Phase I Clinical Trial Data Review Complete - RECCE® 327 as an Intravenous Infusion Formulation

Highlights:

- **Independent examiners confirm Phase I R327 (I.V.) study in 80 human subjects (eight cohorts), achieved all primary study end-points, met international regulatory standards in data and showed R327 to be safe & well tolerated**
- **Dosing was achieved commensurate with efficacy demonstrated in Gram-positive & Gram-negative animal infection models to date**
- **Phase I/II 'fast infusion' dosing of R327 IV is tracking to primary study end-points with expected data read-outs in H2 2023**

SYDNEY Australia, 19 July 2023: Recce Pharmaceuticals Ltd (**ASX:RCE**, **FSE:R9Q**) (the **Company**), the Company developing a New Class of Synthetic Anti-infectives, today announced positive complete and independently verified results from its Phase I (R327-001) study of RECCE® 327 (R327) as an intravenous infusion formulation in 80 healthy male subjects.

The trial was an ascending-dose[1], randomised, placebo-controlled, parallel, double-blind, single-dose, first-in-human study to evaluate the safety and pharmacokinetics of R327 in healthy male subjects. A total of 80 subjects were randomised to eight (8) single-dose cohorts – 60 subjects received R327 with 20 receiving placebo. All enrolled subjects completed dosing per the protocol and completed the trial without dosing interruptions during the study.

In concurrence with the Therapeutic Goods Administration clinical trial regulatory procedures, the **recruitment for the study is closed** and marked '**Complete'** with no '**Serious Adverse Events**' reported.

Summary of Results

- ✓ No serious adverse events (SAEs) or deaths were reported in this study.
- ✓ No clinically significant changes were noted in any hematology parameter(s) in any cohort during the course of the study.
- ✓ No clinically significant changes were noted in any chemistry parameter(s) in any cohort

[1] A single dose of R327 IV was infused in each cohort of healthy male subjects to demonstrate its safety before increasing the dose to another cohort of healthy male subjects.

during the course of the study (Kidney and Liver functions all normal – no change in parameters).

- ✓ All coagulation parameters remained within normal limits or were deemed not clinically significant (Normal blood clotting properties were maintained).
- ✓ No clinically significant changes were noted in any urinalysis parameter(s) in any cohort during the course of the study (i.e. no adverse event/side effect).
- ✓ No clinically significant changes were noted in any vital sign (included systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate, and body temperature) parameter(s) in any cohort during the course of the study.
- ✓ No clinically significant changes were noted in any 12-lead ECG parameter(s) in any subject in any cohort during the course of the study (no cardiac event).
- ✓ No clinically significant changes were noted in any cardiac telemetry parameter(s) in any subject in any cohort during the course of the study (no cardiac abnormalities during continuous heart monitoring whilst under observation).

Safety and Tolerability Results

R327 was found to be well tolerated with a good safety profile across all dose groups from 50 mg to 6,000 mg when administrated intravenously over one hour infusion. All treatment emergent adverse events (TEAEs) across the cohorts (including placebo groups) were classified as mild or moderate. All outcomes for the TEAEs were recovered or resolved.

Adverse Event (TEAEs)	R327	Placebo
Diarrhoea	2%	10%
Infusion Site Pain	38%	20%
Infusion Site Specific Thrombosis	10%	5%
Other Symptoms Noted*	23%	15%

** e.g., itchy skin, nausea, headache, feeling hot*

Pharmacokinetic Results – Potential for R327 to be Used to Treat Sepsis

The results showed a significant dose-dependent concentration of R327 in both the urine and the plasma, highlighting the potential of R327 as a potential treatment of sepsis and complicated/uncomplicated UTIs.

The graph below shows a significant dose dependent concentration of R327 in subjects' plasma (blood). The results demonstrate a consistent, steady, and proportional linear increase across measured doses of R327. With no observed commensurate spike in drug concentration, (which can lead to harder-to-control side effects) this will help provide the Company with an optimised dosing regime – a compelling profile for a sepsis drug candidate.

recce.com.au
ACN 124 849 065

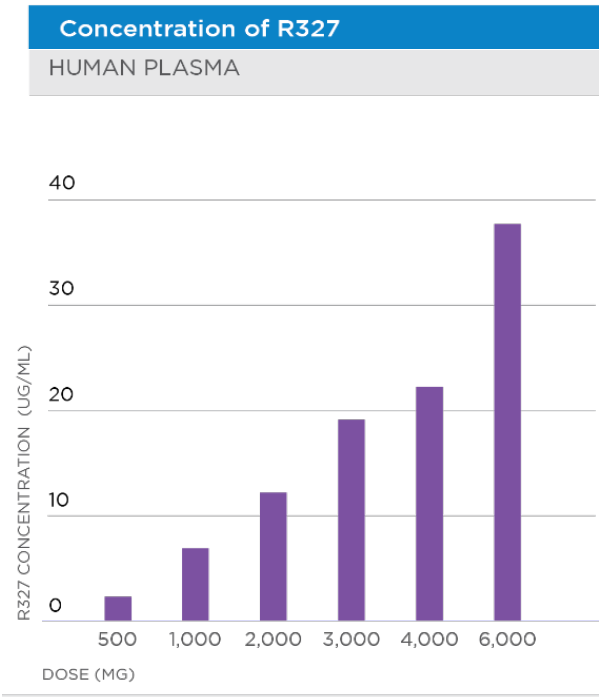
Chief Executive Officer
James Graham
Recce Pharmaceuticals Ltd
james.graham@recce.com.au

Media and Investor Relations

Australia
Andrew Geddes
CityPR
+61 408 677 734
ageddes@citypublicrelations.com.au

USA
Jordyn Temperato
LifeSci Communications
jtemperato@lifescicomms.com

Europe
Guillaume van Renterghem
LifeSci Advisors
gvanrenterghem@lifesciadvisors.com



R327 dosed subjects (60 total)

R327 dose (mg)	Concentration of R327 in Human Plasma – R327 Max Concentration (ug/ml)
500	3.36
1,000	6.72
2,000	12.9
3,000	18.3
4,000	23.8
6,000	36.5

Positive Unexpected Findings:

Potential for R327 to be Used to Treat Urinary Tract Infections (UTIs):

UTI's are responsible for about 30% of all sepsis infections, defined as 'Urosepsis'. R327's potential as a treatment option across the patient infectious disease journey therefore positions it for therapy in this area of unmet medical need.

The R327 clinical results showed a significant dose-dependent concentration of R327 in both the urine and the plasma when the concentration of R327 found in the urine was up to twenty-one-fold higher than in the plasma. It was also found that the primary route of excretion of R327 appeared to be through the kidney into the ureters and down into the bladder.

R327 dose (mg)	CMAX Plasma (ug/ml)	CMAX Urine (ug/ml)	Ratio - urine/plasma
500	3.36	53.5	**16x**
1,000	6.72	110.8	**17x**
2,000	12.9	176.1	**14x**
3,000	18.3	157.2	**9x**
4,000	23.8	490.4	**21x**
6,000	36.5	570.8	**16x**

recce.com.au
ACN 124 849 065

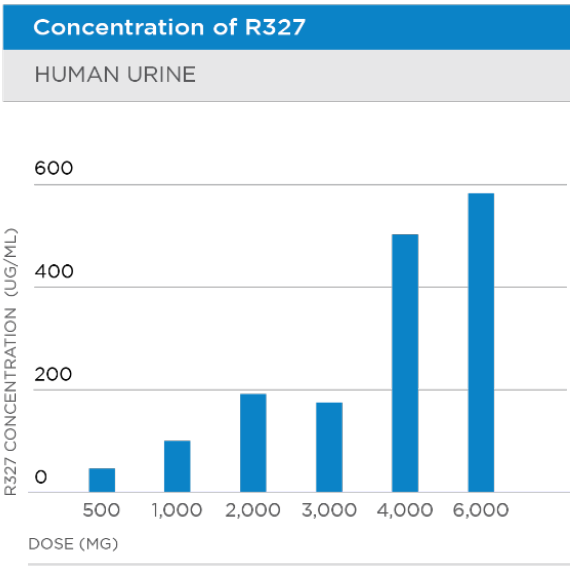
Chief Executive Officer
James Graham
Recce Pharmaceuticals Ltd
james.graham@recce.com.au

Media and Investor Relations

Australia
Andrew Geddes
CityPR
+61 408 677 734
ageddes@citypublicrelations.com.au

USA
Jordyn Temperato
LifeSci Communications
jtemperato@lifescicomms.com

Europe
Guillaume van Renterghem
LifeSci Advisors
gvanrenterghem@lifesciadvisors.com

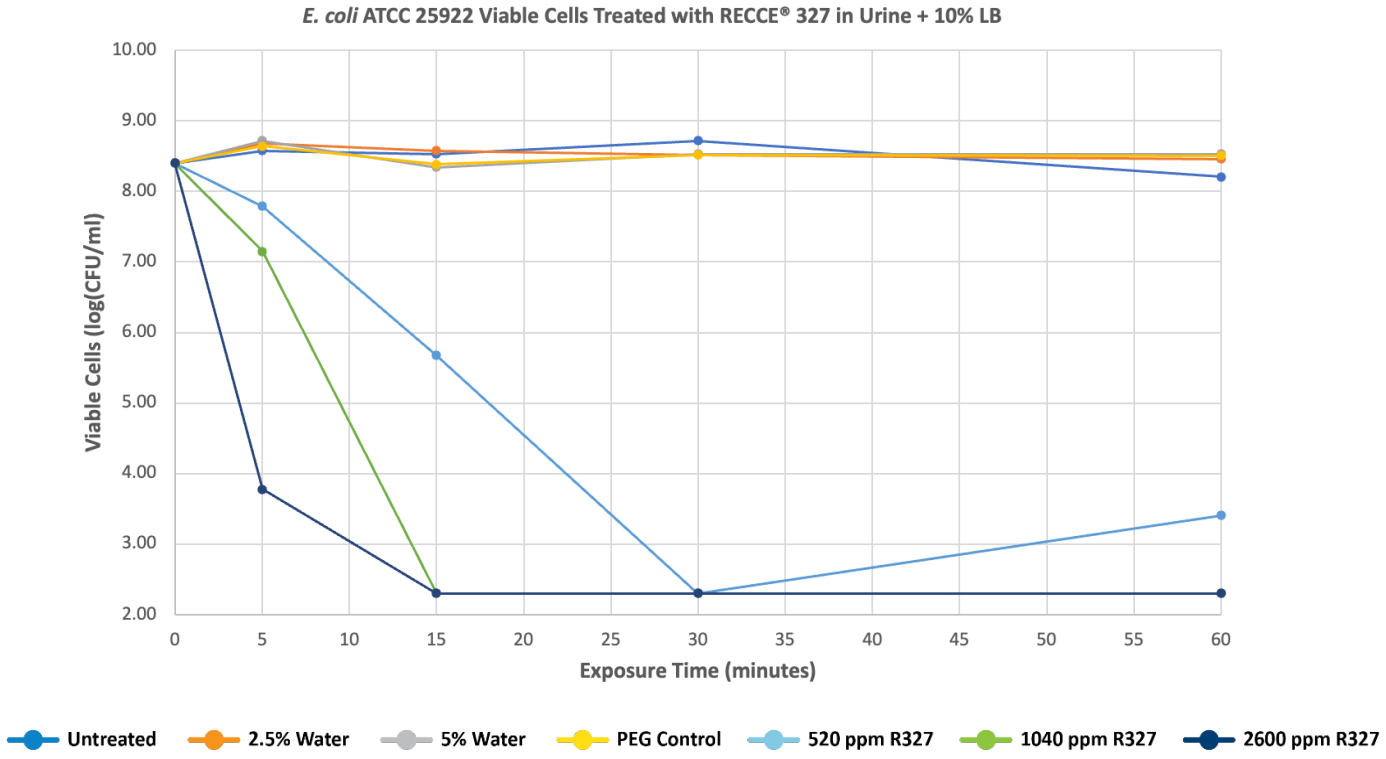


In 60 healthy subjects

R327 dose (mg)	Concentration of R327 in Human Urine – R327 Max Concentration (ug/ml)
500	53.5
1,000	110.8
2,000	176.1
3,000	157.2
4,000	490.4
6,000	570.8

Furthermore, an independent study demonstrated R327 in the presence of human urine could reduce the number of viable *E. coli* bacteria by over 99.99% in a matter of minutes (shown below). This, along with the excellent safety profile of R327, and preclinical *in vivo* kidney and UTI bacterial infections studies, highlights the great potential of R327 in treating complicated and uncomplicated UTIs.

RECCE® 327 Kills Quickly in Urine



recce.com.au
ACN 124 849 065

Chief Executive Officer
James Graham
Recce Pharmaceuticals Ltd
james.graham@recce.com.au

Media and Investor Relations

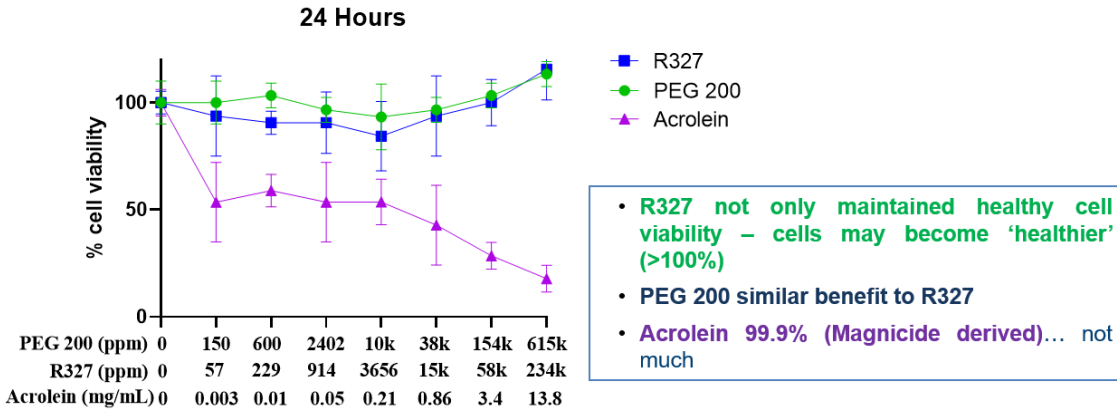
Australia
Andrew Geddes
CityPR
+61 408 677 734
ageddes@citypublicrelations.com.au

USA
Jordyn Temperato
LifeSci Communications
jtemperato@lifescicomms.com

Europe
Guillaume van Renterghem
LifeSci Advisors
gvanrenterghem@lifesciadvisors.com

Healthy Cell viability remained exceptionally high, even improving in the presence of R327

Viability of a Monocyte* Cell Line Treated with R327, PEG 200 and Acrolein

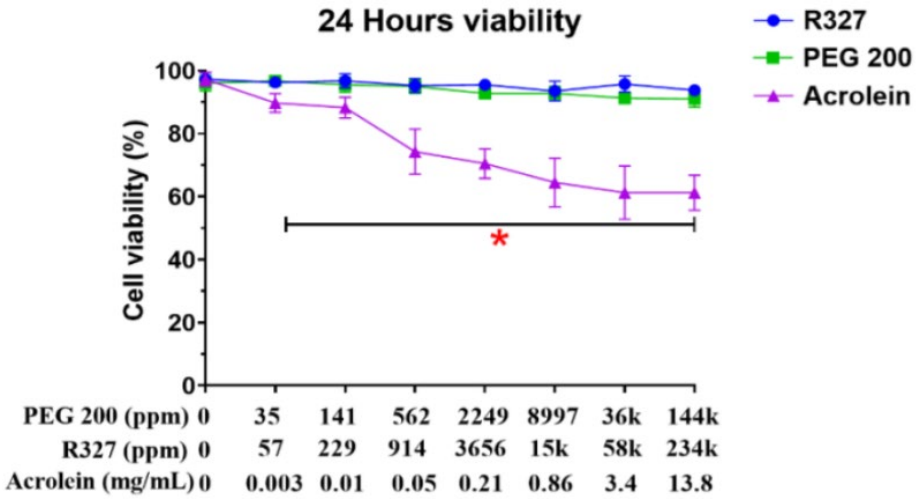


Monocytes are a type of white blood cell that resides in the blood and tissues to find and destroy germs

Another positive, yet unexpected finding was the improvement of healthy human cells in the PK/P.D. analysis, including indications of improved kidney health from R327 as it was excreted from the body.

The above study represents an independent study of the effect of R327 on healthy human cells, indicating cell health improving >100%, since repeated across multiple independent confirmatory investigations. In an unwell patient treatment setting, the wider support of human health is likely a welcomed feature from dosing of R327.

Viability of Healthy Kidney Cells* treated with R327, PEG 200 and Acrolein



***HEK-293 (ATCC CRL 1573)**

A further independent study (above) demonstrated the safety of R327 on viability of mammalian cells. The effect of R327 on a kidney cell line (ATCC CRL 1573). Results show R327 was well tolerated across a wide concentration range without any evident cytotoxicity to the kidney cells.

recce.com.au
ACN 124 849 065

Chief Executive Officer
James Graham
Recce Pharmaceuticals Ltd
james.graham@recce.com.au

Media and Investor Relations

Australia
Andrew Geddes
CityPR
+61 408 677 734
ageddes@citypublicrelations.com.au

USA
Jordyn Temperato
LifeSci Communications
jtemperato@lifescicomms.com

Europe
Guillaume van Renterghem
LifeSci Advisors
gvanrenterghem@lifesciadvisors.com

In most cases, antibiotics can cause kidney damage and can be quite a common occurrence. For example, in hospital wards antibiotics account for approximately 10% of episodes of acute renal failure and 60% of drug-related kidney damage[2]. Moreover, antibiotics can form crystals that don't break down and block urine flow[3]. One such example is one of the world's most widely prescribed commercial antibiotic (generates over US $10bn in revenue), which is known to cause urine crystallisation[4]. Others have substances that can damage certain kidney cells when attempting to filter them out. As previously mentioned, the results of the Phase I demonstrated no change in any chemistry parameter(s) to those dosed with R327, with all kidney and liver functions appearing to be normal.

Non-Executive Director of Recce Pharmaceuticals and Medical Monitor of the Clinical Trial, Alan W Dunton, MD said, "We are pleased to see that, even when administered at doses much higher than the expected therapeutic window, R327 IV does not lead to safety or toxicity issues in healthy subjects. We believe in the potential of R327 to provide a much-needed solution to patients with serious infections and look forward to providing interim proof-of-efficacy data in pre-sepsis patients in H2 2023."

Recce Pharmaceuticals, Executive Chairman Dr John Prendergast said, "We are highly encouraged by the safety and tolerability R327 demonstrated across eight cohorts at doses up to 6,000 mg, which is above the expected therapeutic range. We look forward to building off these results by initiating a Phase II study in patients with early-stage sepsis. There are currently no specific treatment options available for sepsis, with patients generally given broad-spectrum antimicrobials at first and then refined once the antibiograms become available a few hours after treatment initiations, which can be critical for patients with sepsis. Our next-generation anti-infectives have the potential to change the treatment landscape by becoming a universal first-line treatment for patients with life-threatening infections from both Gram-positive and Gram-negative bacteria, including their superbug forms."

Next Steps

The successful Phase I safety and tolerability study of R327 IV in healthy male volunteers has paved the way for the next stage of R327's clinical development in sepsis and UTIs. The Company is currently conducting a Phase I/II UTI clinical trial evaluating R327 IV at faster infusion rates – recently announcing its first cohort dosed, including its first female subject.

This announcement has been approved for release by Recce Pharmaceuticals Board.

[2]https://pubmed.ncbi.nlm.nih.gov/23059939/
[3]https://www.webmd.com/a-to-z-guides/medicine-hurt-kidneys#:~:text=way%20they%20should.-,Antibiotics,try%20to%20filter%20them%20out.
[4]https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8919213/#:~:text=Amoxicillin%20is%20known%20to%20cause,hematuria%20or%20acute%20renal%20failure.

recce.com.au
ACN 124 849 065

Chief Executive Officer
James Graham
Recce Pharmaceuticals Ltd
james.graham@recce.com.au

Media and Investor Relations

Australia
Andrew Geddes
CityPR
+61 408 677 734
ageddes@citypublicrelations.com.au

USA
Jordyn Temperato
LifeSci Communications
jtemperato@lifescicomms.com

Europe
Guillaume van Renterghem
LifeSci Advisors
gvanrenterghem@lifesciadvisors.com

About Recce Pharmaceuticals Ltd

Recce Pharmaceuticals Ltd (ASX: **RCE**, FSE: **R9Q**) is developing New Classes of Synthetic Anti-Infectives designed to address the urgent global health problems of antibiotic-resistant superbugs and emerging viral pathogens.

Recce's anti-infective pipeline includes three patented, broad-spectrum, synthetic polymer anti-infectives: RECCE® 327 as an intravenous and topical therapy that is being developed for the treatment of serious and potentially life-threatening infections due to Gram-positive and Gram-negative bacteria including their superbug forms; RECCE® 435 as an orally administered therapy for bacterial infections; and RECCE® 529 for viral infections. Through their multi-layered mechanisms of action, Recce's anti-infectives have the potential to overcome the hypercellular mutation of bacteria and viruses – the challenge of all existing antibiotics to date.

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. Further to this designation, RECCE® 327 has been included on The Pew Charitable Trusts Global New Antibiotics in Development Pipeline as the world's only synthetic polymer and sepsis drug candidate in development. RECCE® 327 is not yet market approved for use in humans with further clinical testing required to fully evaluate safety and efficacy.

Recce wholly owns its automated manufacturing, which is supporting present clinical trials. Recce's anti-infective pipeline seeks to exploit the unique capabilities of its technologies targeting synergistic, unmet medical needs.

recce.com.au
ACN 124 849 065

Chief Executive Officer
James Graham
Recce Pharmaceuticals Ltd
james.graham@recce.com.au

Media and Investor Relations

Australia
Andrew Geddes
CityPR
+61 408 677 734
ageddes@citypublicrelations.com.au

USA
Jordyn Temperato
LifeSci Communications
jtemperato@lifescicomms.com

Europe
Guillaume van Renterghem
LifeSci Advisors
gvanrenterghem@lifesciadvisors.com