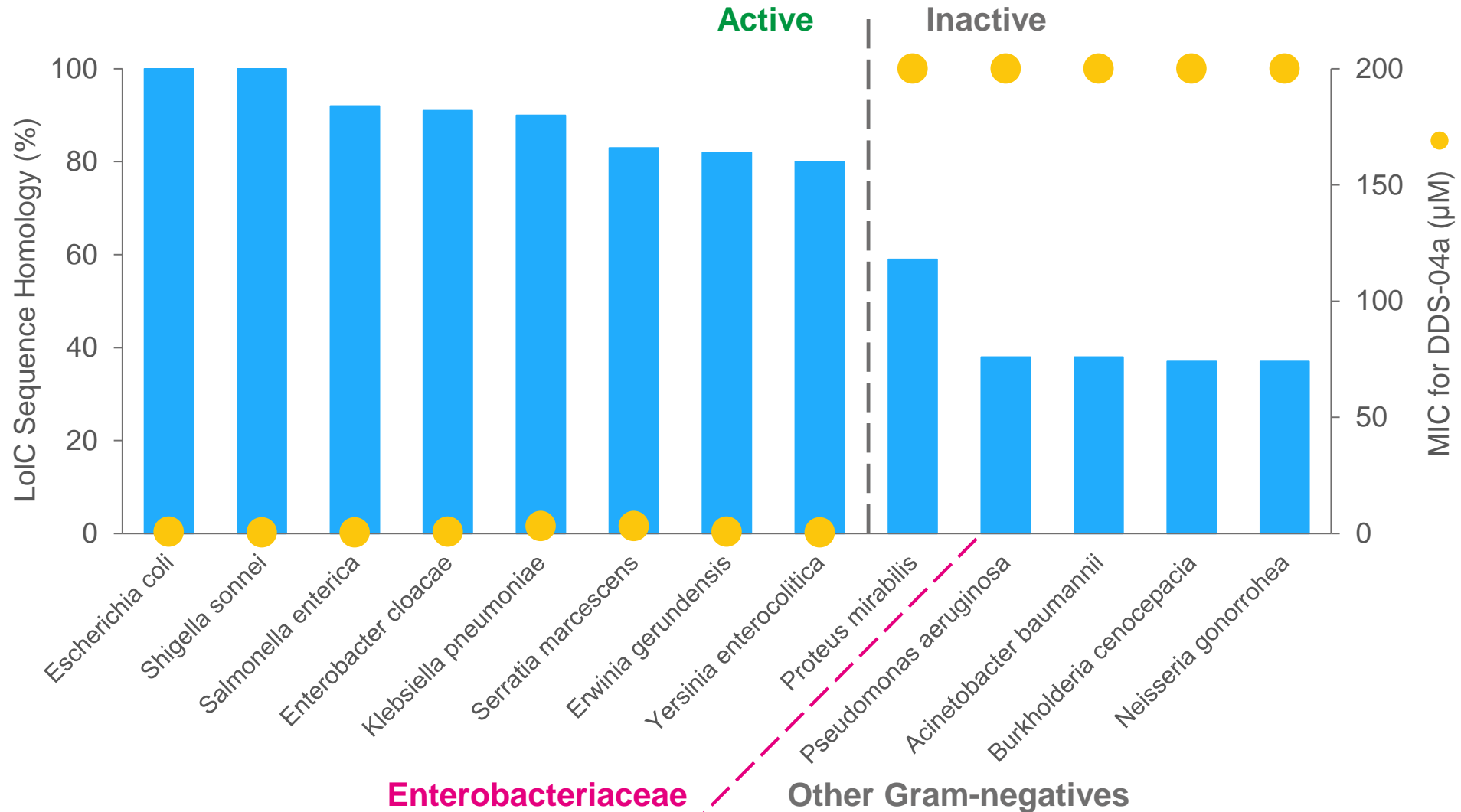
LoIC/E: Novel Clinically Unexploited Molecular Target



LoICDE:

- Essential inner membrane ABC transporter in Gram negative bacteria
- Releases lipoproteins into the periplasm from the bacterial inner membrane
- Protein sequence conserved within most Enterobacteriaceae

Sequence Homology Gives Enterobacteriaceae Specific Activity



Potent Activity Against a Globally Diverse Panel of Clinical Isolates

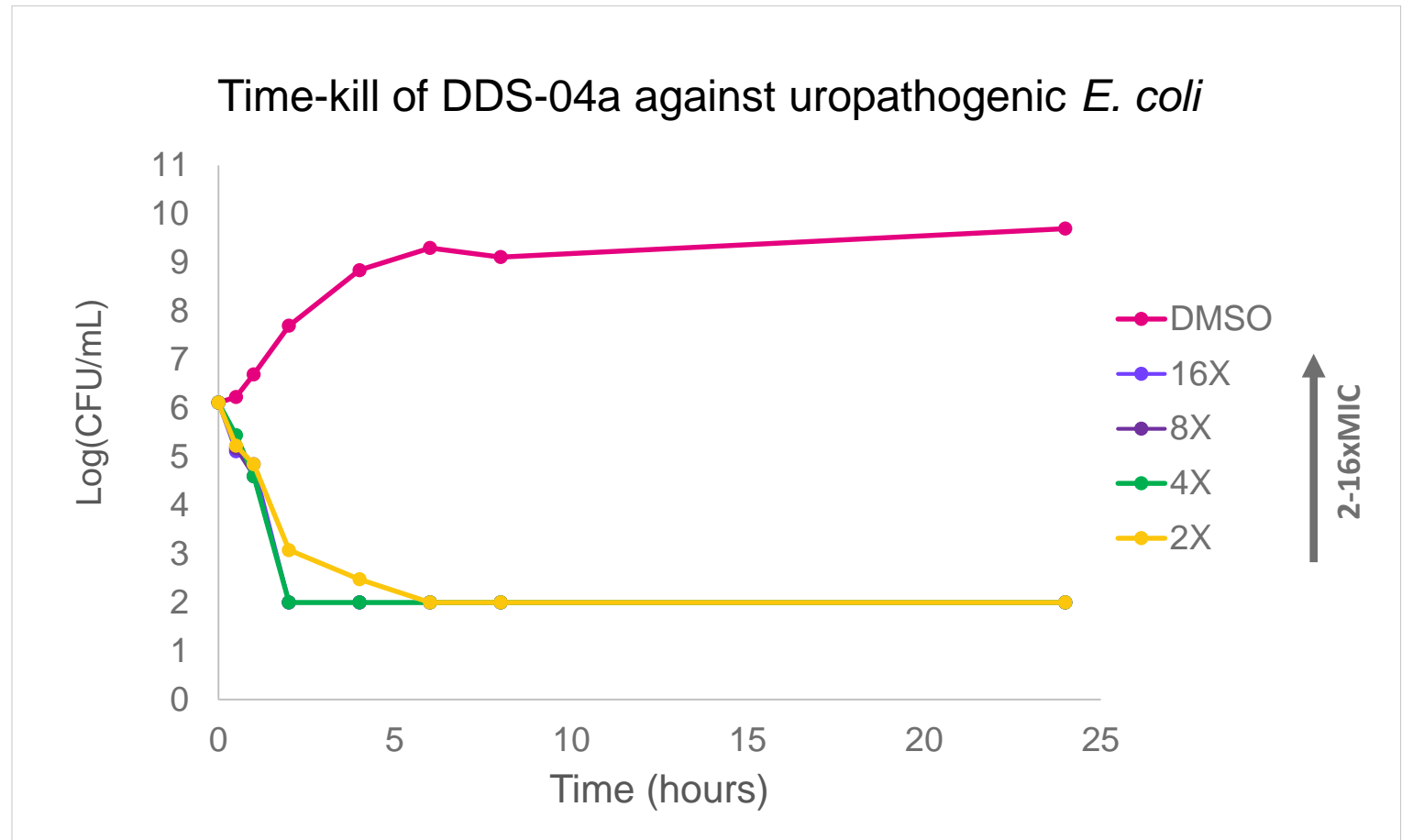
Panel of clinical *E. coli* and *K. pneumoniae* isolates

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

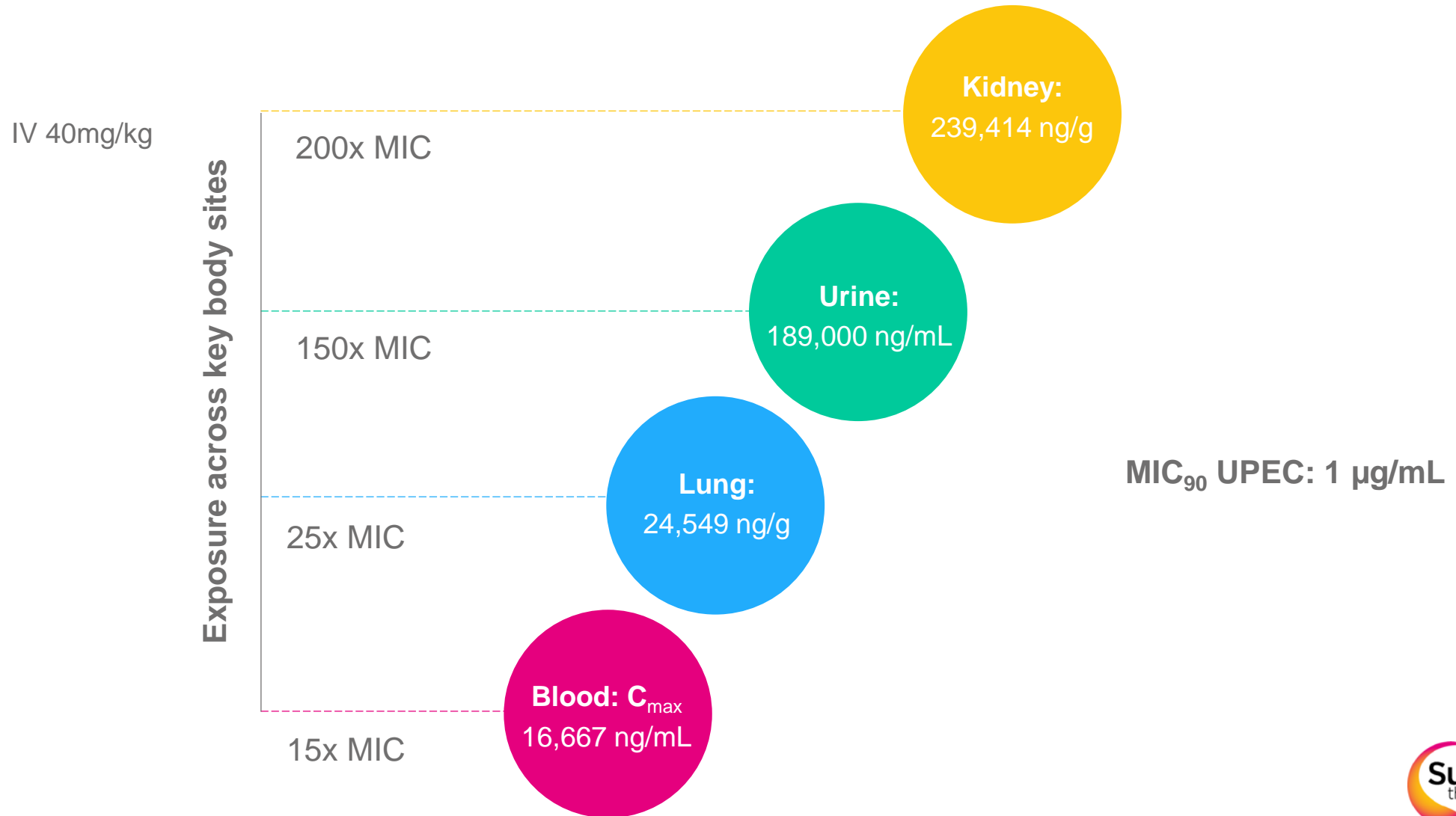
	Range (µg/ml)		MIC ₉₀ (µg/ml)	
	<i>E. coli</i>	<i>K. pneumoniae</i>	<i>E. coli</i>	<i>K. pneumoniae</i>
DDS-04a	0.5 - 2	0.5 - 4	1	2
DDS-04b	0.5 - 1	0.5 - 2	0.5	1
DDS-04c	0.5 - 1	0.5 - 1	1	1
Nitrofurantoin	8 - 128	32 - >128	32	>128
Amoxicillin/Clavulanic Acid	2 - >32	1 - >32	>32	>32
Trimethoprim/Sulfamethoxazole	<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

Low Propensity for Resistance Development

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

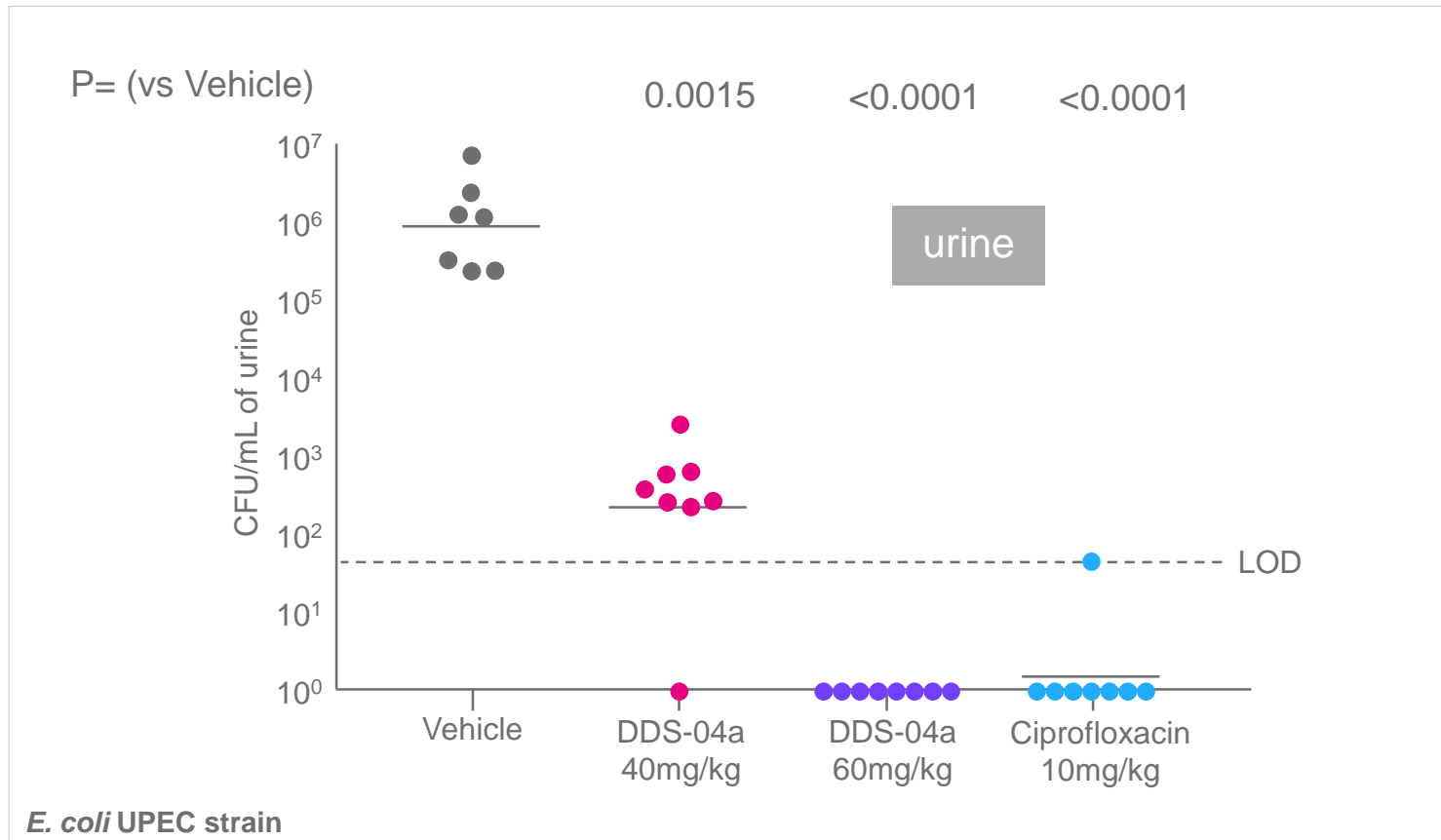


DDS-04a is Well Tolerated with Exposure at Key Infection Sites *In Vivo*



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

Route/Regimen – IV TID over 3 days

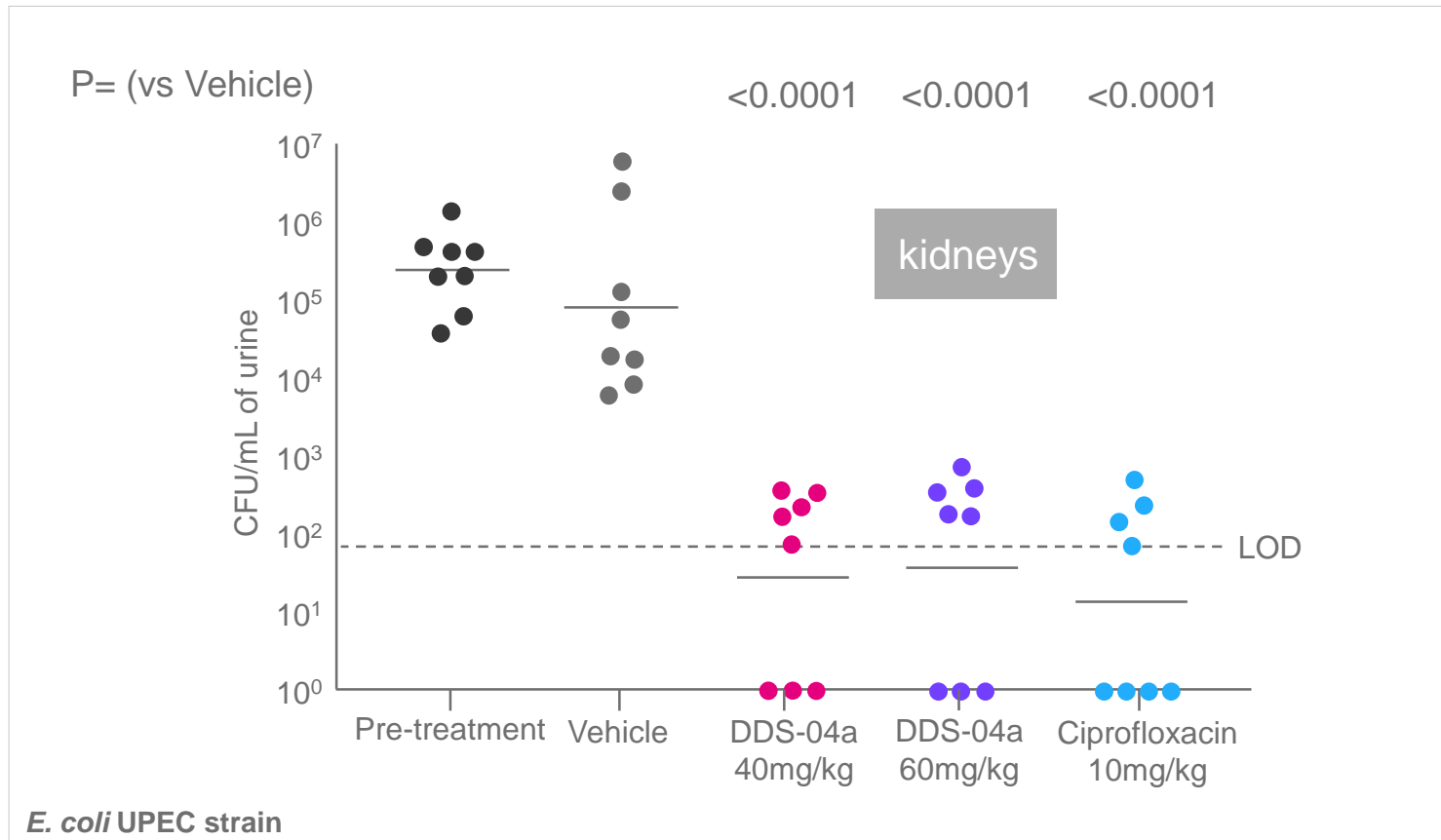


Significant reduction in bacterial burden in the urine

Data generated by Evotec, United Kingdom

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

Route/Regimen – IV TID over 3 days



Significant reduction in bacterial burden in the kidneys

Data generated by Evotec, United Kingdom

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

Programme Highlights

Novel MoA	✔ LoIC/E clinically unexploited (powered by the Discuva Platform)
High Potency	✔ Excellent 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	✔ Excellent drug exposure in the bloodstream, bladder, kidneys and lungs
Safety	✔ Good pharmacological properties and safety profile
Good <i>in vitro</i> / <i>in vivo</i> Correlation	✔ Efficacious with complete clearance of bacterial burden in a UTI <i>in vivo</i> model

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