WORLD AMR
ANTIMICROBIAL RESISTANCE
CONGRESS

# Breaking the Paradigm For New Anti-Infectives

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Recce
Pharmaceuticals

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recce.com.au

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# Lack of Novel/Effective Antibiotics in Development

***Why can't we have an antibiotic which doesn't create resistance?***

**~27 antibiotics** under development in clinical trials against pathogens considered **critical** by World Health Organisation such as *Acinetobacter baumannii* and *Pseudomonas aeruginosa*.

**6**
**out of 27**

'**innovative**' enough to overcome **antibiotic resistance** using WHO criteria

**2**
**of the 6**

target **highly-drug resistant** forms of microbes

**4**
**of the 27**

***may*** have a new mechanism of action; no new drug classes since the 1980s

The **current economic model** for developing new antibiotics **has failed**

Virtually **no practical economic incentives** and most **regulatory authorities have NOT prioritized**

**Antibiotic R&D** is now primarily **driven by small biotech companies**

# About Recce Pharmaceuticals Ltd

***"To address the global health threat of antimicrobial resistance with a revolutionary portfolio of synthetic anti-infectives"***

- Recce Pharmaceuticals Ltd (ASX: RCE, FSE: R9Q) is developing a new class of Synthetic Anti-Infectives, protected by Composition of Matter Patents
- **Australian clinical-stage biotech company**, with a United States presence
- **Strong pre-clinical data package** demonstrating **high bactericidal activity** combined with **very good safety** at expected human therapeutic range
- Now in **Clinical Studies as an I.V. as well as topical liquid/gel**
- **Qualified Infectious Disease Product designation**
  - 10 years market exclusivity plus fast track approval*
- RECCE® 327 (main product candidate) has been included in **The Pew Charitable Trusts Global New Antibiotics in Development Pipeline** as the world's only synthetic polymer and sepsis drug candidate in development

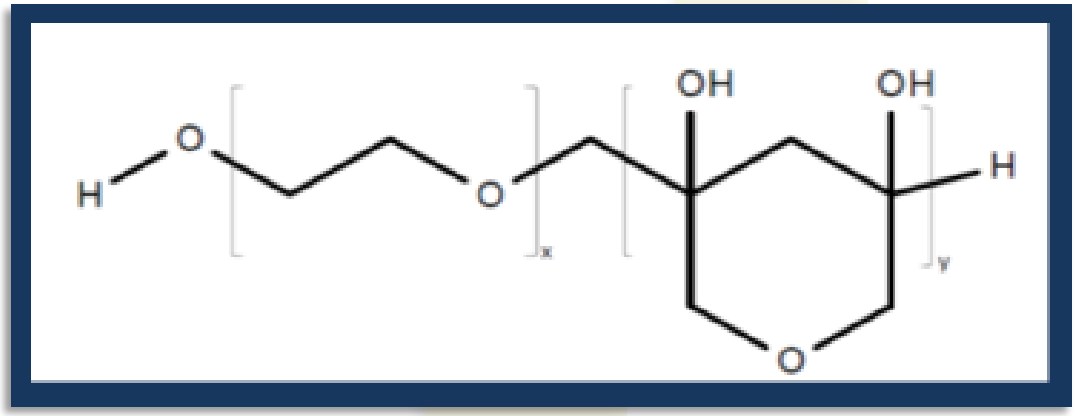



**Awarded by the US FDA in 2017 for R327 bacteraemia (broad-spectrum bacterial sepsis). Time starts only from potential market approval.*

# What is the RECCE® platform technology?

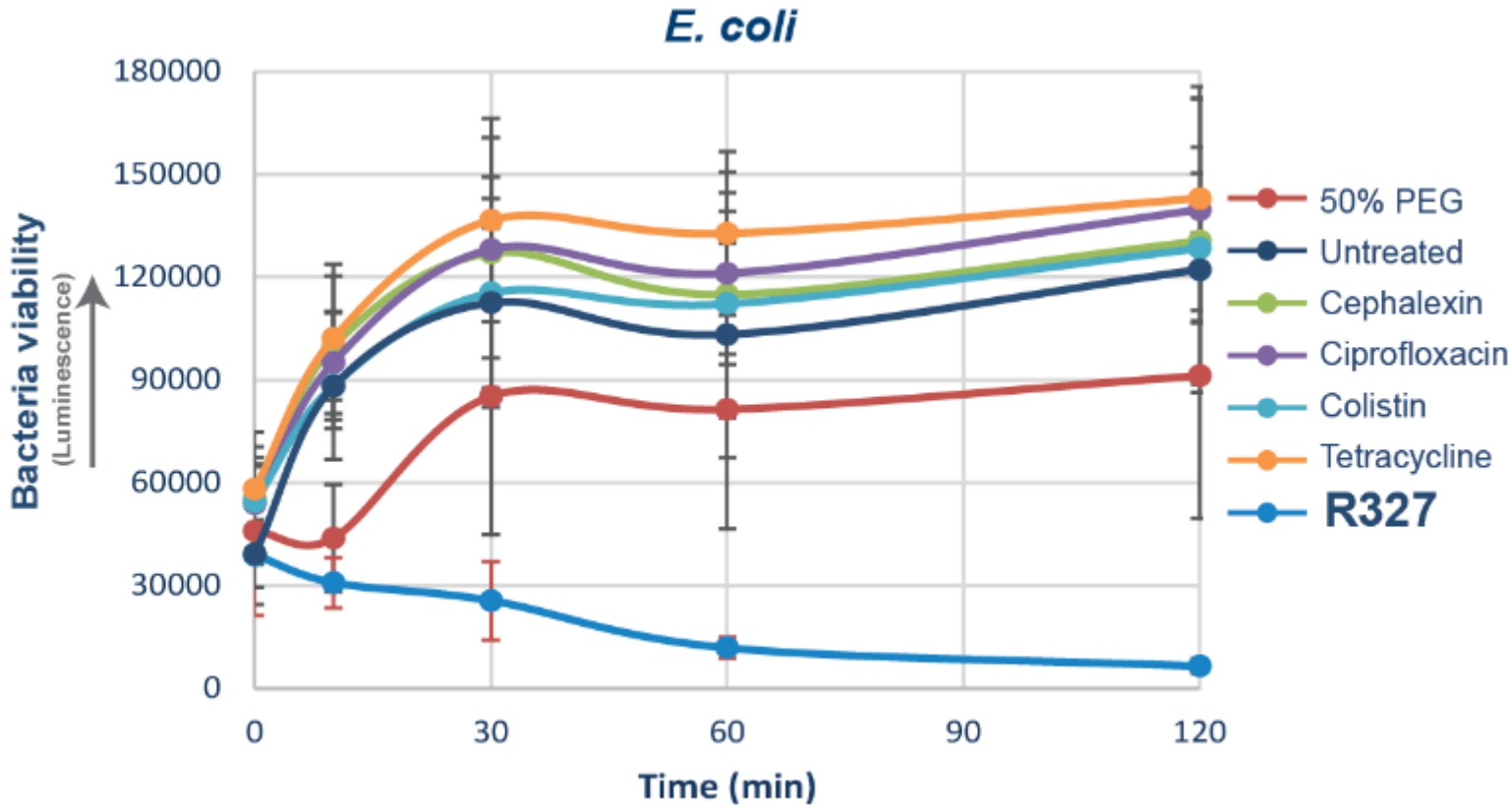
- Synthetic antibiotics, **not derived from nature - limited risk of resistance.**
- Derived from **polymer chemistry expertise** and vision of the founder, Graham Melrose, PhD.
    - Former Executive Director and Head of Research at Johnson & Johnson Australasia
    - Responsible for all research and new product development
    - Advanced several transformative medical technologies in the Infectious Diseases space
    - Head Consultant to all Research Directors, Johnson & Johnson organisations
- A stable, safe, hydrophilic and highly efficacious polymer.
- 100% Soluble at all pH's – even to the very acidic (low) pH of the stomach.

***Basic structure***



# RECCE® 327 Faster Acting than Existing Antibiotics

***No prolonged exposure needed, minimizing possibility of toxicity.***

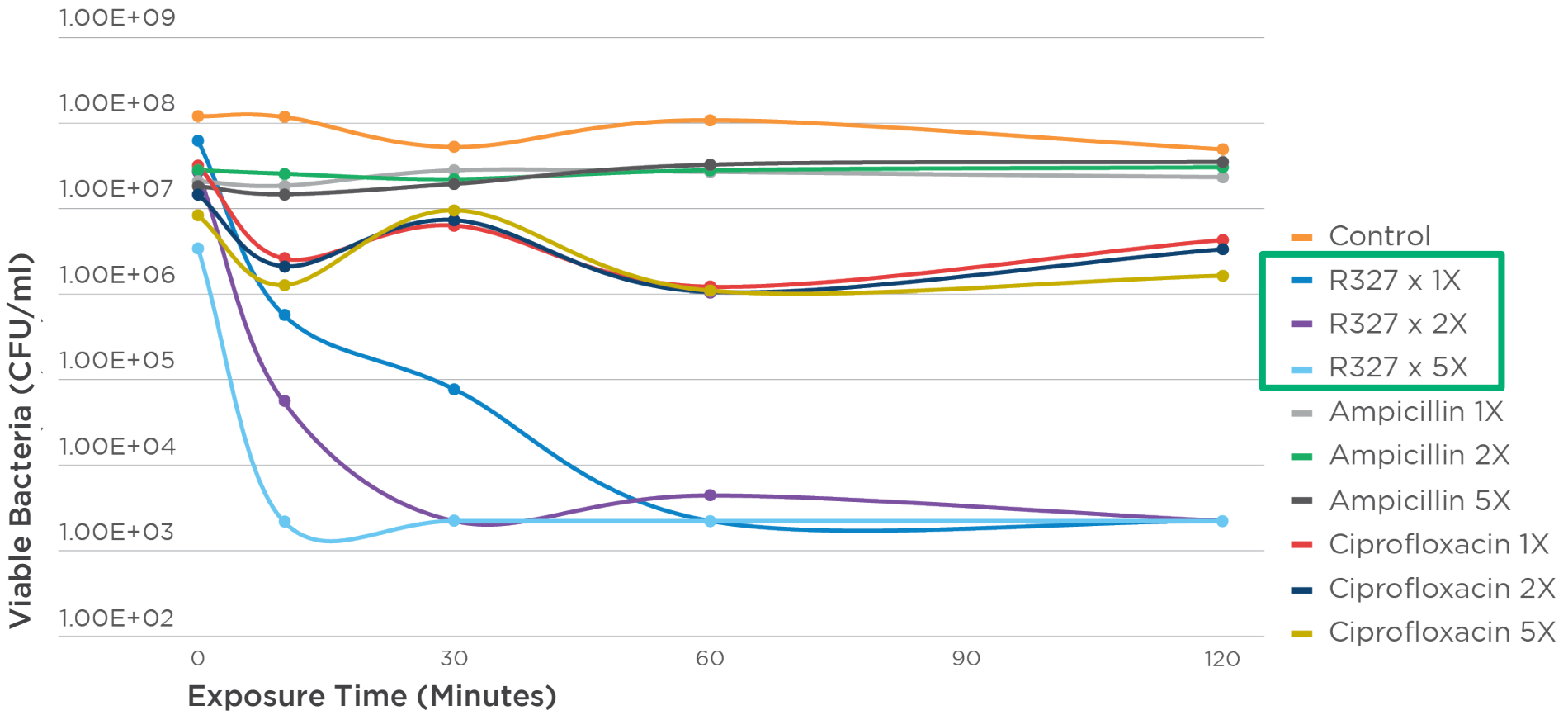



***Activity seen in just 10 minutes***



**Xen14 (a reduction in luminescence correlates with decrease in cell viability)*
**All compounds used at 2X Minimum Inhibitory Concentration (MIC)*

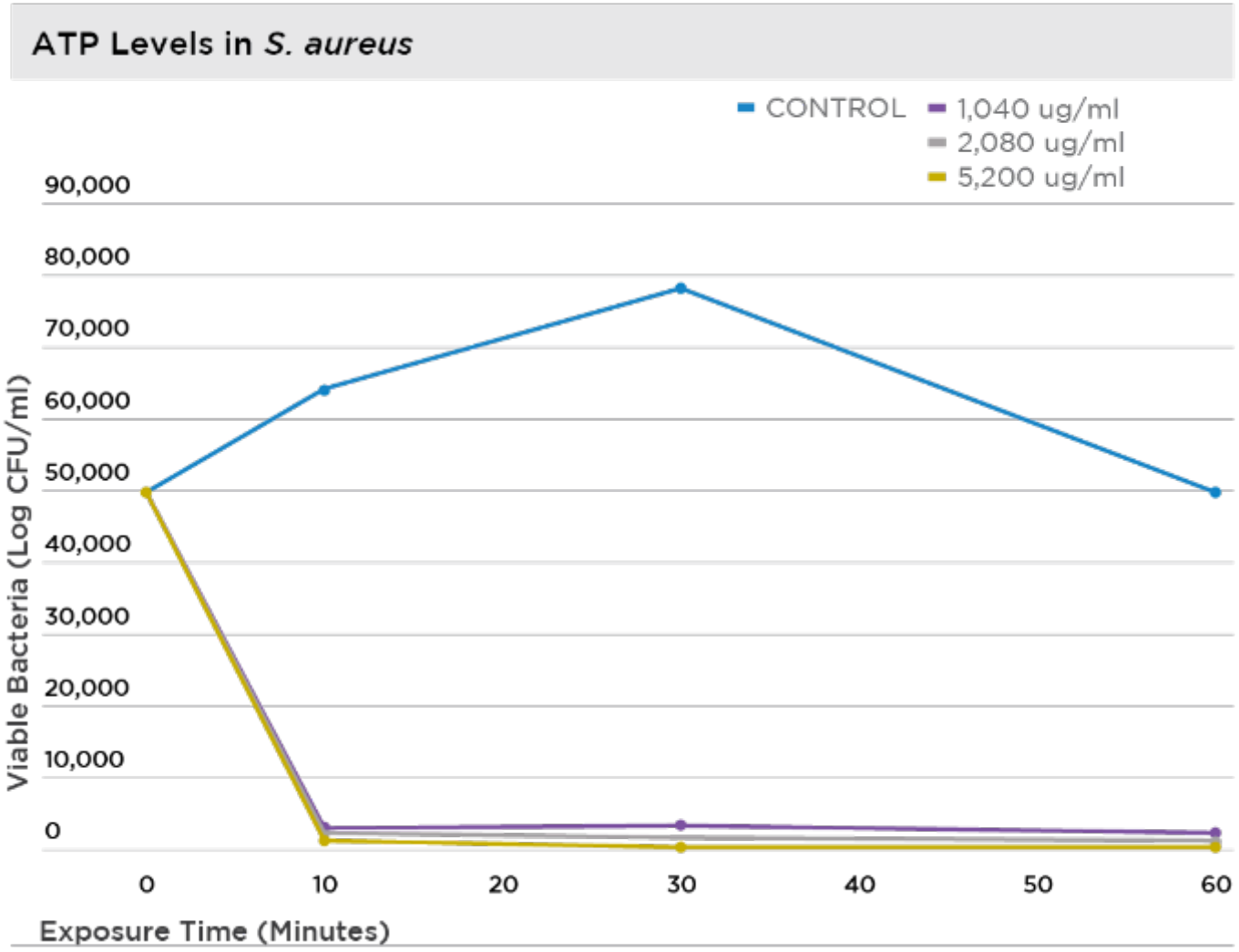
# RECCE® 327 Rapidly Kills Non-growing *E. coli* ATCC 25922




***"Many antibiotics will not kill non-growing cells… R327 kills non-growing cells and kills them very rapidly and irreversibly"***

***Marc Sharp, PhD,***
***Chief Scientific Officer, Linnaeus Bioscience***

# *S. aureus* XEN36* treated with RECCE® 327




***"Very rapid decrease in ATP levels, correlated with a very rapid decrease in viable bacterial counts"***

***Marc Sharp, PhD,***
***Chief Scientific Officer, Linnaeus Bioscience***

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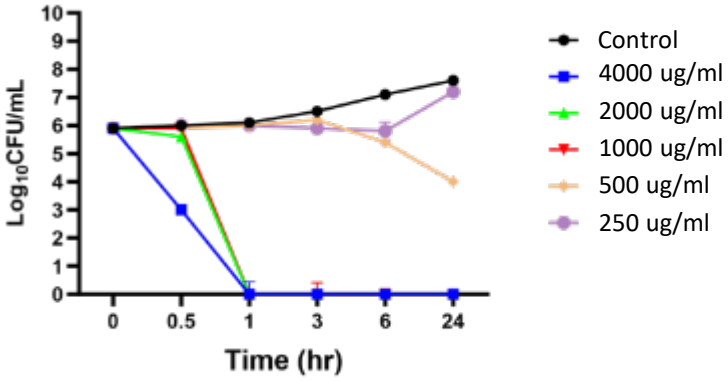
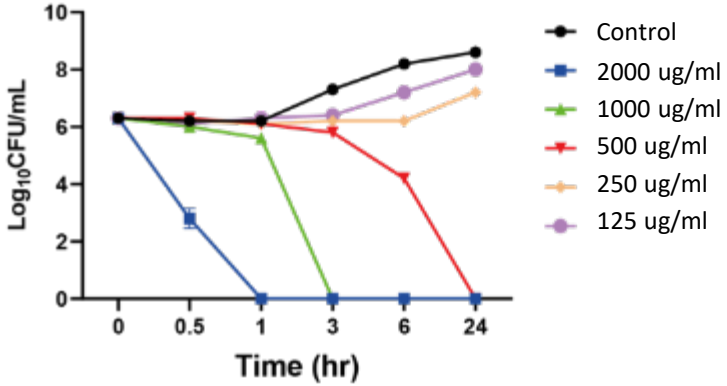
**Staphylococcus aureus Xen36 was derived from the parental strain Staphylococcus aureus ATCC 49525 (Wright), a clinical isolate from bacteraemia patient. Experiments conducted using 10% LB*

# Bactericidal Effect of RECCE® 327 on ESKAPE Pathogens

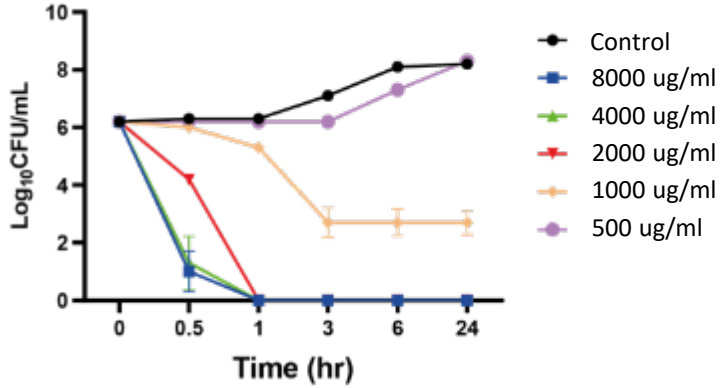
### *Enterococcus faecium*



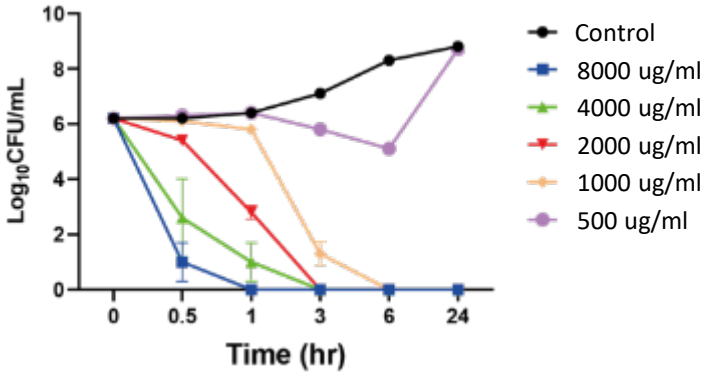

### *Staphylococcus aureus*



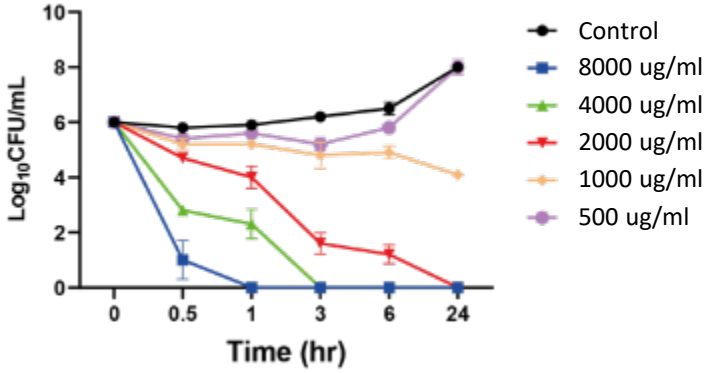

### *Klebsiella pneumoniae*



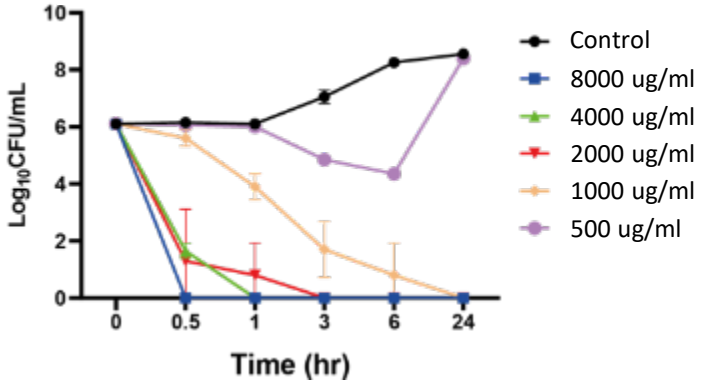

### *Acinetobacter baumannii*




### *Pseudomonas aeruginosa*




### *Enterobacter cloacae*




- ***Average time-kill curves of R327 at various concentrations against strains of ESKAPE pathogens (tested in duplicate)***
- Time-kill study was performed to determine the bacterial killing effect of R327 at a total of five concentrations, ranging from 0.5X to 8X, MIC and to measure killing kinetics of treatment with R327 against each strain.

***All bacteria derived from ATCC collection**

# RECCE® 327 Activity Against *Escherichia coli*

- *E. coli* grows fast. Eukaryotic cells healthy and not affected.

- R327 at 3,000 ppm shown to be highly effective against *E. coli* without affecting growing, healthy eukaryotic cells.

- R327 rapidly and irreversibly shuts down the ATP in *E. coli*, not allowing it to divide and grow.

***Without R327***

***R327 (3,000 ppm)***

**eukaryotic cells** ***E. coli***

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# How does the RECCE® technology work?

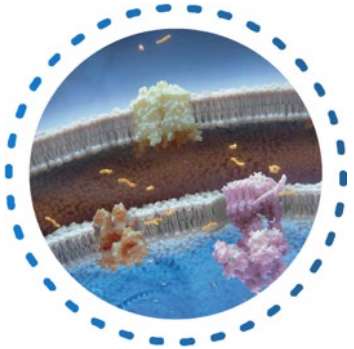
- Novel mechanism which targets rapid access to and shut down of bacterial energy production (ATP) which results in bacterial death of both active and resting bacteria.
- **Activity of R327 is measured in minutes** not hours like most other antibiotics.
- Host cells not negatively impacted by RECCE® compounds.
- Activity of R327 does not knowingly contribute to the development of mechanisms associated with AMR.

**Stage 1**

**R327 arrests cell growth and permeabilizes cell membranes**

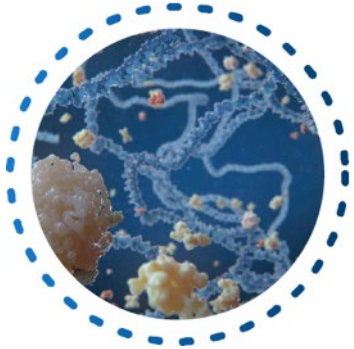
**Stage 2**

**R327 disrupts bacterial cellular energetics, depleting ATP**



**Stage 3**

**R327 inhibits major bacterial metabolic pathways including protein synthesis and cell division**

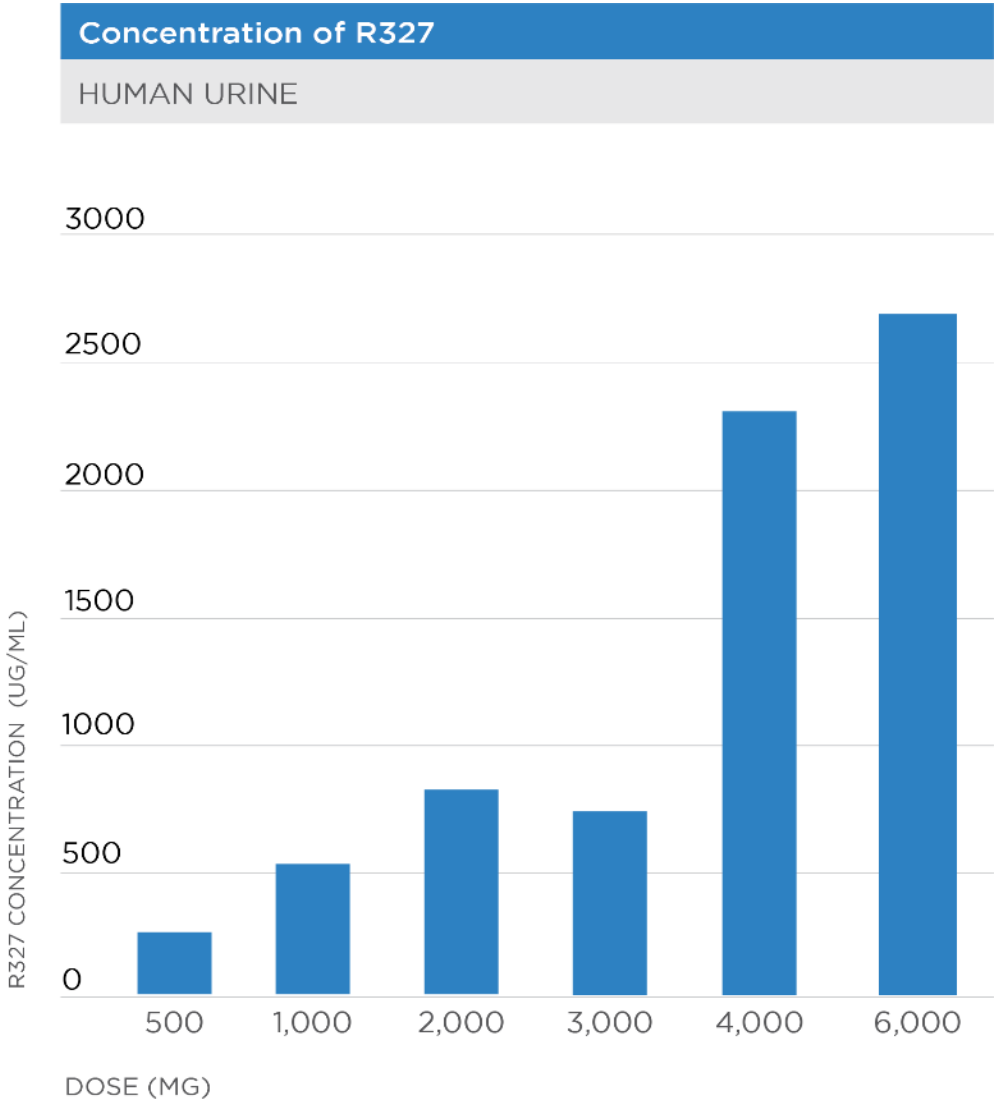


**Stage 4**

**R327 is rapidly and irreversibly bactericidal**

# RECCE® 327 Concentrates Safely in the Urine

## Intravenous Formulation – Phase I Results show R327 Ideal for UTI /Urosepsis



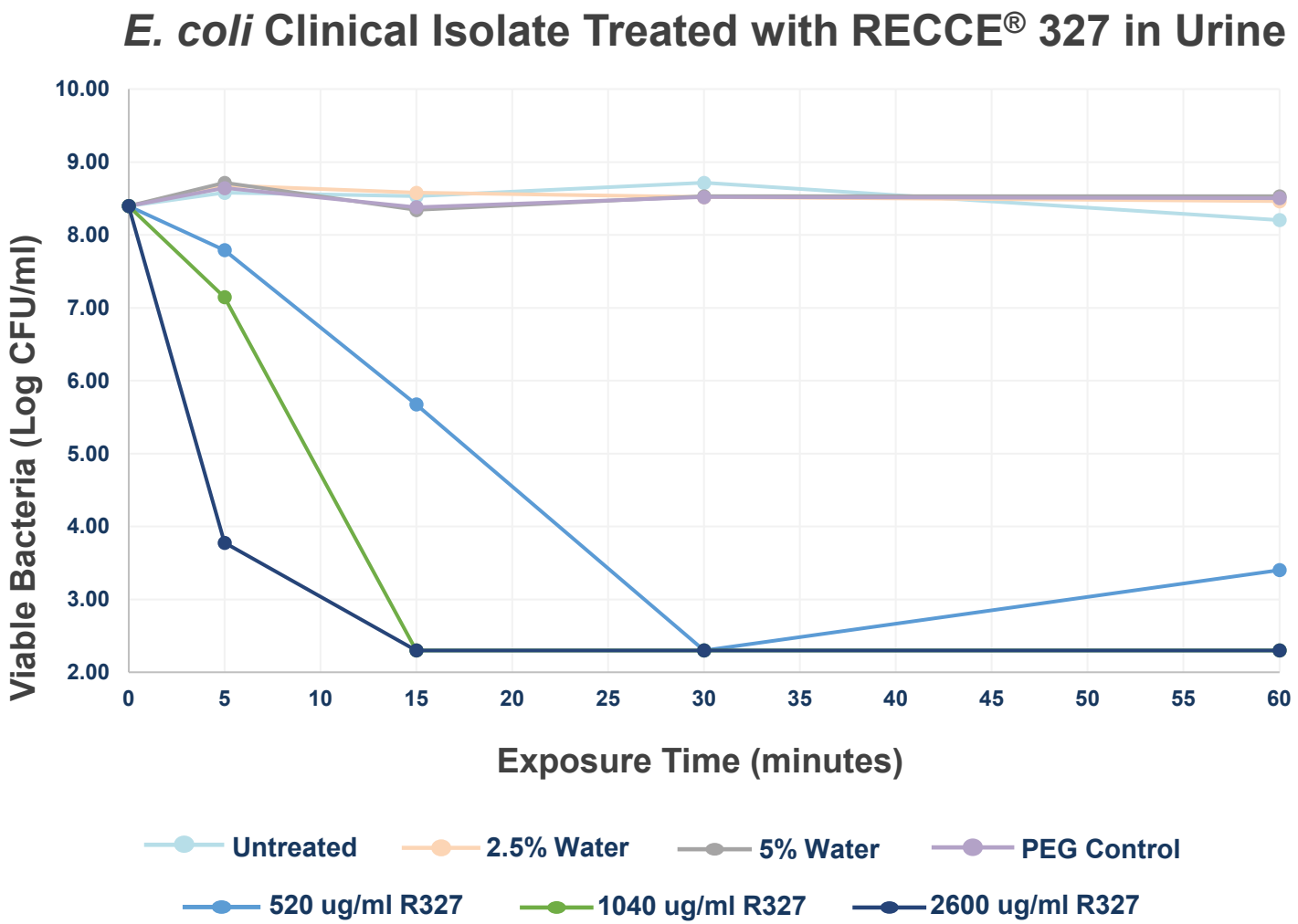

- **No serious adverse events** noted in single-dose Ph I clinical trial
  - **80 healthy male subjects**
- **Safe up to and including 6,000mg** using a 1-hour infusion
- **High concentrations of R327** noted in the urine of Ph I healthy subjects
  - **R327 excreted/safely concentrates in urine**
- No laboratory, ECG of PE changes noted
- Plasma concentrations are linear vs. dose and "predictable"
- Insight consistent with pre-clinical *in-vivo* kidney and UTI bacterial infection studies

**Concentration of R327 in Urine Compared to Plasma**

| R327 dose (mg) | Ratio Urine/Plasma |
|---|---|
| 500 | 16x |
| 1,000 | 17x |
| 2,000 | 14x |
| 3,000 | 9x |
| 4,000 | 21x |
| 6,000 | 16x |

# RECCE® 327 Kills *E. coli* within Minutes in Human Urine

## Efficacy in Humans with UTI can be predicted



# Independent Study Undertaken on R327 sub-MIC

***Conducted by Leading Experts in Bacterial MoA Analysis***


- Recce Pharmaceuticals and Linnaeus Bioscience Inc. performed a daily sub-MIC **serial passaging experiment for 30 days using R327**
- **No lasting change in the MIC to R327 was found**
- Repeat/new experiments continue
- ***"The development of resistance is unlikely because of target diversity***: We believe **R327 targets multiple critical proteins**, bacteria would have to alter all of these proteins to gain resistance."

***Marc Sharp, PhD,***
***Chief Scientific Officer, Linnaeus Bioscience***

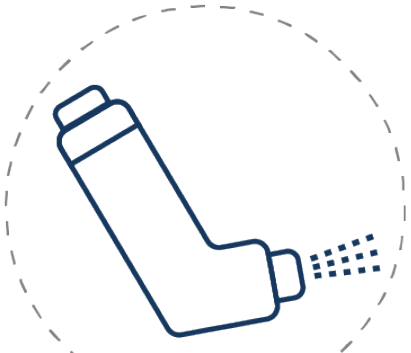
# RECCE® Anti-Infectives Have a Range of Formulations

## *Suitable for Various Indications*

Intravenous

Topical Gel

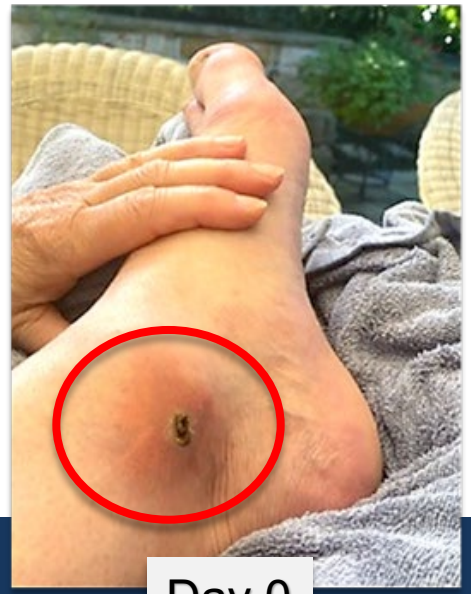
Topical Liquid



Aerosol for inhalation

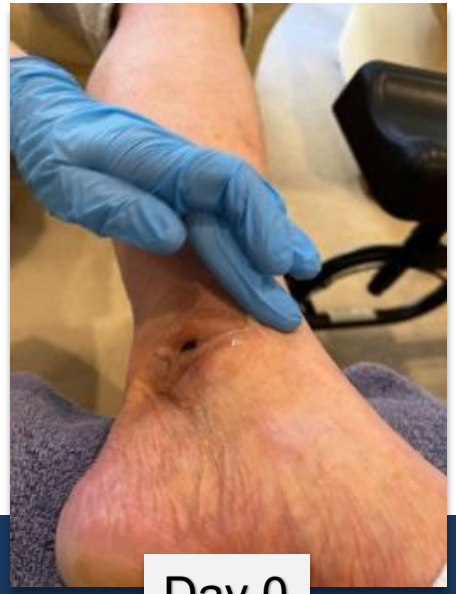
Aerosol and liquid for intranasal administration

# Patient Case Study – TGA Special Access Scheme Category A



Day 0

Pre-treatment infection

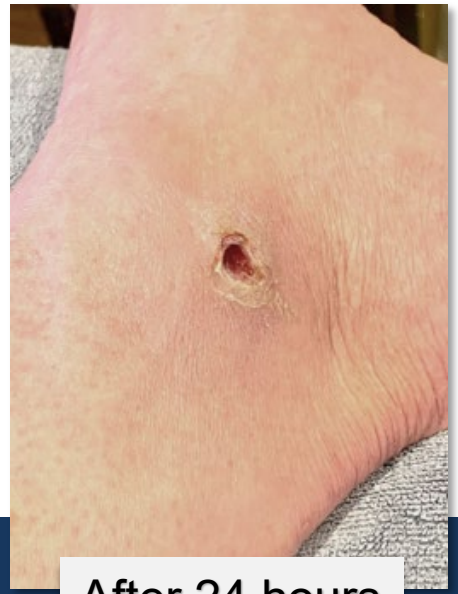


Day 0

First Recce Gel Applied

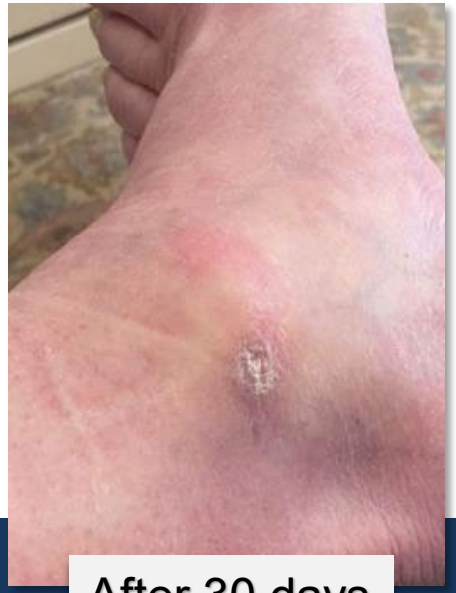
Day 0

Gel Application Complete



After 24 hours

Post Treatment



After 30 days

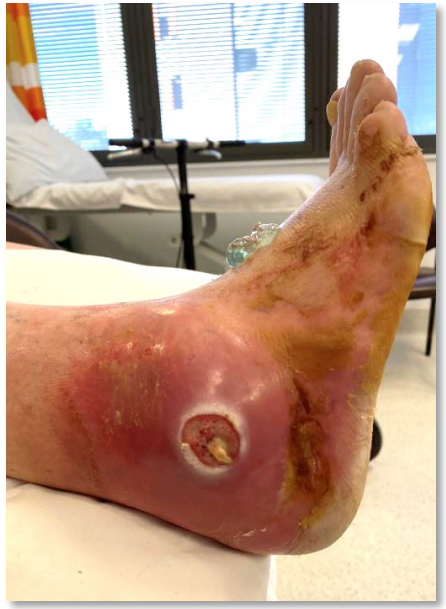
Post Treatment

- Patient Y **unresponsive to 4 x daily Cephalexin for 10 days**
  - Infection spreading and hospital ready.
- With only **one dosing application**, after 24 hours the **infection had clinically responded**
  - Redness and Swelling reduced.

- No pre-treatment wound debridement.
- No stinging at any point reported.
- **R327 Gel worked quickly and effectively**

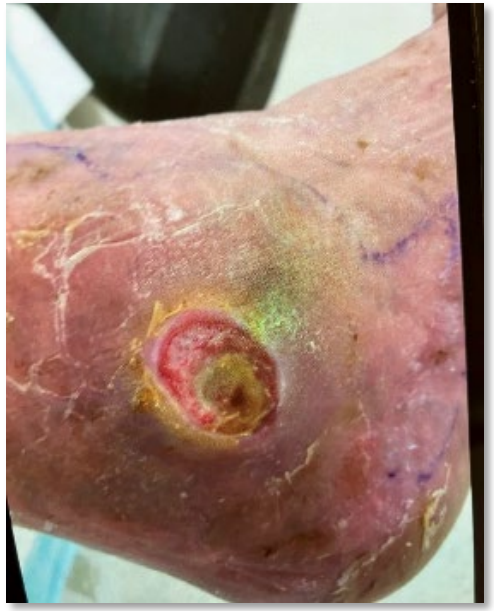
# Patient Case Study – TGA Special Access Scheme Category A

## *Pre-Treatment*



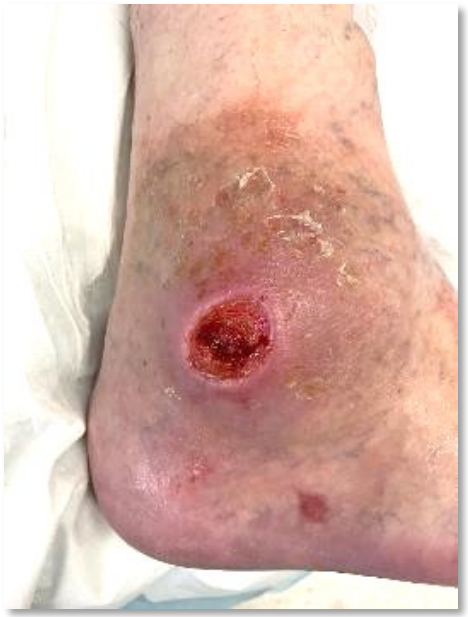
**Day 0 – Recce treatment**
**Significant bacterial infection**

## *Day 7*



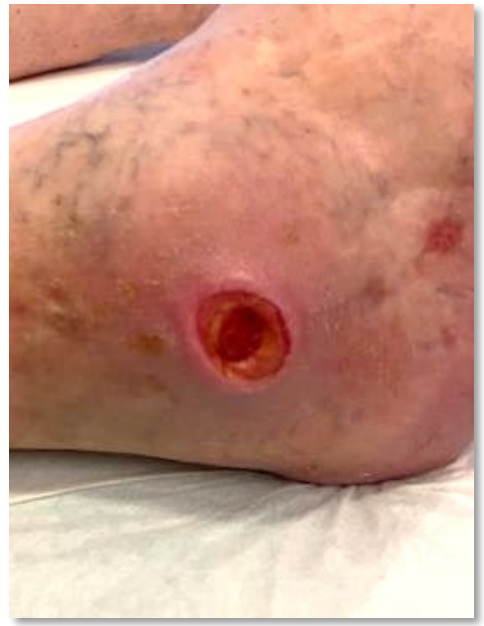
**Day 7 – Recce treatment**
**Initial redness and swelling minimising, wound drying up**

## *Day 10*



**Day 10 – Recce treatment**
**No signs of infection, no signs of pus formation, wound clearing up**

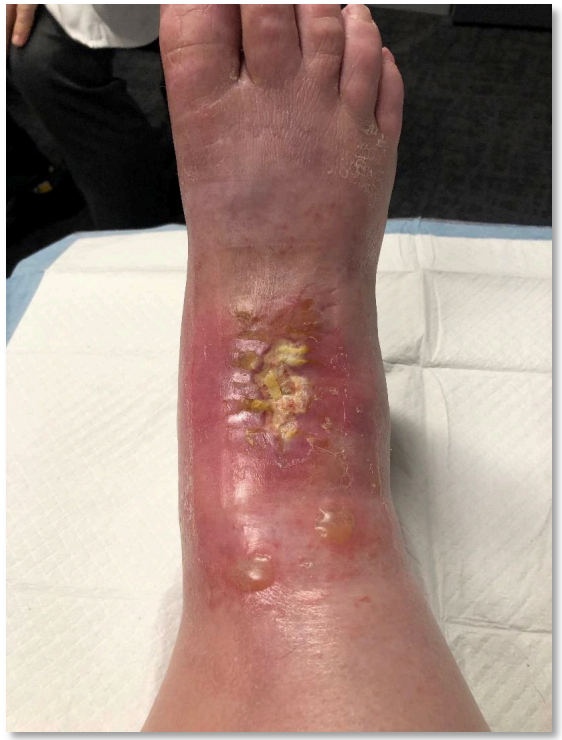
## *Day 14*



**Day 14 – Recce treatment**
**Wound improved, well tolerated**

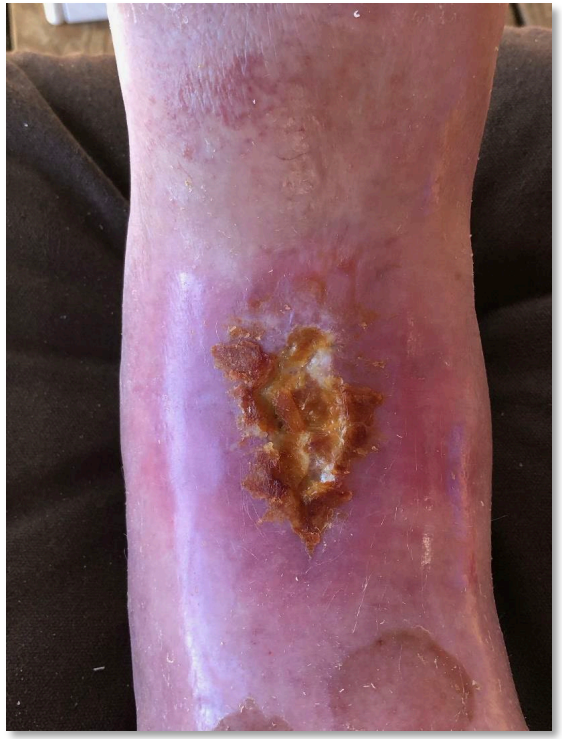
# Patient Case Study – TGA Special Access Scheme Category A

## *Pre-Treatment*



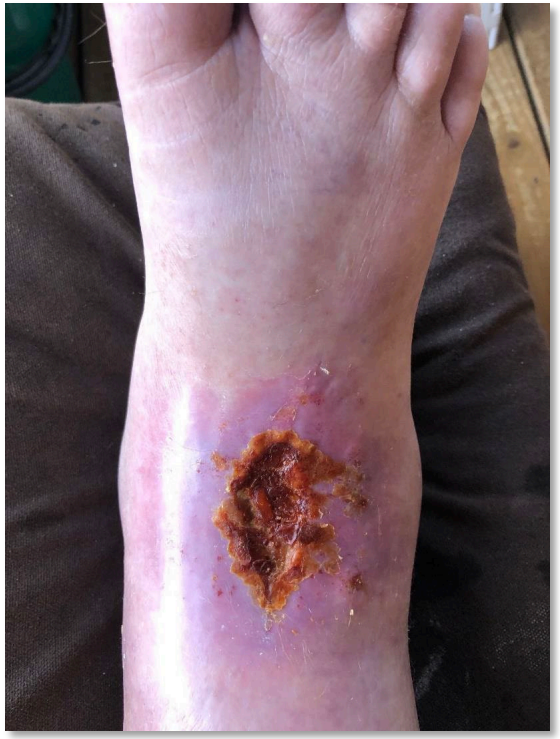
**Day 0 – Pre-treatment wound swab**
**Growing culture of Gram-positive and Gram-negative bacilli**

## *Day 7*



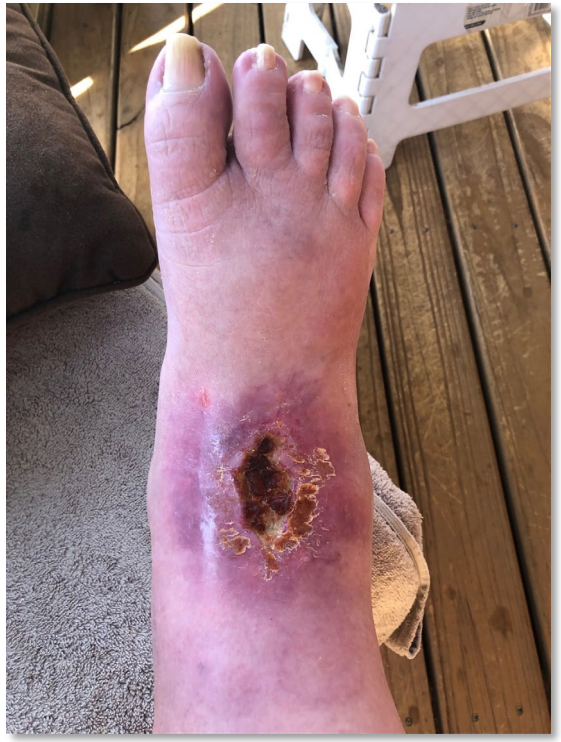
**Day 7 – Recce treatment**
**Initial redness and swelling of the wound had minimised and found to be drying up.**

## *Day 14*



**Day 14 – Recce treatment**
**No signs of bacterial growth surrounding the wound**

## *Day 21*



**Day 21 – Recce treatment**
**Wound had successfully healed, closed and dried up, with no signs of bacterial infection. R327G treatment well tolerated**

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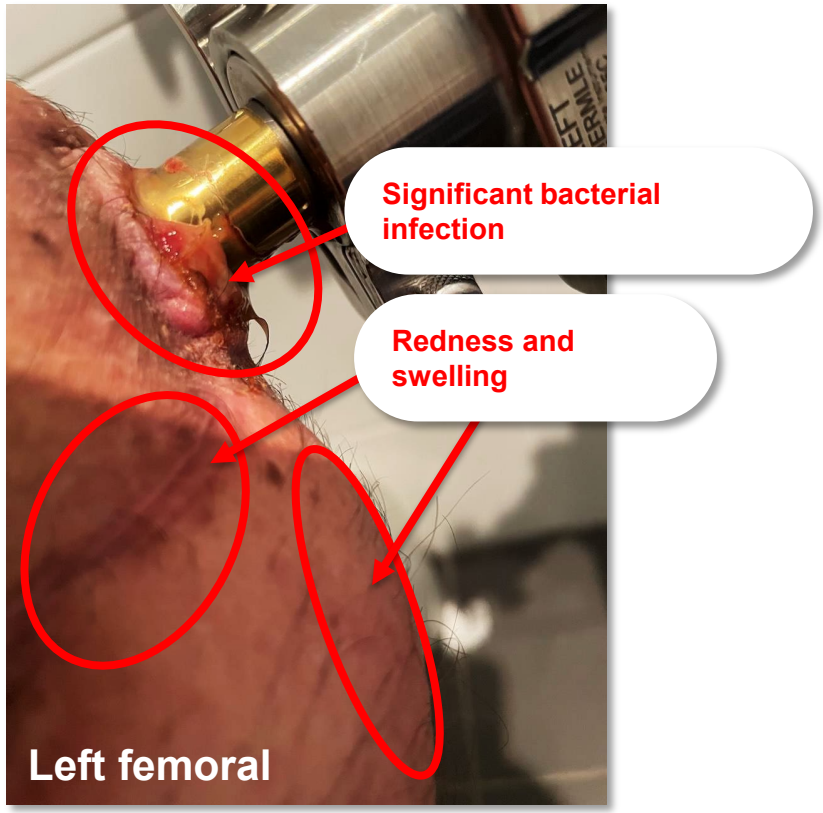
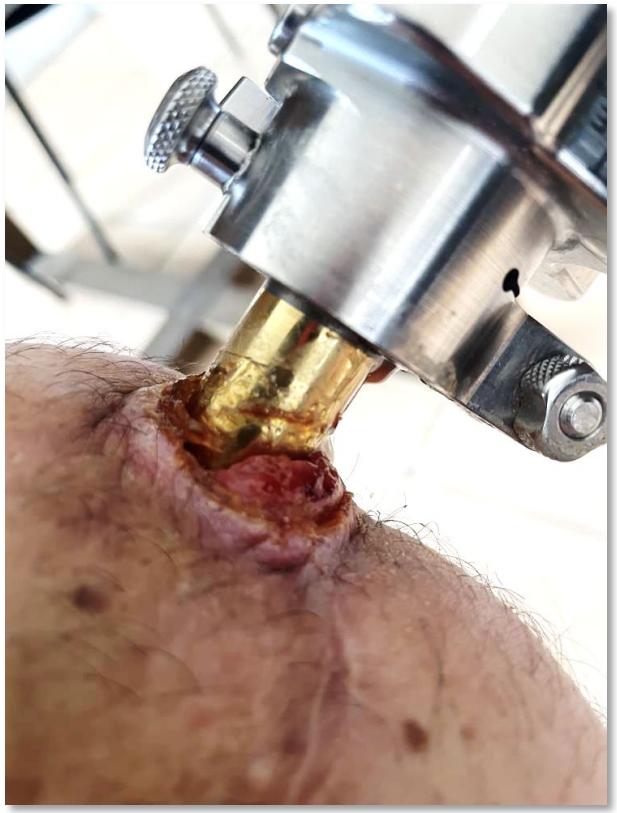
# Patient Case Study – TGA Special Access Scheme Category A

## *Pre-Treatment*



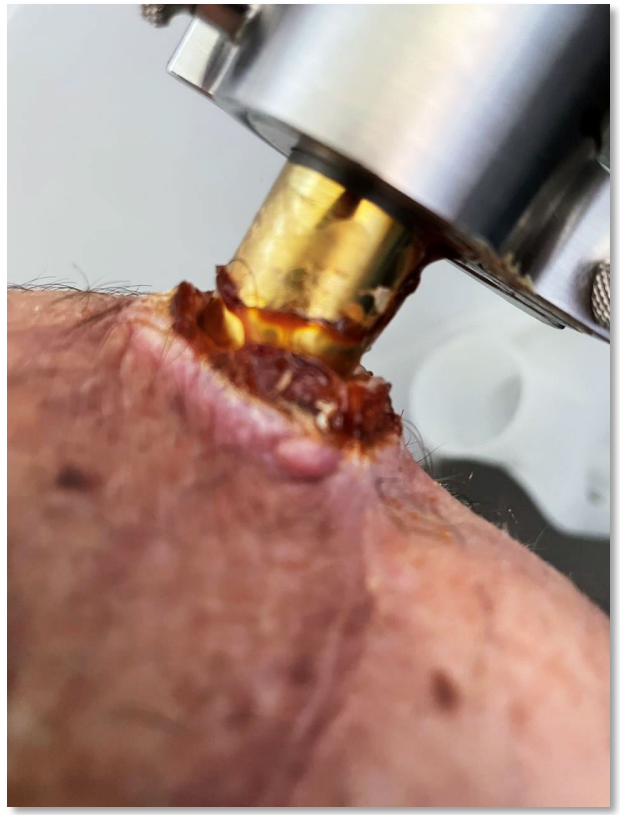

**Day 0 – Pre-treatment**
**Significant bacterial infection, redness and swelling around the implant (upper left thigh)**

## *Day 3*



**Day 3 – Recce treatment**
**Initial redness and swelling minimising, wound healing and drying up**

## *Day 7*



**Day 7 – Recce treatment**
**Wound was dried up and had improved with no signs of redness or swelling. R327G was applied daily and was well-tolerated.**

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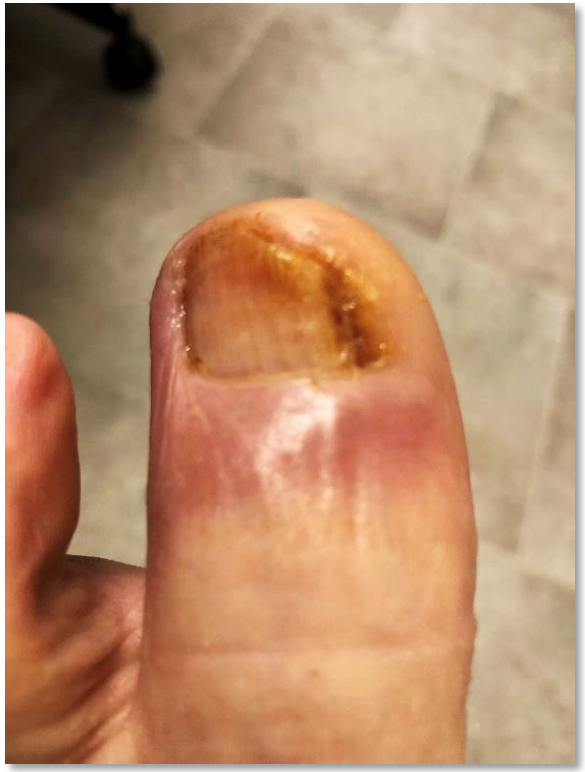
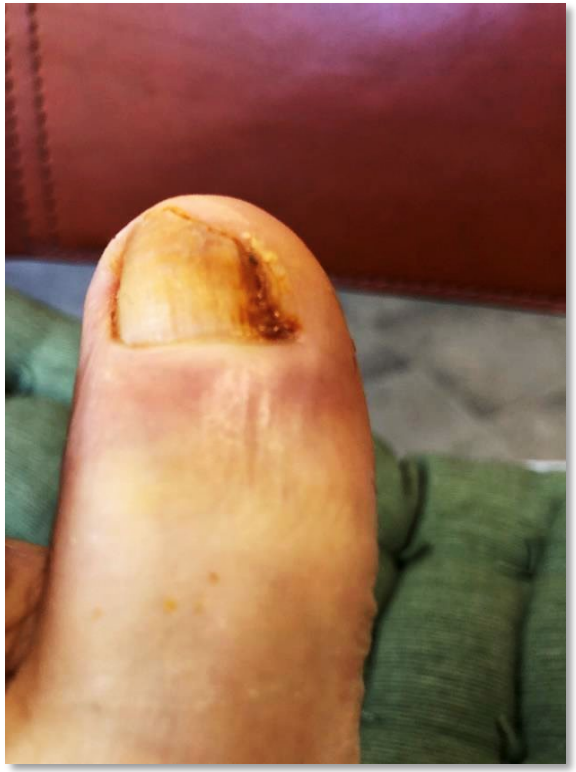
# Patient Case Study – TGA Special Access Scheme Category A

## *Pre-Treatment*



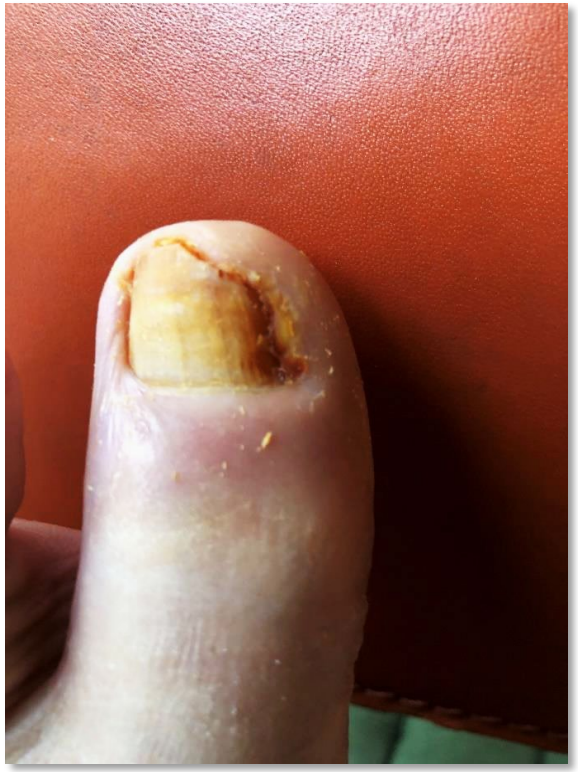
**Day 1 – Pre-treatment**
**Osteomyelitis (serious infection of the bone), signs of initial biofilm formation, not responding to antibiotics**

## *Day 3*



**Day 3 – Recce treatment**
**Wound drying up with infection clearing, toe responding to R327G treatment**

## *Day 7*



**Day 7 – Recce treatment**
**Wound completely dried up, no signs of biofilm surrounding toenail, swelling significantly reduced**

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# Fast-acting, Broad-Spectrum Platform Enables Recce to address Serious, Life Threatening, and/or Resistant Bacterial Infections

***Intravenous** Products – Potential Indications*

- Urinary Tract Infections: complicated, recurrent
- Sexually Transmitted Diseases (resistant)
- Complicated Skin and Soft Tissue Infections (trauma, burn wounds)
- Prosthesis Related Infections
- Ventilator-Acquired Pneumonia
- Hospital-Acquired Pneumonia
- Sepsis

***Topical** Products – Potential Indications*

- Infected burn wounds
- Complicated Skin and Soft Tissue Infections
  - Trauma, burn and other environmental wounds
- Prosthesis-Related Infections
- Infected Diabetic Foot Ulcers


*For illustrative purposes only – not final product*

# Robust Worldwide Intellectual Property Portfolio

***Recce's patent portfolio contains over 40 patents and patent applications in the world's major markets.***

| Filed | Patent Family 1 | Expiry | Patent Family 2 | Expiry | Patent Family 3 | Expiry |
|---|---|---|---|---|---|---|
| Australia | ✓ | 2028 | ✓ | 2037 | ✓ | 2037 |
| USA | ✓ | 2029 | ✓ | 2037 | ✓ | 2037 |
| Europe | ✓ | 2028 | ✓ | 2037 | ✓ | 2037 |
| Germany | ✓ | 2028 | ✓ | 2037 | ✓ | 2037 |
| Spain | ✓ | 2028 | ✓ | 2037 | ✓ | 2037 |
| France | ✓ | 2029 | ✓ | 2037 | ✓ | 2037 |
| UK | ✓ | 2028 | ✓ | 2037 | ✓ | 2037 |
| Italy | ✓ | 2028 | ✓ | 2037 | ✓ | 2037 |
| Sweden | ✓ | 2028 | ✓ | 2037 | ✓ | 2037 |
| Japan | ✓ | 2028 | ✓ | 2037 | ✓ | 2037 |
| China | ✓ | 2028 | Pending | 2037 | ✓ | 2037 |
| HK | Pending | 2028 | Pending | 2037 | ✓ | 2037 |

**Family 1** group relates to the Company's Unique and Highly Economical Manufacturing Process and use of the Polymer in Treatment of Diseases.

**Family 2** relates to the Method of Manufacture, Administration and Application to Treat a Broad Range of Common Human Infections.

**Family 3** relates to a Method of Treatment of a Broad Range of Viral Infections, particularly Parenteral Viral Infection.

**Family 4** relates to Process for Preparation of Biologically Active Copolymer (**Australia Granted expiry 2041**, other Patent Cooperation Treaty countries pending)

# Board Structure

**Dr John Prendergast** – Executive Chairman
*BSc (Hons), MSc (UNSW), PhD (UNSW), CSS (HU)*

**James Graham** – Chief Executive Officer
*BCom (Entrepreneurship), GAICD*

**Alan W Dunton MD** – Non-Executive Director & Chief Medical Advisor
*BSc (BioChem) Hons, M.D. (NYU)*

**Michele Dilizia** – Executive Director & Chief Scientific Officer
*BSc (Med Sci), Grad Dip Bus (Mkting), BA (Journ), GAICD, MASM*

**Dr Justin Ward** – Executive Director & Head of QA/QC
*BSc (Chem), PhD (Chem), M Pharm, MRACI, CChem*

**Alistair McKeough** – Non-Executive Director

# Conclusions

## Recce's Portfolio of Anti-Infectives

- **Rapid onset of effect** and a **broad spectrum of activity** (including against ESKAPE pathogens)
  - Potentially **effective as a single-dose**
  - Straightforward, inexpensive manufacturability, **starting product from USA**
- Technology of Synthetic Anti-Infectives – **does not develop resistance**
- **Multiple methods of administration** suitable for various indications, currently are untreatable due to AMR
- **Platform technology** with products in clinical development
- Products are **positively differentiated from those currently approved/in development**
- **Patent protected through 2041**
- **Planned US IND** to expand development and build broader US presence

# Thank you