# POSITIVE DATA FROM RECCE® 327 ANTIBIOTIC RANGE FINDING TOXICITY (SAFETY) STUDIES IN ANIMALS

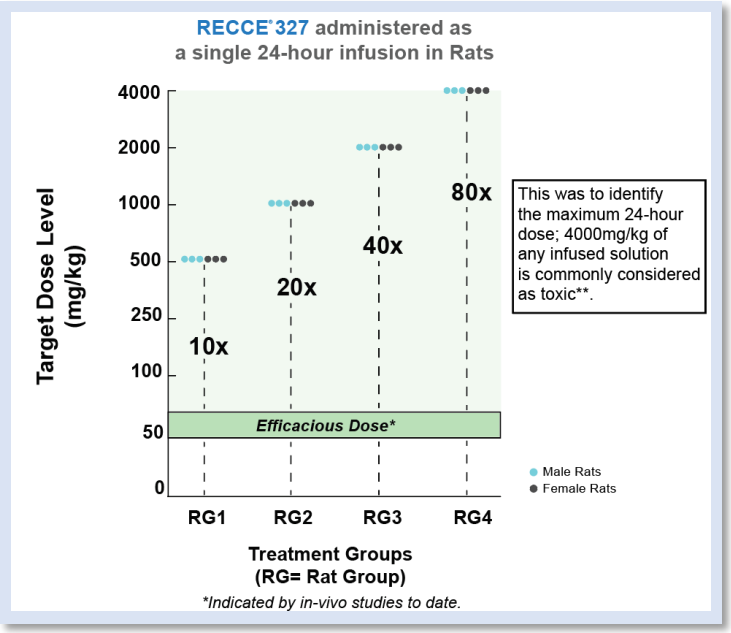
Highlights:

- **24-hour dosing up to 4000mg/kg (80x indicated efficacious dose) in Rats & Dogs well tolerated**
- **NOAEL (No Observed Adverse Effect Level) of 24-hour 500mg/kg (10x indicated efficacious dose)**
- **Expanded daily dosing to 7 days, up to 4000mg/kg – dosing limits identified**
- **Therapeutic dose window appears considerably wider than Vancomycin and other antibiotics**
- **Phase I Human Clinical Trial Protocol reduced in size/number**

**SYDNEY Australia, 10 February 2020:** Recce Pharmaceuticals Ltd (ASX: RCE) (**Company**), the company developing a new class of antibiotics, is pleased to announce successful *in-vivo* Toxicity (Safety) studies in small and large animal species, conducted by an industry leading independent research laboratory, has further reinforced indications of a wide therapeutic window.

The studies indicated a No Observed Adverse Effect Level (NOAEL) in either animal species tested, at any time during or post the study periods, when dosed at 500mg/kg. *In-vivo* studies continue to indicate efficacy at 50-70mg/kg of RECCE® 327, suggesting a wide therapeutic dosing window.

## Single Dose Acute Phase (Phase Ia) - Rats




Groups were dosed sequentially at dose levels of 525mg/kg, 1025mg/kg, 2000mg/kg and 4000mg/kg and were selected based upon clinical observations in the preceding group of animals.

- 4 groups of 6 rats (M/F)
- Rats were given doses of up to 80x efficacious dose amount over 24 hours
- RECCE® 327 is indicated to be efficacious from as little as 50mg/kg.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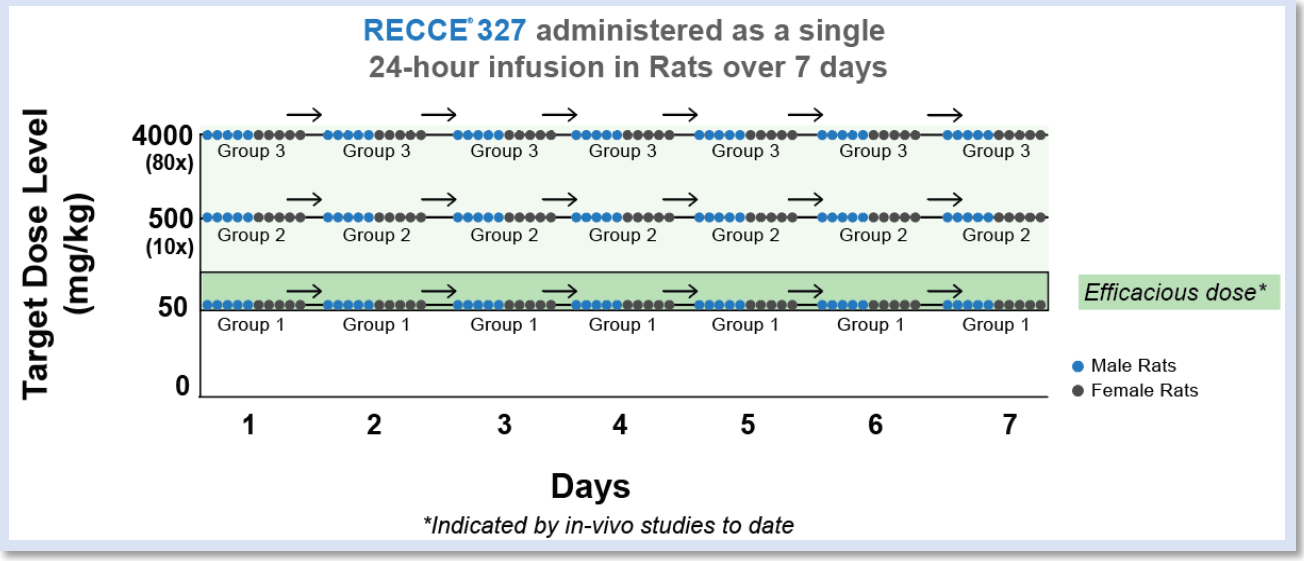
** The Food and Drug Administration Industry Guidance for Safety Assessment of New Pharmaceuticals: “limit doses for acute, sub chronic and chronic toxicity studies of 1,000 mg/kg for rodents and nonrodents are considered appropriate in all cases… doses in the toxicity studies should be limited by a 10-fold exposure margin or a dose of 2,000 mg/kg/day or the Maximum Feasible Dose whichever is lower[1].”

**Range-Finding Repeat Dosing (Phase Ib) up to 4,000 mg/kg - Rats**




The RECCE® 327 dose levels administered in the Range Finding Repeat Dosing Study (Ib) were based upon on a 24-hour single dose study of 4 groups of 6 rats up to 4000mg/kg without any clinical adverse effect.

- 3 groups of 10 rats (M/F) at 50 mg/kg, 500 mg/kg and 4000 mg/kg
- Rats were given same dose over 7 days
- RECCE® 327 is indicated to be efficacious from as little as 50mg/kg and here shows tolerability can be sustained over at least 7 days of continuous daily exposure at doses up to and including 500 mg/kg.

**Study Observation:**

A single 24-hour intravenous infusion administration of RECCE® 327 up to 4,000 mg/kg and 7-day continuous intravenous infusion administration of up to and including 500 mg/kg/day were well tolerated; with no mortalities, clinical signs, changes in body weight, coagulation, clinical chemistry or macroscopic abnormalities. Some minor indications of a dosing limit were observed in some animals beyond the 7-day continuous intravenous infusion administration at 4,000 mg/kg (80x indicated efficacious dose).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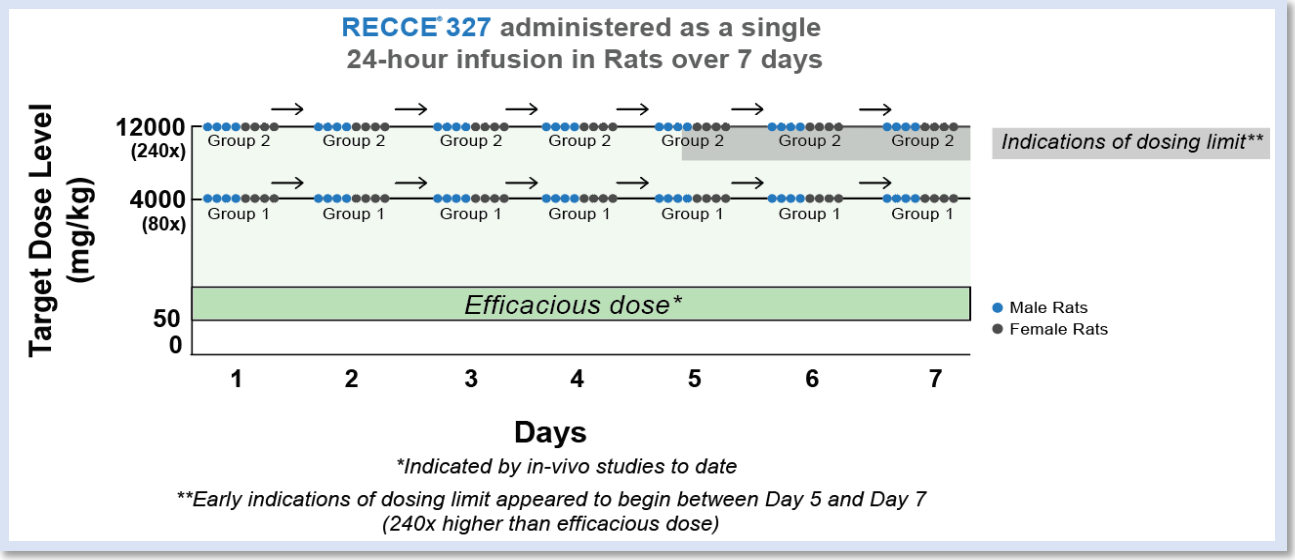
Comparatively, Vancomycin, a commercially successful broad-spectrum antibiotic, indicates efficacy at 50mg/kg when IV administered, but is highly toxic at 400mg/kg, with all rats dying in a study before completion of a course[2].

**Range-Finding Repeat Dosing (Phase Ib) up to 12,000 mg/kg - Rats**



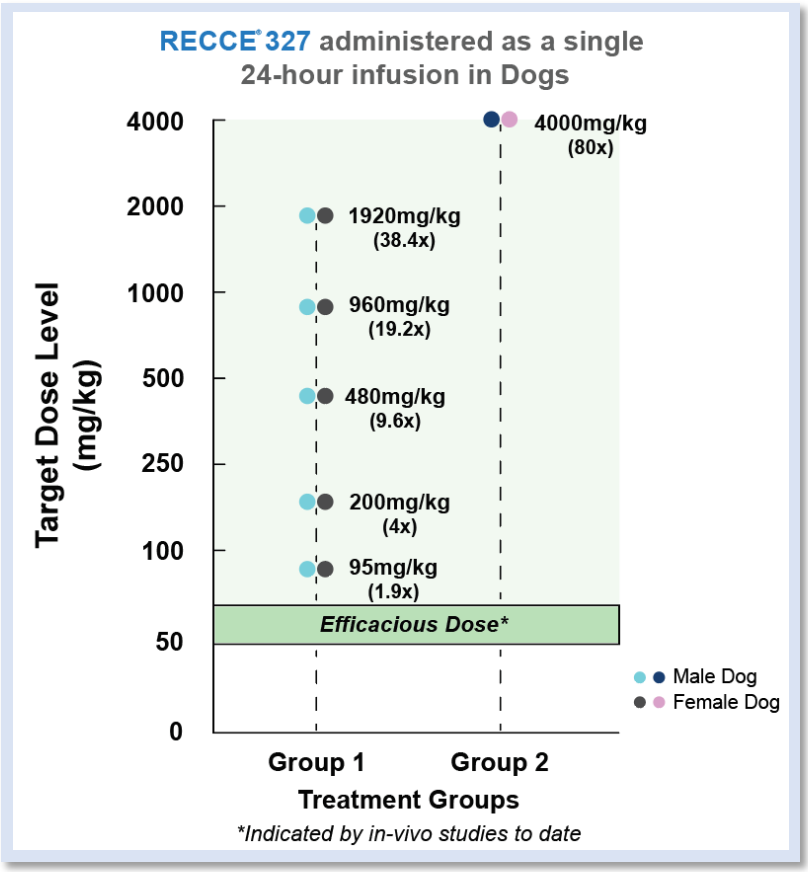

The RECCE® 327 dose levels administered in the Range Finding Repeat Dosing Study (Ib) were based upon on a 24-hour single dose study of 4 groups of 6 rats up to 4000mg/kg without any clinical adverse effect.

- 2 groups of 8 rats (M/F) at 4,000 mg/kg and 12,000 mg/kg
- Rats were given same dose over 7 days

**Study Observations:**

A single 24-hour intravenous infusion administration of RECCE® 327 up to 12,000 mg/kg over the course of 7-days was carried out. Results of up 12,000 mg/kg/day was well tolerated from Days 1 to 4 (inclusive); with no mortalities or clinical signs. Day 5 onwards, there were indications of anticipated toxicity commencement. Some minor indications of a dosing limit were observed in some animals beyond the 7-day continuous intravenous infusion administration at 4,000 mg/kg (80x indicated efficacious dose).

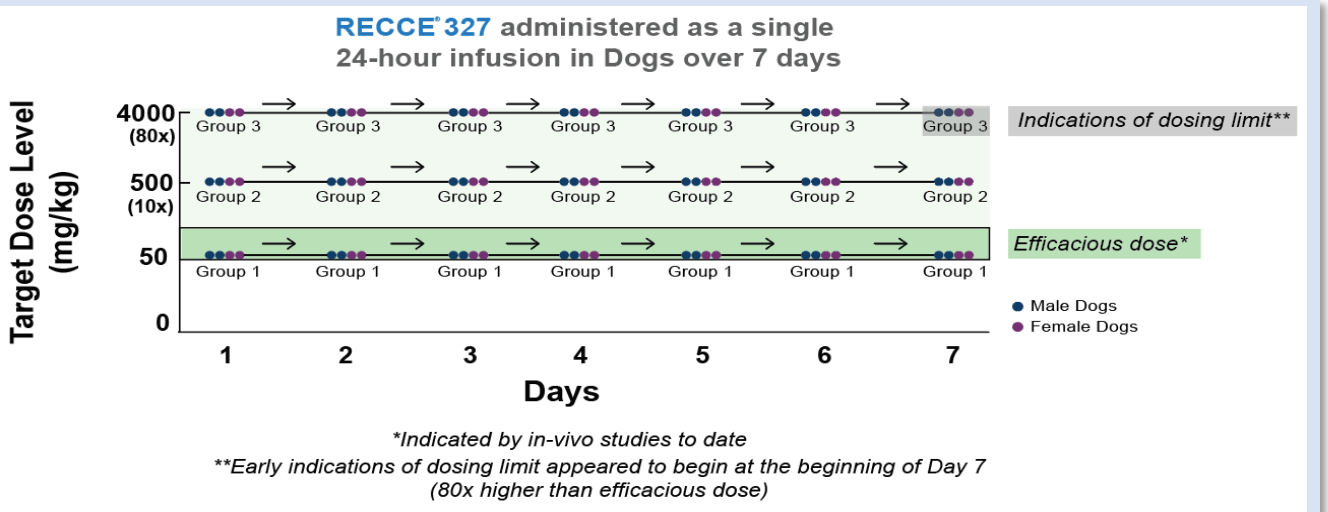
## Single Dose Acute Phase (Phase Ia) - Dogs




Doses were escalated over the 24-hour period at 95mg/kg, 200mg/kg, 480mg/kg, 960mg/kg, 1920mg/kg and 4000mg/kg.

- 1 group of 2 dogs (M/F) at 95 mg/kg, 200 mg/kg, 480 mg/kg, 960 mg/kg and 1,920 mg/kg
- 1 group of 2 dogs (M/F) at 4,000 mg/kg (separate study)
- Dogs were given up to 80x the efficacious dose, which was well tolerated
- RECCE® 327 is indicated to be efficacious from as little as 50mg/kg

## Range-Finding Repeat Dosing (Phase Ib) up to 4,000 mg/kg - Dogs




- 3 groups of 4 dogs (M/F) at 50 mg/kg, 500 mg/kg and 4,000 mg/kg
- Dogs were given same dose over 7 days
- RECCE® 327 still tolerated even when dosed 10 times higher than its lowest dose at 50mg/kg

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The dose levels administered in the Range Finding Repeat Dosing Study (Ib) were based on a previous 24-hour single dose study of RECCE® 327 on 1 group of 2 (M/F) dogs for doses 95 mg/kg – 1,920 mg/kg and 1 group of 2 dogs (M/F) for a 4,000 mg/kg dose.

**Study Observations:**

As per rat 7-day repeat data, it can be concluded that there was an indication of dose limit at very high levels. A single 24-hour intravenous infusion administration of RECCE® 327 up to 4000 mg/kg and 7-day continuous intravenous infusion administration of RECCE® 327 up to 500 mg/kg/day were well tolerated; with no mortalities, clinical signs, changes in body weight, coagulation, clinical chemistry or salient macroscopic abnormalities.

RECCE® 327 is positioned as a first-line therapy via a 24-hour intravenous infusion administration, with the goal of treating infection quickly, regardless of the type of bacteria, including mutated superbug forms.

Chairman Dr John Prendergast commented *"We are delighted by our in-vivo animal studies that continue to demonstrate the potential of RECCE® 327 as a first-line-therapy for the treatment of superbug infections. This sees us in an encouraging position ahead of our anticipated Phase I human clinical studies".*

References

[1] Food and Drug Administration – *Guidance for Industry* – https://www.fda.gov/media/71542/download

[2] National Center for Biotechnology Information – *Vancomycin-induced nephrotoxicity in rats: is enzyme elevation a consistent finding in tubular injury?-* https://www.ncbi.nlm.nih.gov/pubmed/17879216

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**About Recce Pharmaceuticals Ltd**

Recce Pharmaceuticals Ltd (ASX: RCE) is pioneering the development and commercialisation of a New Class of Synthetic Antibiotics with Broad Spectrum activity designed to address the urgent global health problem of antibiotic resistant superbugs.

Recce antibiotics are unique – their potency does not diminish even with repeated use, which is a common failure associated with existing antibiotic use and the resulting emergence of resistant superbugs.

Patented lead candidate RECCE® 327, wholly owned and manufactured in Australia, has been developed for the treatment of blood infections and sepsis derived from *E. coli* and *S. aureus* bacteria – including their superbug forms.

The FDA has awarded RECCE® 327 *Qualified Infectious Disease Product* designation under the *Generating Antibiotic Initiatives Now* (GAIN) Act – labelling it for Fast Track Designation, plus 10 years of market exclusivity post approval.

Recce wholly owns its automated manufacturing, ready to support first-in-human clinical trials. Recce's anti-infective pipeline seeks to exploit the unique capabilities of RECCE® technologies targeting synergistic, unmet medical needs.

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