Recce Pharmaceuticals
recce.com.au
ACN 124 849 065

Anti-Infective Portfolio Update

SYDNEY Australia, 19 October 2022: Recce Pharmaceuticals Ltd (**ASX:RCE**, **FSE:R9Q**) (the **Company**), the Company developing a New Class of Synthetic Anti-infectives, is pleased to announce a live online presentation to provide a comprehensive update on new pre-clinical data-sets, interim clinical trial data, and its expanding operational activities. The event will feature segments from experts in their respective fields and highlights the Company's significant progress across its portfolio of anti-infective programs.

The event will be held online via Zoom on **19th of October 2022 at 11AM AEDT**.

A full recording will be made available via Recce Pharmaceuticals website following the conclusion of the online presentation. Please register using the link below:

https://us02web.zoom.us/webinar/register/WN_JCRB3fBHTauHOTnJwatVDg

Please find provided below a copy of the agenda and presentation slides to be presented by speakers from Recce Pharmaceuticals, Linnaeus Bioscience, and LifeSci Advisors.

Topic	Speaker	Company
Introductory remarks	**James Graham** Managing Director & CEO	Recce Pharmaceuticals
R327 Phase I Intravenous - **Interim PK Data** - **Achieving Primary Endpoints** - **Next Steps (Ph Ib/IIa + Ph II UTI)**	**Dr Alan Dunton** Non-Executive Director	Recce Pharmaceuticals
R327 Mechanism of Action **Broad spectrum activity against:** - **ESKAPE pathogens** - **Biofilms** - **Growing and stationary phase pathogens** - **World Health Organisation Priority Pathogens**	**Dr Marc Sharp** Chief Scientific Officer	Linnaeus Bioscience
Pre-Clinical Datasets - **Bacterial Sinusitis** - ***H.pylori*** - ***M. abscessus***	**Dr Philip Sutton** VP of Translational Sciences	Recce Pharmaceuticals Formerly Murdoch Children's Research Institute
Biotech Global Market Update - **UTI Commercial and Market Opportunities** - **USD $66 million UTI GSK Deal** - **Rising capital market interests in antibiotic**	**Guillaume van Renterghem** Managing Director	LifeSci Advisors
Scientific Strategy - **Full therapeutic road map: R327** - **Addressing unmet medical needs** - **Multiple clinical-stage therapeutic indications**	**Michele Dilizia** Executive Director & CSO	Recce Pharmaceuticals

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

Chief Executive Officer
James Graham
Recce Pharmaceuticals Ltd
+61 (02) 9256 2571
james.graham@recce.com.au

Media and Investor Relations (AU)
Andrew Geddes
CityPR
+61 (02) 9267 4511
ageddes@citypublicrelations.com.au

Media and Investor Relations (USA)
Jordyn Temperato
LifeSci Communications
jtemperato@lifescicomms.com

Anti-Infective Portfolio Update

recce.com.au

ASX:RCE FSE:R9Q

October 2022

Disclaimer

DISCLAIMER

This presentation has been prepared by Recce Pharmaceuticals Ltd (the "Company"). It does not purport to contain all the information that a prospective investor may require in connection with any potential investment in the Company. You should not treat the contents of this presentation, or any information provided in connection with it, as financial advice, financial product advice or advice relating to legal, taxation or investment matters.

No representation or warranty (whether express or implied) is made by the Company or any of its officers, advisers, agents or employees as to the accuracy, completeness or reasonableness of the information, statements, opinions or matters (express or implied) arising out of, contained in or derived from this presentation or provided in connection with it, or any omission from this presentation, nor as to the attainability of any estimates, forecasts or projections set out in this presentation.

This presentation is provided expressly on the basis that you will carry out your own independent inquiries into the matters contained in the presentation and make your own independent decisions about the affairs, financial position or prospects of the Company. The Company reserves the right to update, amend or supplement the information at any time in its absolute discretion (without incurring any obligation to do so).

Neither the Company, nor its related bodies corporate, officers, their advisers, agents and employees accept any responsibility or liability to you or to any other person or entity arising out of this presentation including pursuant to the general law (whether for negligence, under statute or otherwise), or under the Australian Securities and Investments Commission Act 2001, Corporations Act 2001, Competition and Consumer Act 2010 or any corresponding provision of any Australian state or territory legislation (or the law of any similar legislation in any other jurisdiction), or similar provision under any applicable law. Any such responsibility or liability is, to the maximum extent permitted by law, expressly disclaimed and excluded. Nothing in this material should be construed as either an offer to sell or a solicitation of an offer to buy or sell securities. It does not include all available information and should not be used in isolation as a basis to invest in the Company.

FUTURE MATTERS

This presentation contains reference to certain intentions, expectations, future plans, strategy and prospects of the Company.

Those intentions, expectations, future plans, strategy and prospects may or may not be achieved. They are based on certain assumptions, which may not be met or on which views may differ and may be affected by known and unknown risks. The performance and operations of the Company may be influenced by a number of factors, many of which are outside the control of the Company. No representation or warranty, express or implied, is made by the Company, or any of its directors, officers, employees, advisers or agents that any intentions, expectations or plans will be achieved either totally or partially or that any particular rate of return will be achieved.

Given the risks and uncertainties that may cause the Company's actual future results, performance or achievements to be materially different from those expected, planned or intended, recipients should not place undue reliance on these intentions, expectations, future plans, strategy and prospects. The Company does not warrant or represent that the actual results, performance or achievements will be as expected, planned or intended.

US DISCLOSURE

This document does not constitute any part of any offer to sell, or the solicitation of an offer to buy, any securities in the United States or to, or for the account or benefit of any "US person" as defined in Regulation S under the US Securities Act of 1993 ("Securities Act"). The Company's shares have not been, and will not be, registered under the Securities Act or the securities laws of any state or other jurisdiction of the United States, and may not be offered or sold in the United States or to any US person without being so registered or pursuant to an exemption from registration including an exemption for qualified institutional buyers.

Introduction and Agenda

Topic	Speaker	Company
Introductory Remarks	**James Graham** Managing Director and CEO	Recce Pharmaceuticals Ltd
R327 Phase I Intravenous - Interim PK Data - Achieving Primary Endpoints - Next Steps (Ph Ib/IIa + Ph II UTI)	**Dr Alan Dunton** Non-Executive Director	Recce Pharmaceuticals Ltd

R327 Mechanism of Action
- Broad spectrum activity against:
  - ESKAPE pathogens
  - Biofilms
  - Growing and stationary phase pathogens
  - World Health Organisation Priority Pathogens
	Dr Marc Sharp
	Chief Scientific Officer
		Linnaeus Bioscience

Pre-clinical Datasets - Bacterial Sinusitis - ***Helicobacter pylori*** - ***Mycobacterium abscessus***	**Dr Philip Sutton** VP of Translational Sciences	Recce Pharmaceuticals Ltd *Formerly Murdoch Children's Research Institute*
Biotech Global Market Update - UTI Commercial and Market Opportunities - USD $66 million UTI GSK Deal - Rising capital market interests in antibiotic	**Guillaume van Renterghem** Managing Director	LifeSci Advisors
Scientific Strategy - Full therapeutic road map: R327 - Addressing unmet medical needs - Multiple clinical-stage therapeutic indications	**Michele Dilizia** Executive Director and CSO	Recce Pharmaceuticals Ltd

Pre-Clinical/Clinical Studies

Alan W Dunton, M.D., Non-Executive Director, Recce Pharmaceuticals Ltd

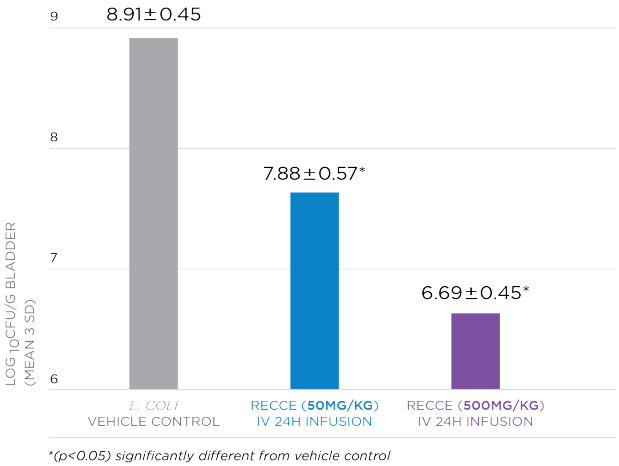
Former President and Managing Director,
Janssen Research (Johnson & Johnson)

Former Vice President of Global Clinical R&D
R.W. Johnson Pharmaceutical Research Institute

Recce
Pharmaceuticals

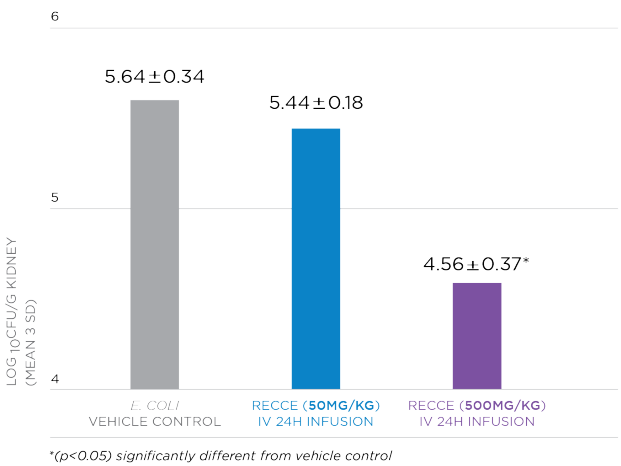
Pre-Sepsis UTI and Kidney Models in Rats

Efficacy: Bladder



*(p<0.05) significantly different from vehicle control

Efficacy: Kidneys



*(p<0.05) significantly different from vehicle control

Single 24-hour intravenous infusion

Group 1 – *E. coli* infection + vehicle control

Group 2 – *E. coli* infection + R327 50mg/kg

Group 3 – *E. coli* infection + R327 500mg/kg

- R327 as a treatment of Kidney and other UTIs caused by *E. coli*, (pre-sepsis) 'early stage'
- R327 showed dose dependent antibacterial effect in the kidney and bladder at 50mg/kg and 500mg/kg when compared to vehicle control (p<0.050).
- Rats treated with RECCE® 327: no adverse clinical signs were observed

Phase I Clinical Single-dose safety and PK study

Reason for Optimism in Treating UTI/Sepsis

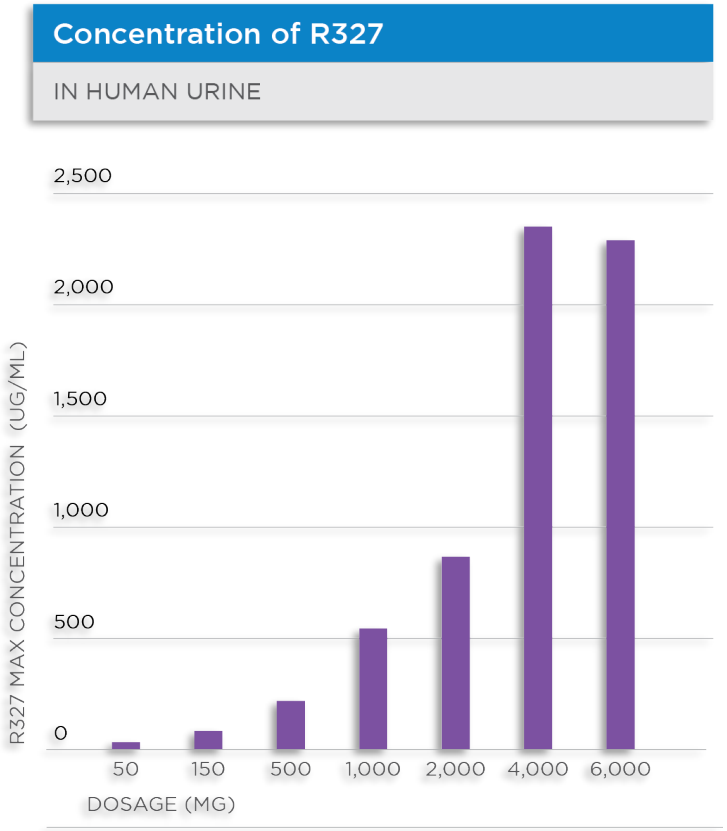
- **R327 primary route of elimination** appears to be through the kidney to the ureters and bladder.
- **High concentrations of R327** noted in the urine of Phase I healthy subjects.
- **Insight consistent** with pre-clinical *in-vivo* kidney and UTI bacterial infection studies.
- **Opportunities for therapeutic in array of UTIs (uncomplicated UTI - single dose, complicated UTI, recurrent UTI, treatment resistant etc).**
- Suggests **broader anti-infective treatment model** in pre-sepsis.

Concentration of R327 in Urine Compared to Plasma

In over 60 healthy subjects

Dose (mg)	Concentration of R327 in Human Plasma – R327 Max Concentration (ug/ml)	Concentration of R327 in Human Urine – R327 Max Concentration (ug/ml)	Ratio Urine/Plasma -
50	1.4	21.3	**15x**
150	5.1	68.5	**13x**
500	13.5	204.5	**15x**
1,000	32	529.5	**17x**
2,000	60.5	860.7	**14x**
4,000	115	2352.2	**20x**
6,000	175	2295.7	**13x**

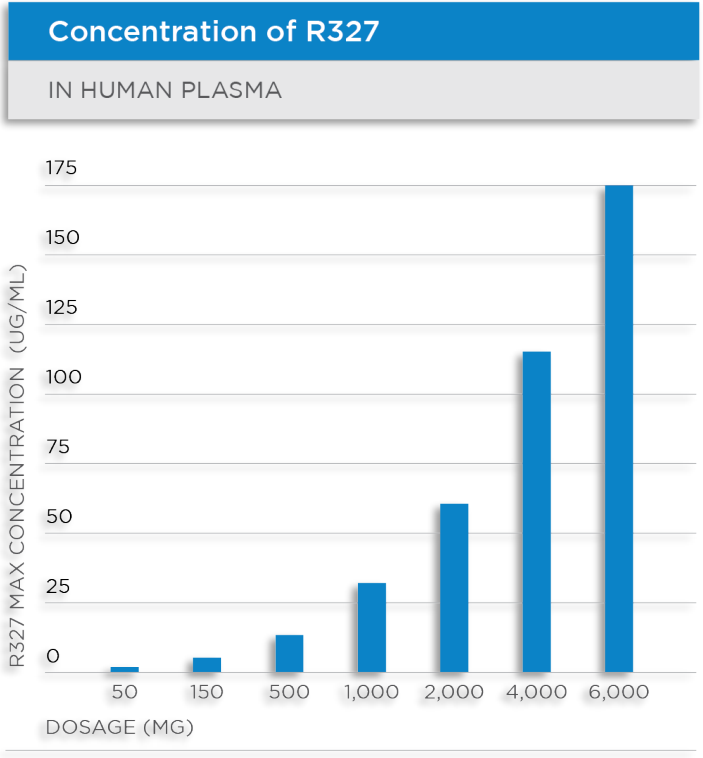
Phase I Single-dose clinical study – R327 in the Urinary Tract



- Significant dose dependant concentration of R327 in subjects urine
- Compound concentrated in the urinary tract – potential for site specific interreaction with bacteria
- Compelling profile for a UTI drug candidate

Dose (mg)	Concentration of R327 in Human Urine - R327 Max Concentration (ug/ml)
50	21.3
150	68.5
500	204.5
1,000	529.5
2,000	860.7
4,000	2352.2
6,000	2295.7

Phase I Single-dose clinical study – R327 in Human Plasma



- Significant dose dependant concentration of R327 in subjects plasma (blood)
- R327 in human plasma – potential for interreaction with bacteria in the blood
- Compelling profile for a sepsis drug candidate

Dose (mg)	Concentration of R327 in Human Plasma – R327 Max Concentration (ug/ml)
50	1.4
150	5.1
500	13.5
1,000	32
2,000	60.5
4,000	115
6,000	175

Pre-Clinical and Clinical Studies

- ***In vivo pre-clinical***
  - Pre-Sepsis UTI Models in Rats ✓
- **Phase I clinical trials**
  - R327 I.V. Single Dose, Safety/Tolerability/PK study in healthy subjects ✓
- **Phase II UTI clinical trial (Pre-Sepsis)**
  - Single (as now completed Phase I) efficacy study – Q1 2023
  - Multiple-dose treatment of UTIs - complicated/resistant/chronic/etc. H1 2023
- **Phase Ib/IIa Sepsis clinical trial**
  - R327 I.V. Multiple Dose, Safety/Tolerability/PK study in healthy subjects (First patient dosing Q4 2022)
  - Multiple-Dose efficacy study in **urosepsis*** (sepsis derived from UTI infections) – efficacy signal

Urosepsis – 25 percent of sepsis cases originate from the urogenital tract

RECCE® 327 Mechanism of Action

Marc Sharp, PhD, Chief Scientific Officer Linnaeus Bioscience Inc., USA

RECCE® 327 (R327) is a synthetic polymer 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.

Through its unique and multi-layered mechanism of action (MoA), R327 ***permeabilizes*** *the* ***cell membrane,*** *causing* ***lysis*** *at high concentrations;* ***disrupts*** *bacterial cellular energetics;* ***arrests cell division*** *and* ***kills*** *even* ***non-dividing cells****.*

Recce
Pharmaceuticals

Mechanism of Action – RECCE® 327

- The activity of **RECCE® 327** (R327) was investigated against a wide array of **Gram-positive**, **Gram-negative**, and **mycobacterial species**
  - Including the **ESKAPE pathogens**, ***Bacillus subtilis*** and ***Escherichia coli*** biofilms to determine the effects of R327 on these bacterial species
- Graphs convey ATP levels and viable cells for different bacterial strains treated with 0, 1X, 2X and 5X the MIC (varying PPM's) of R327 for one hour in 10% LB
  - By testing it in 10% LB we were able to **treat all of the strains at the same relative concentrations**

"A unique mode of action that we've not seen before"

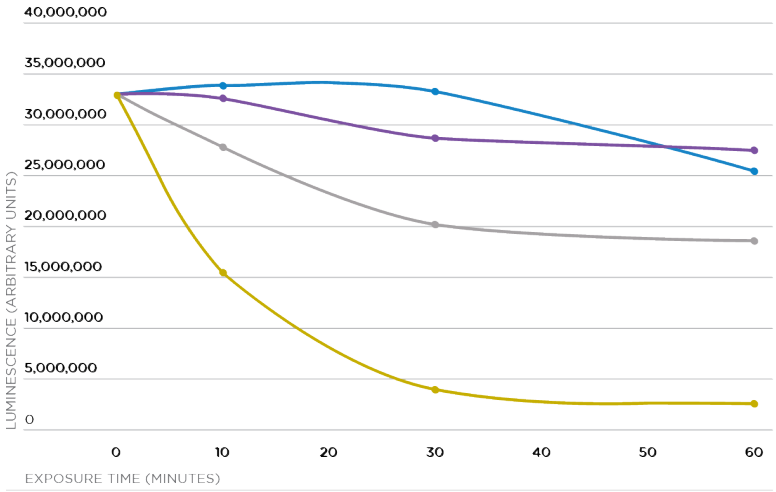
World Health Organisation List of Most Threatening Antibiotic Resistant Bacteria

PRIORITY 1: CRITICAL	RECCE® 327
• *Pseudomonas aeruginosa*, carbapenem-resistant	✓ 1
• *Enterobacteriaceae*, carbapenem-resistant, ESBL-producing	✓ 2
• *Acinetobacter baumannii*, carbapenem-resistant	✓ 3
PRIORITY 2: HIGH	
• *Enterococcus faecium*, vancomycin-resistant	✓ 4
• *Staphylococcus aureus*, methicillin-resistant, vancomycin-intermediate and resistant	✓ 5
• *Helicobacter pylori*, clarithromycin-resistant	✓ 6
• *Neisseria gonorrhoeae*, cephalosporin-resistant, fluoroquinolone-resistant	✓ 7
• *Campylobacter spp.*, fluoroquinolone-resistant	Not Tested
• *Salmonellae*, fluoroquinolone-resistant	Not Tested
PRIORITY 3: MEDIUM	
• *Streptococcus pneumoniae*, penicillin-non-susceptible	✓ 8
• *Haemophilus influenzae*, ampicillin-resistant	Not Tested
• *Shigella spp.*, fluoroquinolone-resistant	Not Tested

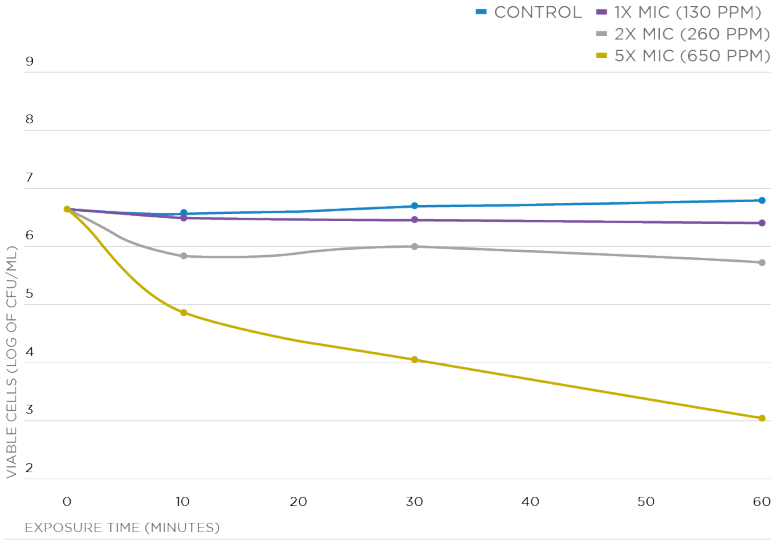
1 Active *in vitro* against Recce's own superbug of this bacterium
2 Active *in vivo* against a member of this family CRE *E. coli*
3 Active *in vitro* and against superbug variant CRAB
4 Active *in vitro* against a very closely related species, *Enterococcus faecalis*,
5 Active both *in vitro* and *in vivo* against MRSA, Methicillin-resistant *S. aureus*
6 Active both *in vitro* and *in vivo* against three strains (2 of which were superbugs)
7 Active *in vitro* (superbug not available)
8 Active *in vitro* against related superbug *Klebsiella pneumoniae*
* List as of 2017

RECCE® 327 activity in 10% LB: *E. coli* ATCC 25922*

ATP Levels in *E. coli* ATCC 25922 Treated with RECCE® 327 in 10% LB



Viable Cells in *E. coli* ATCC 25922 Treated with RECCE® 327 in 10% LB



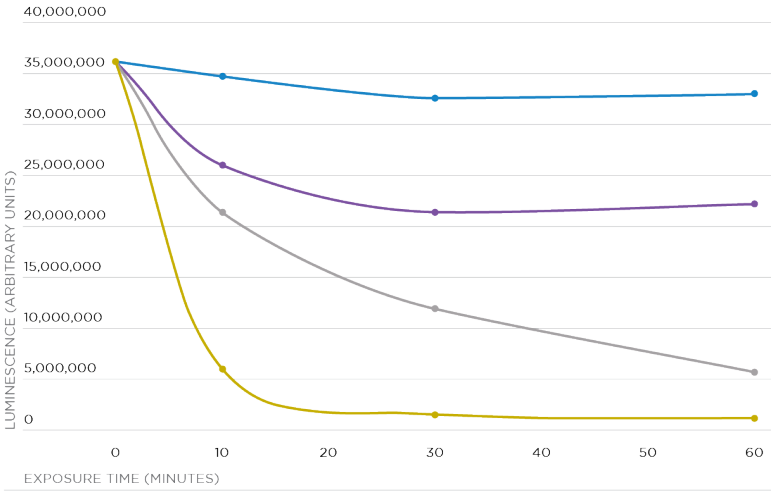
"R327 is killing all the cells in that culture within an hour"

recce.com.au

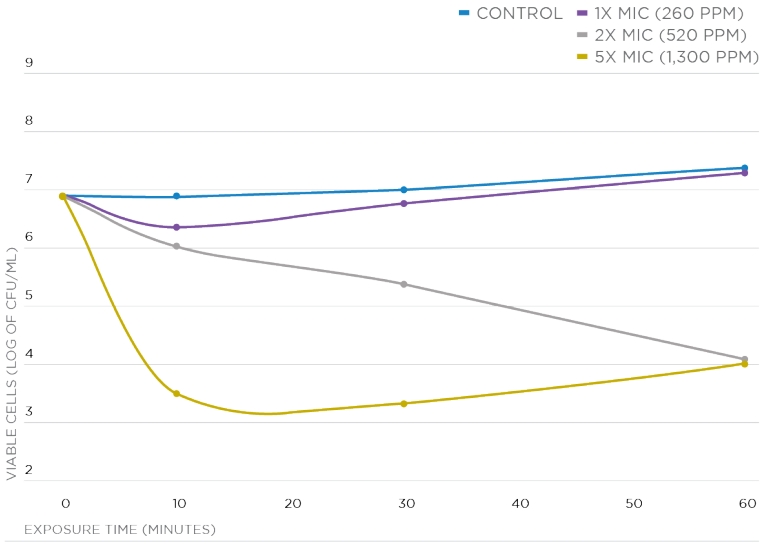
**Originally isolated from a human clinical sample collected in Seattle and WA (1946). It is of serotype O6 and biotype 1*

RECCE® 327 activity in 10% LB: *B. subtilis* PY79*

ATP Levels in *B. subtilis* PY79 Treated with RECCE® 327 in 10% LB



Viable Cells in *B. subtilis* PY79 Treated with RECCE® 327 in 10% LB



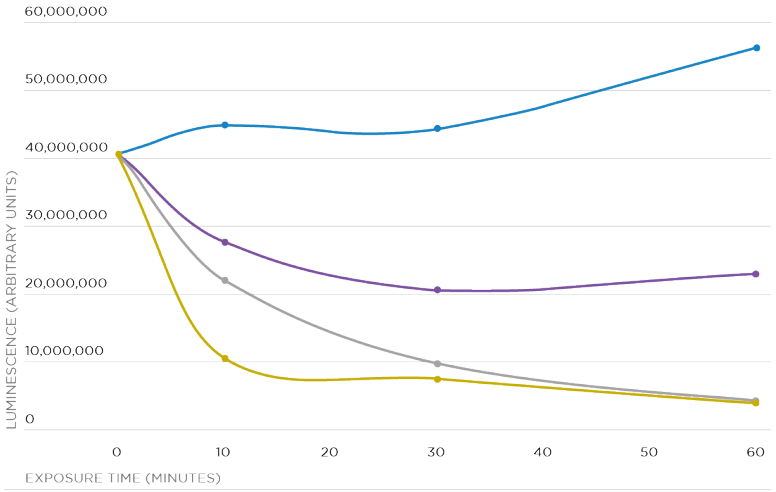
"Rapid decrease in ATP levels when you treat with R327"

recce.com.au

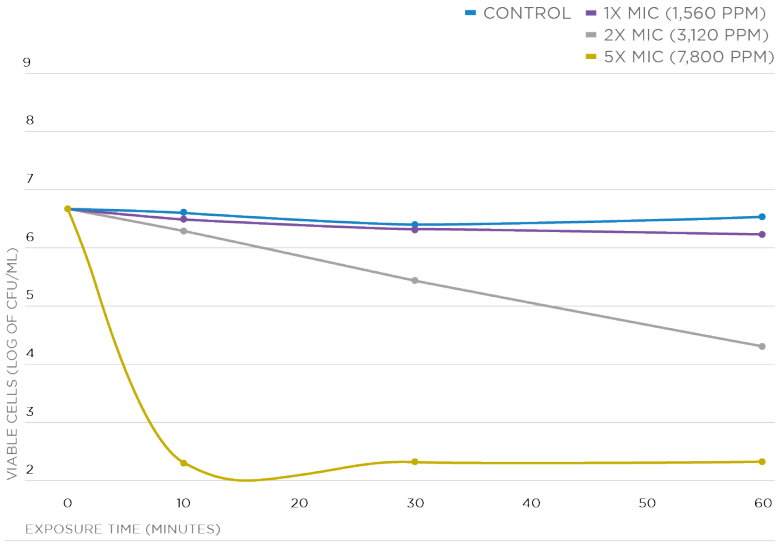
**Prototrophic laboratory strain that has been highly used for studying a wide variety of cellular pathways*

RECCE® 327 activity in 10% LB: *P. aeruginosa* PAO1*

ATP Levels in *P. aeruginosa* PAO1 Treated with RECCE® 327 in 10% LB



Viable Cells in *P. aeruginosa* PAO1 Treated with RECCE® 327 in 10% LB

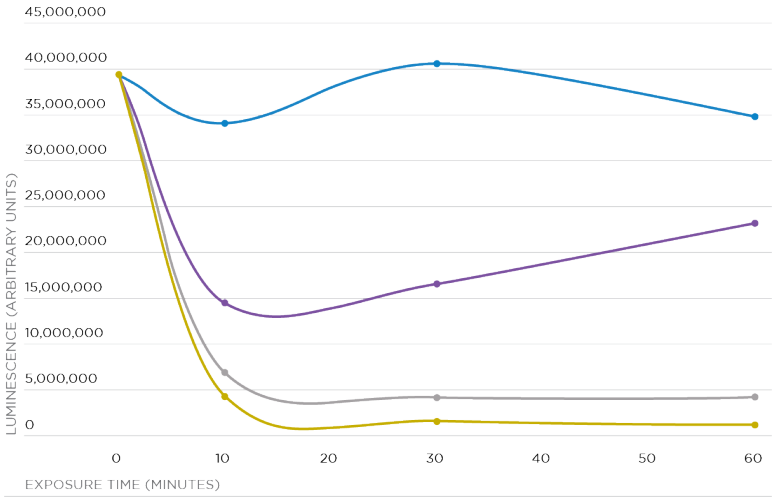


"Extremely resistant pathogen, very few drugs affect this pathogen and we're seeing again very strong effects from R327"

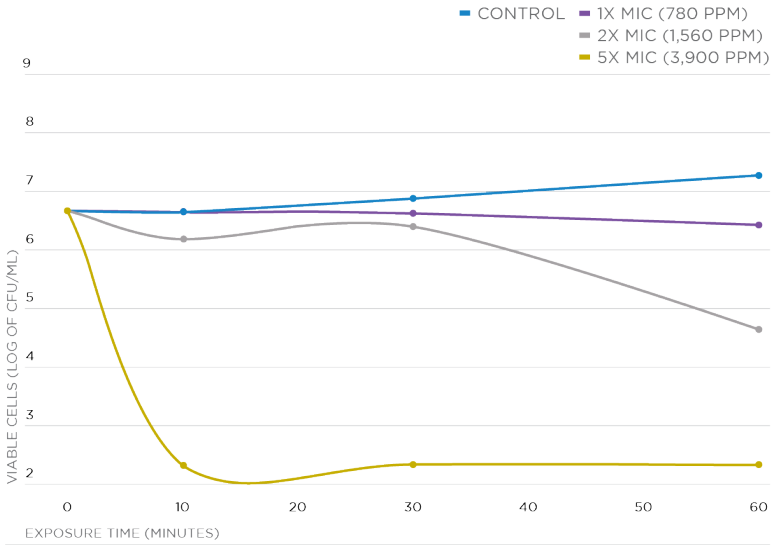
**Isolated from human wound*

RECCE® 327 activity in 10% LB: *A. baumannii* ATCC 17978*

ATP Levels in *A. baumannii* ATCC 17978 Treated with RECCE® 327 in 10% LB



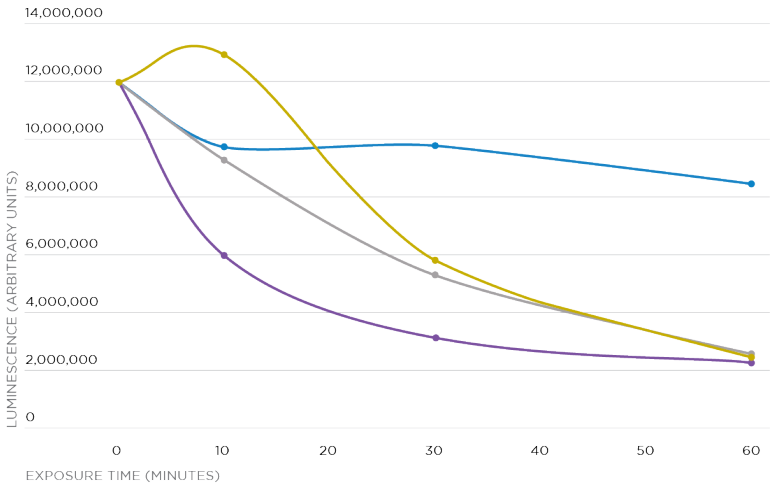
Viable Cells in *A. baumannii* ATCC 17978 Treated with RECCE® 327 in 10% LB



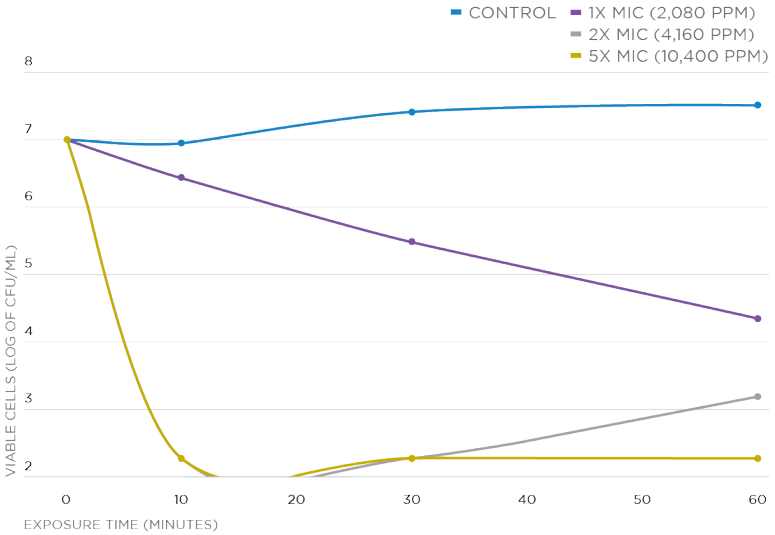
**Isolated from a fatal case of meningitis in a 4-month-old human*

RECCE® 327 activity in 10% LB: *K. pneumoniae* ATCC 700603*

ATP Levels in *K. pneumoniae* ATCC 700603 Treated with RECCE® 327 in 10% LB



Viable Cells in *K. pneumoniae* ATCC 700603 Treated with RECCE® 327 in 10% LB

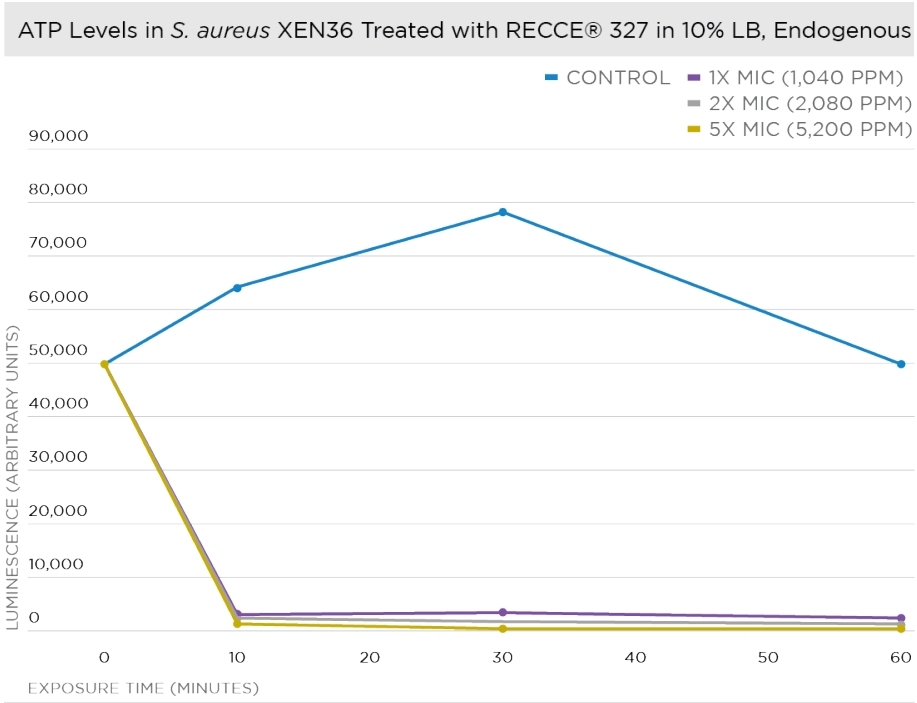


"Very significant effect as quick as we can test this, within 10 minutes of treatment you're seeing very strong decreases"

recce.com.au

**Isolated from urine from hospitalised patient*

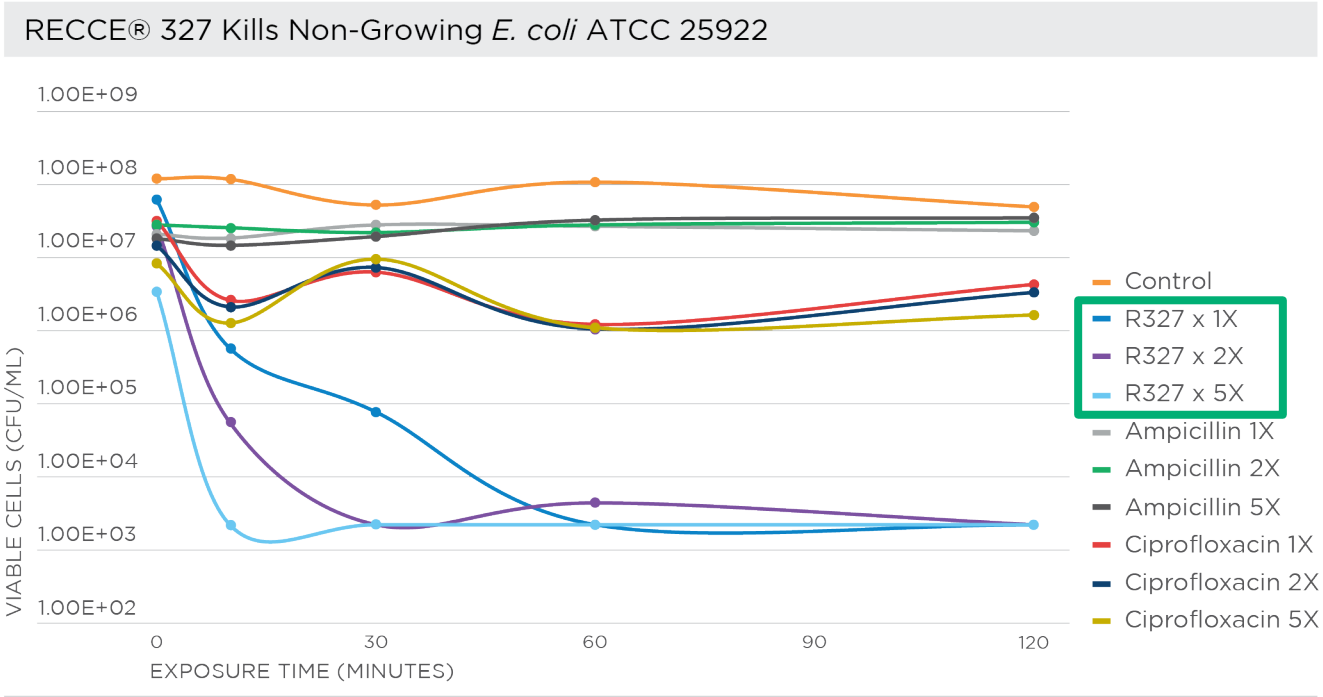
RECCE® 327 activity in 10% LB: *S. aureus* XEN36*



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

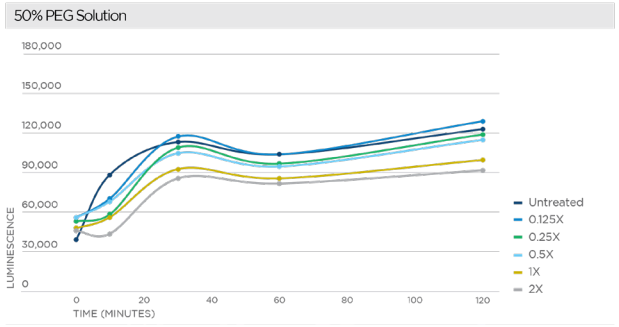
**Staphylococcus aureus Xen36 was derived from the parental strain Staphylococcus aureus ATCC 49525 (Wright), a clinical isolate from bacteraemia patient.*

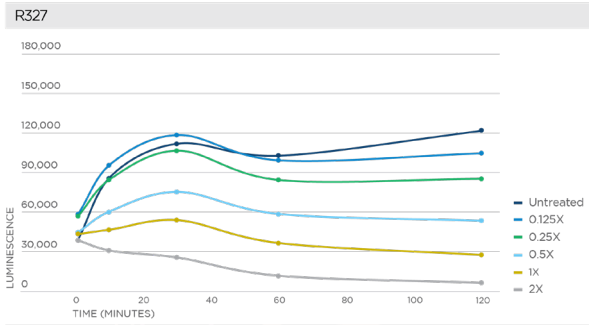
RECCE® 327 rapidly kills non-growing *E. coli*

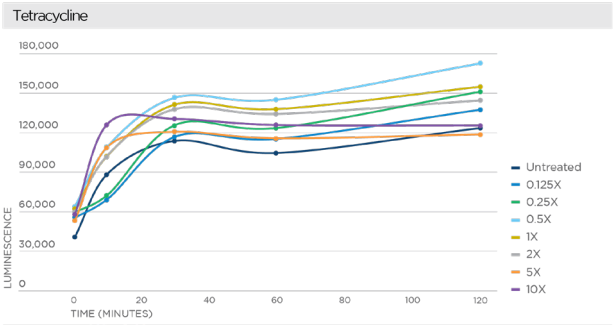


"Many antibiotics will not kill non-growing cells… R327 kills non growing cells and kills them very rapidly and irreversibly"

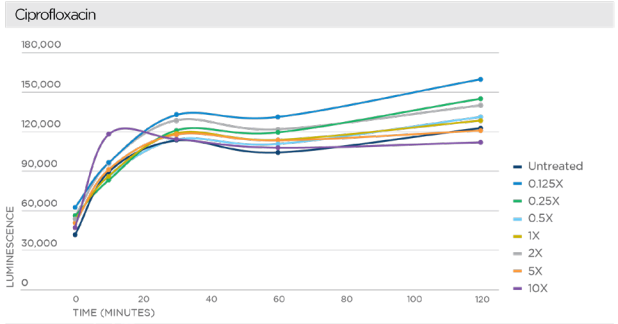
RECCE® 327 efficiently kills *E. coli* in a Biofilm

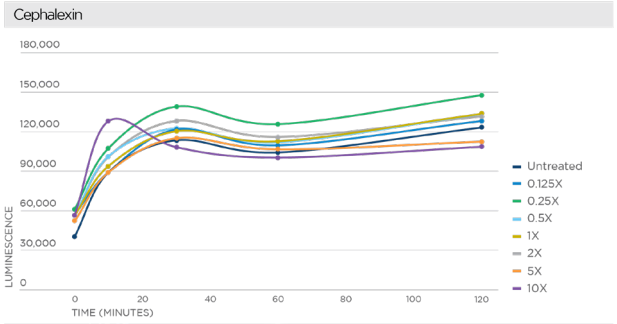


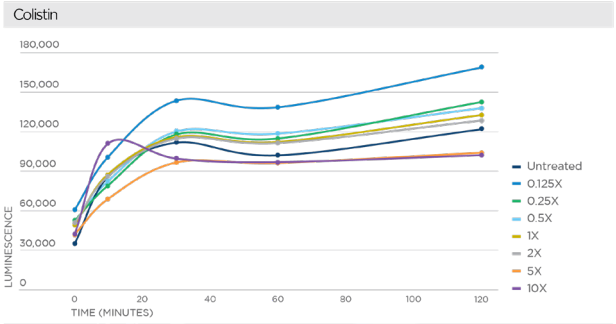




Unlike many common antibiotics, ***R327 disrupts cellular bioenergetics and efficiently kills E. coli in a biofilm***







Mechanism of Action – Linnaeus Biosciences

Results

R327 is **rapidly bactericidal, reducing viable cell counts** across all tested bacterial species and conditions.

Cells treated with **R327** showed **rapid, dose-dependent, decreases in cellular ATP levels** in luciferase-based *in vitro* ATP assays.

Conclusion

These results confirm that R327 is:

- **Broad Spectrum**
- **Bactericidal**
- **Effective** against **growing** and **non-growing** cells

*R327 demonstrates great potential as a **new anti-infective***

Pre-clinical Update

Dr Philip Sutton – Vice President of Translational Sciences, Recce Pharmaceuticals Ltd

Former Group Leader/Senior Principal Research Fellow, Mucosal Immunology
Murdoch Children's Research Institute

Agenda:

Bacterial Sinusitis

Helicobacter pylori

Mycobacterium abscessus

Recce
Pharmaceuticals

Bacterial Sinusitis

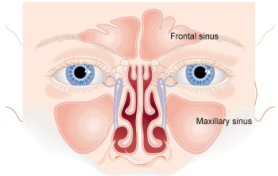
Bacterial Sinusitis affects ***28.9 million people in the U.S. each year****, making it* ***one of the most common health problems,*** *with 11.6% of U.S. adults diagnosed with Chronic Sinusitis annually.*

The most common causative bacteria: ***Streptococcus pneumoniae***

Recce Pharmaceuticals

Sinusitis is a typically mild infection or inflammation of the tissue lining the sinuses that is treated in the outpatient setting

Disease Overview



The maxillary and frontal sinuses can both be infected causing manifestation of sinusitis

- **Infection of the sinuses causes symptoms such as facial pain, congestion, nasal obstruction, and fever**
- Most cases of uncomplicated acute bacterial sinusitis have strong prognosis, but frontal or sphenoid sinusitis may require hospitalization
- Estimated 12% of U.S. population affected by acute and chronic rhinosinusitis (~40 million people); acute bacterial rhinosinusitis (ABRS) most commonly occurs as a complication of viral infection

Sinusitis is a highly prevalent condition that can be treated via intranasal antibiotics, providing rationale for development of a novel antibiotic agent

Pathogen Context

Key Pathogens

Increasing Frequency

- *S. pneumoniae*
- *H. influenzae*
- *M. catarrhalis*
- *S. aureus*
- *P. aeruginosa*

- There is significant heterogeneity in pathogens, though gram-negative bacteria are more common in hospital settings and immunocompromised patients

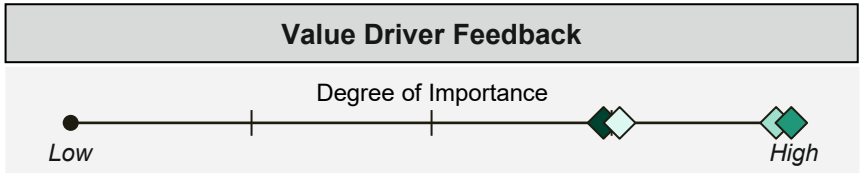
Patient / Population Context

- Patients with severe complications such as high, persistent fever, inflammation, and altered mental status may be urgently referred given potential for severe disease course
- Immunocompromised patients with ABRS are at higher risk for severe disease and warrant immediate antibiotic therapy
- Approximately 80% of all ABRS cases are believed to be self-limiting and may not require antibiotic treatment

ABRS: Acute Bacterial Rhinosinusitis. Source: Cingi. Nature Public Health Emergency Collection. 2019; UpToDate; Physician Interviews; ClearView Analysis.

KOLs were impressed with the value drivers for R327 and believed it could have strong utility in poorly managed recurrent patients

Physician Perceptions of R327



Efficacy Against Drug Resistant Pathogens

- KOLs noted that difficult-to-treat sinusitis is often due to resistant pathogens, and saw significant value in R327's broad set of targets

"This would be a great alternative to surgery. There's a subset of patients that need it if antibiotics cannot resolve the sinusitis." – ENT KOL

Maintained Activity With Repeat Use

- The ability to repeatedly administer R327 could fit well into antibiotic stewardship for an infection that can be recurrent

Multiple ROAs

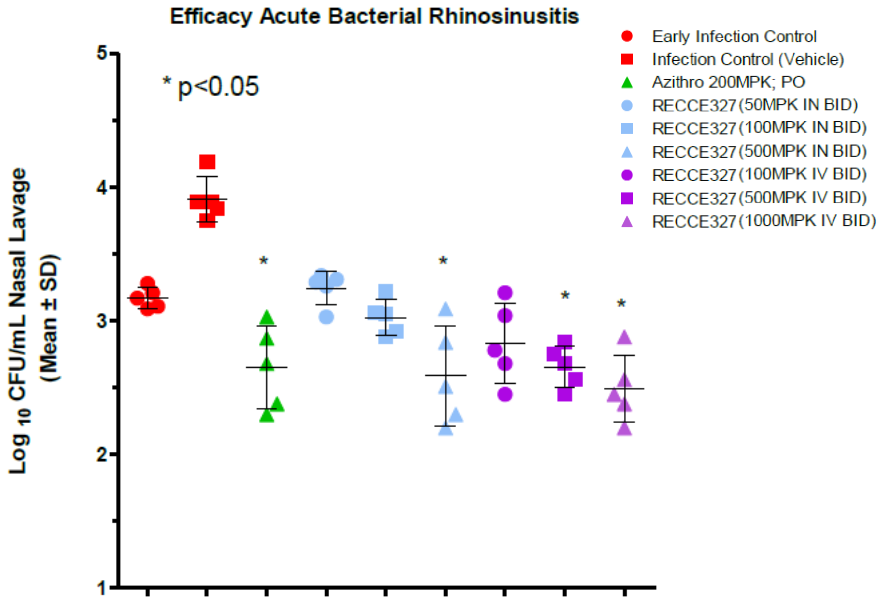
- Physicians were enthusiastic about an intranasal ROA if it demonstrated novelty and efficacy over current intranasal formulations

"If this really targets both bacteria and viruses, it would be highly useful and probably broaden the number of patients it is used in." – ENT KOL

Source: Physician Interviews; ClearView Anaysis.

Bacterial Sinusitis

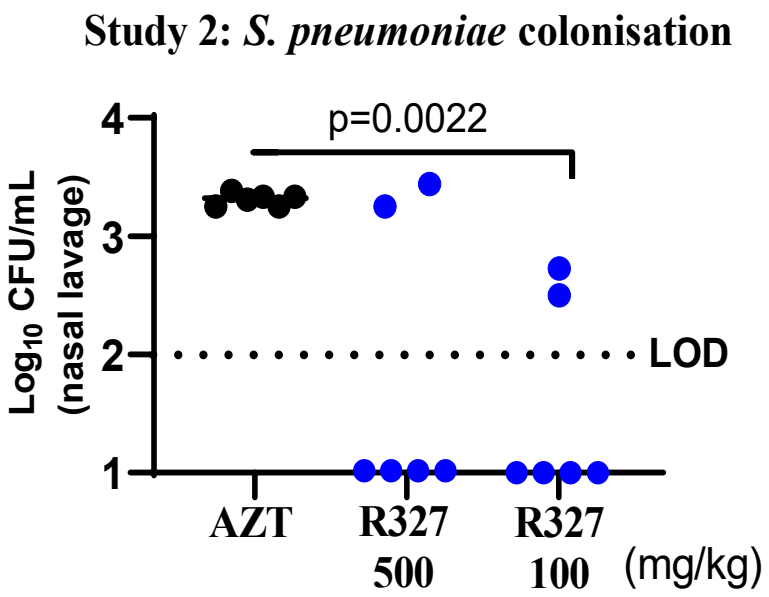
Study 1: By independent Contract Research Organisation (CRO)



- Nasal cavities of mice infected with *S. pneumoniae* (clinical isolate – ATCC 49619)
- Treatment of anaesthetised mice with R327 by both intranasal and intravenous routes significantly reduced nasal infection by *S. pneumoniae*
- R327 efficacy in this study was similar to positive control group treated with Azithromycin

Bacterial Sinusitis

Study 2: By Murdoch Children's Research Institute using improved protocol



LOD: Limit of detection

Mice infected with *S. pneumoniae* (clinical isolate – ATCC 49619) were treated nasally, twice daily for 5 days, with R327

Treatment of non-anaesthetised mice with R327 by intranasal route:

- **Significantly reduced nasal infection by *S. pneumoniae***
- **Eradicated infection in 8/12 treated mice**
- **Superior to positive control group** treated with Azithromycin (in which infection was not eradicated in any mice)

Bacterial Sinusitis

Key Findings so far:

- R327 treatment via the nasal route **can eradicate nasal *S. pneumoniae* infection** (the most common bacterial cause of sinusitis) in mice
- Successful treatment of a patient's multidrug-resistant *Pseudomonas aeruginosa* sinusitis infection with R327 via nasal passage
  - Under TGA Special Access Scheme Category A
  - Patient reported a **substantial reduction in infected discharge with no side effects** after 3-day treatment with R327 topical nasal spray
- Sufficient and compelling data now creates the potential to start a Phase I/II clinical trial

Helicobacter pylori

*There is a global unmet medical need for the treatment of **Helicobacter pylori (H. pylori)** with **no first-line therapy curative in all patients**.*

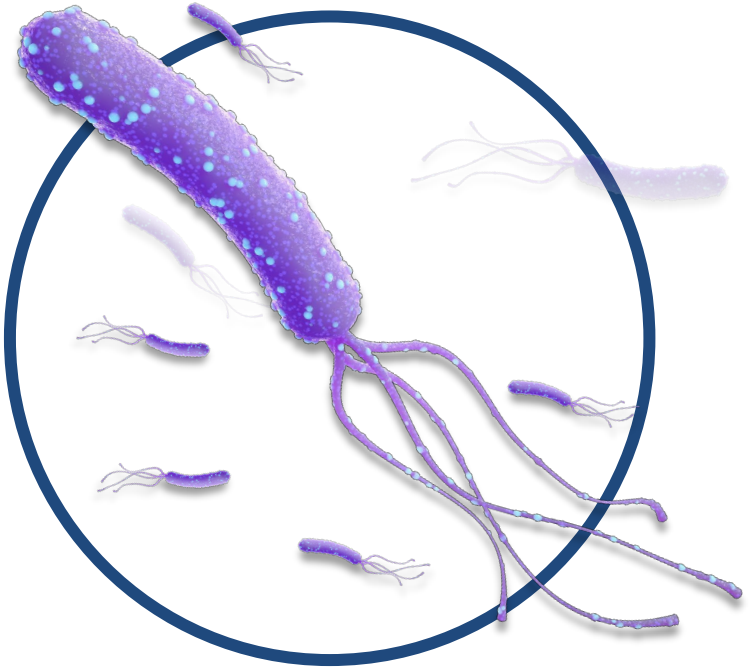
*To date, **half the world's population is estimated to be infected with H. pylori.***

Recce
Pharmaceuticals

Helicobacter pylori (H. pylori)

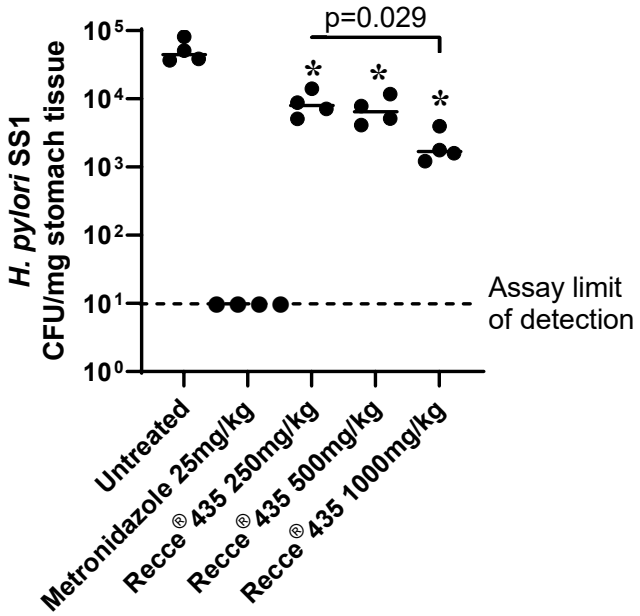
What is *H. pylori?*

- Gram-negative bacterium
- Infects during childhood and typically colonises for life
- An estimated half the world's population is infected
- Causes chronic gastritis that is the driver of a range of pathologies including:
  - Stomach adenocarcinoma
  - Gastric MALT lymphoma
  - Gastric ulcers
  - Duodenal ulcers
- Treated with oral antibiotic cocktails (triple or quadruple therapy; standard frontline therapies)
  - **Antibiotic resistance** a **large** and **increasing problem**
  - WHO recently listed *H. pylori* amongst **top ten bacteria where new antibiotics are most urgently needed**



H. pylori

Summary
Good efficacy in culture and reduces *H. pylori* colonisation by 1-2 logs (90-99% reduction) *in vivo (mice)* demonstrating R435 effectively kills *H. pylori,* but suggests more formulation work and dosing optimisation is required to improve delivery to site of infection.



MIC (µg/mL)			
H. pylori strain	Metronidazole	Clarithromycin	R435
CI1	8	<0.125	16
CI2	256	0.25	32
CI3	64	<0.125	4
CI4	1	<0.125	4
B128	4	0.25	<0.125
11637	0.5	<0.125	0.25
SS1	0.5	<0.125	8

Using the broth dilution method, **R435 was demonstrated to have efficacy against all seven strains of *H. pylori* tested** having different virulence factors and similar efficacy as metronidazole and clarithromycin (cell culture assays), including four human clinical isolates (C1-C4), and mouse colonising strains SS1, B128 and lab type strain 11637.

Mycobacterium abscessus

and other Non Tuberculous Mycobacteria (NTM)

Mycobacterium abscessus (M. abscessus) *drug therapy can take up to 2 years and its failure causes an accelerated lung function decline.*

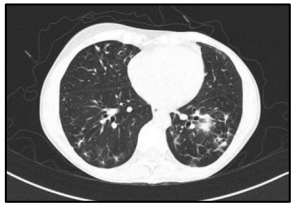
M. abscessus ***is intrinsically resistant*** *to several classes of antibiotics and the* ***incidence of multidrug-resistant strains is steadily rising.***

No effective standard antibiotic treatments currently exist for ***M. abscessus*** *infection.*

Recce
Pharmaceuticals

NTM infections may result in a chronic lung disease defined by nonspecific symptoms and is primarily caused by MAC, *M. kansaii,* and *M. abscessus*

Disease Overview



An abnormal thoracic CT scan of a patient with NTM lung disease demonstrates diffuse bronchiectasis

- NTM lung disease may manifest as the less progressive nodular bronchiectasis and the more progressive cavitary disease
- Symptoms may be nonspecific including chronic cough, weight loss, fatigue, fever, night sweats, shortness of breath, chest pain, and recurring respiratory infections

Disease Area	Primary ROA	Setting of Care
Respiratory	Oral, Inhaled, Intranasal, IV	Community

NTM lung disease is an orphan indication with significant unmet need that is chronically treated in the community setting

Pathogen Context

Key Pathogens

Increasing Frequency

- *M. avium* complex
- *M. kansaii*
- *M. abscessus*
- *M. gordonae*
- *M. fortuitum*

- Nontuberculous mycobacteria are commonly found in water and soil
- Incidence of specific pathogens vary by region with *M. abscessus* most frequent in the West
- Pathogens may be distinguished based on rate of growth on solid culture medium

Patient / Population Context

- Infections are most common in the elderly and postmenopausal women, immunocompromised patients, and patients with underlying lung disease
- Though NTM occurs throughout the U.S., the Mid-Atlantic, Southeast, California, and Texas have the highest rates of infection

CF: Cystic Fibrosis; ILD: Interstitial Lung Disease; MAC: *M. avium* complex. Source: Cowman. European Respiratory Journal. 2019; Spaulding. *Ann Am Thorac Soc.* 2017; Kwon. J Korean Med Sci. 2016; UpToDate; Physician Interviews; ClearView Analysis.

KOLs perceived significant unmet need for novel agents that could reduce duration of therapy and improve NTM treatment tolerability

Key NTM Unmet Needs

Increasing Need

Unmet Need	Description	Physician Perspectives
Novel Therapies with Shorter Treatment Course	• Strong desire for an effective option with a shorter duration of treatment relative to the current 12 – 24 month course of antibiotics, with hesitance initiating treatment noted[1] • Physicians noted the large burden on patients given the length of treatment, highlighting resulting adherence issues	*"This is a long treatment to keep patients on and it doesn't make them feel that much better very quickly."* – *Pulmonologist KOL*
Therapeutic Regimens with Safer, More Tolerable Profile	• Further adherence problems noted given poor safety and tolerability of current agents, with one physician stating that demonstrating just superior safety/tolerability (with comparable efficacy) to SoC would be sufficient to drive early use of a novel agent	*"The side effect profile of these medications makes patients feel sick. This is a long treatment to stay on when you already don't feel well."* – *Pulmonologist KOL*
More Efficacious and Convenient Treatments	• Physicians believed there was remaining unmet need for patients who are refractory to current treatments, especially patients with RGM who must resort to surgical intervention[2] • Current regimens utilize multiple agents which can pose burdens for patients, and a novel monotherapy may be quickly adopted	*"If a patient has M. abscessus, they're fortunate if they get any improvement, and there's sometimes potentially permanent damage."* – *Pulmonologist KOL*

A novel therapy that will experience meaningful uptake will likely need to significantly improve upon duration of therapy, tolerability, or ability to treat refractory disease

[1]Physicians noted that given the long treatment course, treatment initiation is often delayed until a persistent infection is very clear so as not to risk starting the course in a patient that ultimately does not need it and may drop off prior to completion; [2] Approved agent Arikayce was not viewed as highly impactful, particularly given that use is limited to patients with refractory MAC infections. RGM: Rapidly Growing Mycobacteria. Source: Physician Interviews; ClearView Analysis.

M. abscessus

Study 1: Successfully demonstrated activity (MIC) of R327 against *M. abscessus* in culture

Study 2: Investigated the effect of R327 against *M. abscessus* infecting macrophages

- In the human lung, *M. abscessus* infect macrophages (type of immune cell)
- Inside these cells, the bacteria are protected from immune attack
- Many antibiotics cannot enter cells and therefore do not reach these *M. abscessus*

Human stem cell-derived macrophages (used due to their physiological similarity to macrophages in the human lung) were infected with *M. abscessus* ATCC 19977 then treated with R327.

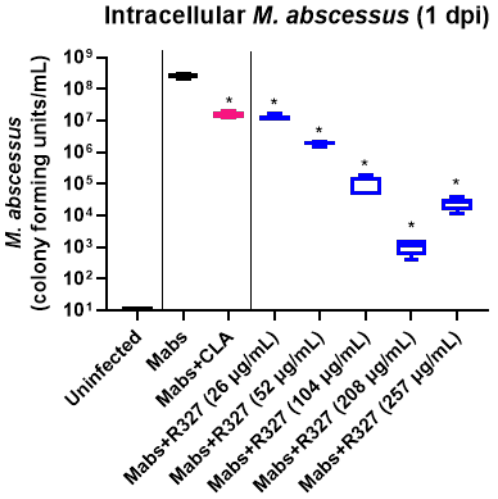
1 and 3 days later, live *M. abscessus* inside the cells were quantified by colony-forming assay.

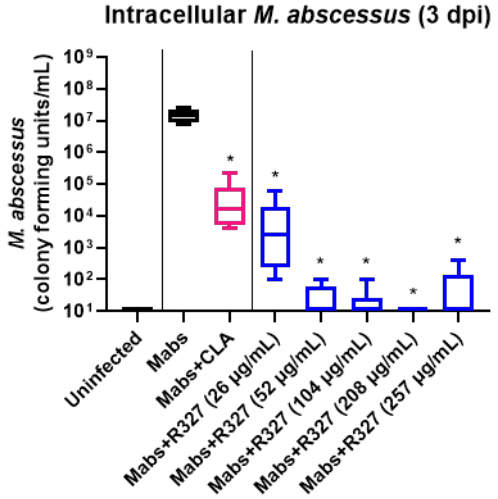
R327 was extremely effective at killing intracellular *M. abscessus*

- No toxic effect on the macrophages
- Dose-dependent killing of *M. abscessus* with eradication of bacteria obtained at 3 days post infection (dpi)

R327 superior to Clarithromycin positive control

- Clarithromycin was one of the rare antibacterial agents used in the 1990s with some success and became the treatment of choice[1]





M. abscessus

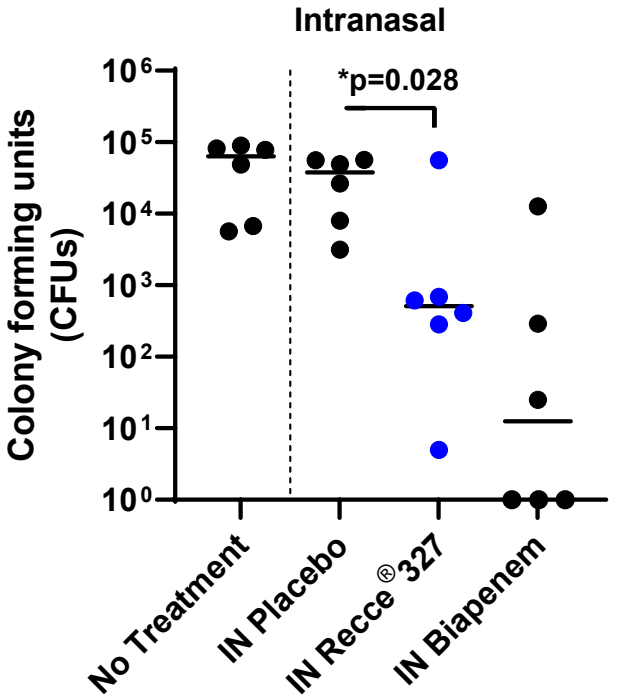
Study 3: Examine the efficacy of R327 treatment against *M. abscessus* lung infection in mice

In a pilot study (unoptimized conditions), mice infected in their lungs with *M. abscessus* were treated with R327, nasally (intranasal), twice daily for five days.

Levels of *M. abscessus* in the lungs were then quantified by colony-forming assay.

- **No adverse events were observed in the mice**, while treating a lung infection
- Nasal R327 treatment **significantly reduced *M. abscessus* levels**
- Despite using unoptimized dose and delivery, efficacy of R327 was only slightly inferior to that of the positive control antibiotic, Biapenem

Pulmonary *M. abscessus*



IN = intranasal

M. abscessus - Summary

M. abscessus has emerged as one of the most important lung pathogens in cystic fibrosis

- *Major driver of disease progression*
- *Contraindication for end-stage lung transplantation*
- *Current treatments ineffective and toxic*

R327

- **No toxicity observed against treated (physiologically relevant) human macrophages, or in infected mice**
- **Very good activity against intracellular *M. abscessus* within human macrophages**
  - Complete eradication of infection achieved
  - Able to **penetrate cells** and **kill these bacteria inside macrophages**
- **Proof of concept achieved in killing of *M. abscessus* infection in mice following nasal delivery**

Future Direction for Indications – Summary

Bacterial Sinusitis

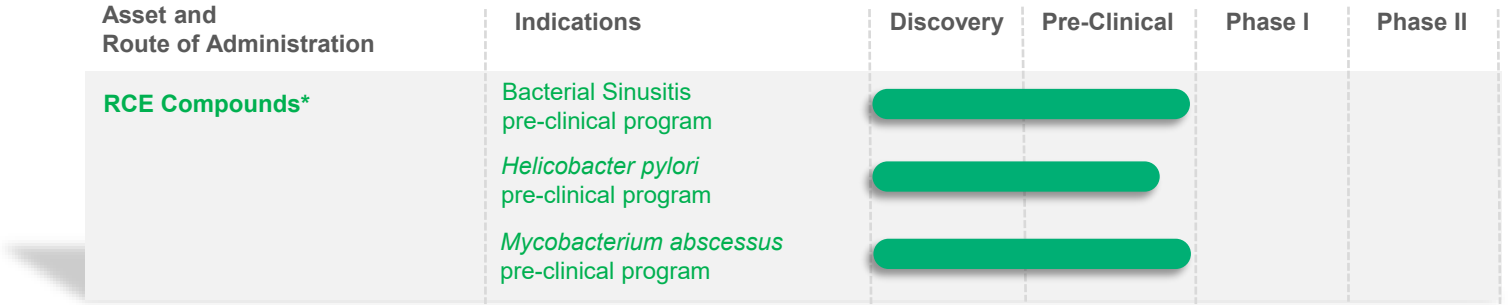
- Sufficient and compelling data creates the potential to start a Phase I/II clinical trial.
  - Expected commencement H1 2023

H. pylori

- Further formulation work and dosing optimisation is required to improve delivery to site of infection.

M. abscessus

- Proof of concept achieved.
  - Compelling data for a potential human study



Market and Commercial Opportunities

Guillaume van Renterghem, Managing Director LifeSci Advisors Switzerland, Zurich

Former Associate Vice President, Investor Relations
Sanofi

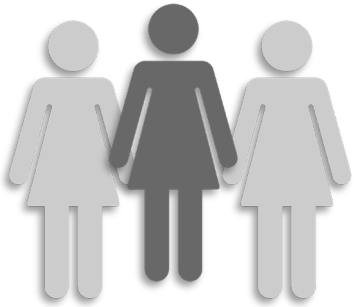
Biotech and Specialty Pharma Analyst
UBS Investment Bank

Biotech and Specialty Pharma Analyst
Canaccord Adams

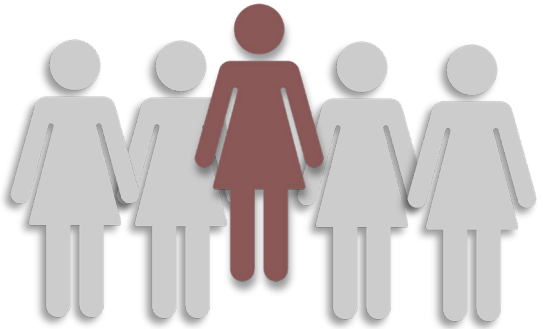
Recce
Pharmaceuticals

Market Update – Background on UTIs

- **Urinary tract infection** (UTI) is **one of the most common infectious diseases**
- The most common pathogen causing UTIs is *Escherichia coli* (*E. coli*) with 62%
  - The **resistance** among the **isolates of *E. coli*** are: ampicillin (86%), amoxicillin (76%), tetracycline (71%), trimethoprim-sulfamethoxazole (64%), cephalexin (61%), and cefalothin (60%)
- **Globally, more than 404.6 million individuals had UTIs in 2019**
  - USD $6 billion dollars in direct health care expenditure
  - Previous years have demonstrated the likelihood of antibiotics killing most UTIs is rapidly dropping



One in three uncomplicated UTIs in young healthy women are Bactrim-resistant



One in five are resistant to five other common antibiotics.

Market Update

- The **global urinary tract infection therapeutics** market is in **great demand** as the **number of UTI cases is rising** constantly.
- Driving factors of global UTI infections market are the sudden rise in prevalence rates and the disease's diagnosis.
- **Outpatient therapies** for UTIs are becoming **limited due to antimicrobial resistance.**
- **UTIs already cost Australia's health system $909 million per year**, not including indirect costs such as lost productivity.

Report Attribute	Details
Market Size in 2020	USD 8.9 billion
Projected Market Size in 2027	USD 11.6 billion
CAGR Growth Rate	4.56% CAGR
Base Year	2020
Forecast Years	2021-2027
Key Market Players	Achaogen, Allergen, Aquinox, AstraZeneca, Almirall, S.A, Bayer AG, Bristol-Myers Squibb Company, Cipla, C.H. Boehringer Sohn, Dr. Reddy's Laboratories Ltd., F. Hoffmann-La Roche, GlaxoSmithKline plc., Janssen Global Services, LLC, Lipella Pharmaceuticals, Lupin Ltd., MediciNova, MerLion Pharmaceuticals, Merck & Co., Inc, Novo Nordisk, Novartis, Pfizer, Sun Pharmaceuticals Industries, Shionogi, Teva Pharmaceuticals Industries, Urigen, Zavante Therapeutics, and others
Key Segment	By Age Group, By Indication, By Distribution Network, By Drug Group, and By Region
Major Regions Covered	NA, EU, APAC, LATAM, Middle East & Africa

Market Update – Case Study (1/2)

GSK and Spero Therapeutics announce exclusive licence agreement for late-stage antibiotic that may treat complicated urinary tract infections

Spero Therapeutics receives **USD $66 million upfront**, with **potential for future milestone** payments and **tiered royalties**

Spero will start a new Phase III clinical trial in 2023, following encouraging US FDA regulatory feedback on the proposed clinical trial design

First oral carbapenem antibiotic to potentially treat complicated **urinary tract infections** (cUTI), including pyelonephritis, caused by certain bacteria

Market Update – Case Study (2/2)

Spero Market Cap before announcement **USD$28M** (21st September) **increased** to **USD $73m** (6th October) following the announcement – up **160%**

GSK pays USD **$66m** to Spero upfront and USD **$9m** in Equity Investment (Spero in charge of paying for the new Phase 3)

Market cap increase only reflects ~ **60%** of the cash injected by GSK into Spero

No further probability of success regarding stronger commercial efforts behind the drug if/when approved

Potential milestones of "up to" $525m plus royalties on sales

Rare for companies to provide such detailed break-down of milestones and royalties on sales levels

Events	Milestone Payments (up to)
Delivery of Phase III Programme	$150m
Total commercial milestone payments based on first sale (US/EU)	$150m
Sales Milestone Events	
Net sales greater than $200m	$25m
Net sales greater than $300m	$25m
Net sales greater than $400m	$25m
Net sales greater than $500m	$50m
Net sales greater than $750m	$50m
Net sales greater than $1,000m	$50m
Total sales milestone payments:	$225m
Royalties	Low-single digit to low-double digit (if sales exceed $1b) tiered royalties on net product sales.

Scientific Strategy

Michele Dilizia, Executive Director and Chief Scientific Officer, Recce Pharmaceuticals Ltd

Recce
Pharmaceuticals

Strong Pipeline

Over Various Indications and Upcoming Inflection Points

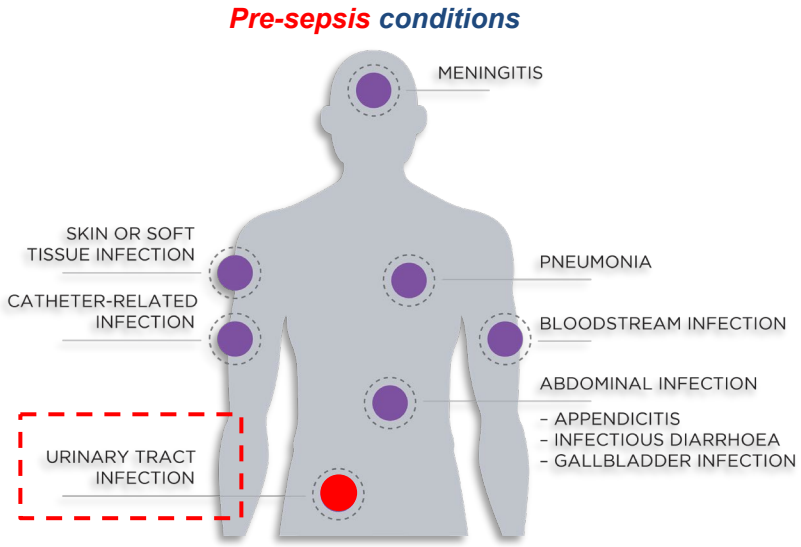
Asset and Route of Administration	Indications	Discovery	Pre-Clinical	Phase I	Phase II	Phase III	Market
R327 Intravenous*	Serious/life threatening bacterial infections including sepsis						
	Urinary tract infections including urosepsis						
	Multidose, early stage sepsis efficacy study						
R327 Topical*	Wound infections including infected burns						
	Diabetic Foot Ulcers						
RCE Compounds*	*Helicobacter pylori* pre-clinical program						
	Bacterial Sinusitis pre-clinical program						
	Mycobacterium abscessus pre-clinical program						
R327 Nasal**	COVID & Influenza						
R529 Intravenous & Intranasal**	COVID						

**Anti-bacterial program*
***Anti-viral program*

Patient Example*

UTI/Sepsis

- Patient woke up feeling unwell, intense back pain, fever.
- Doctors diagnosed her with sepsis and put into induced coma.
- Patient spent nine weeks in a coma and had her hands and legs amputated after **developing sepsis following a common urinary tract infection.**
- Approximately 25% of sepsis cases originate from the urogenital tract.



The Solution

- Potential of R327 in **new indications**.
  - Form part of a **broader anti-infective treatment model** supported by pre-clinical data.
- **Full therapeutic road map** for **pre-sepsis** and **sepsis conditions** – early to advanced stage infections.
- Confidently and quickly administer the antibiotic at first patient presentation potentially improving the outcome.

Recce Pharmaceuticals

*Patient example only of how sepsis can develop from a UTI. Patient was not treated with R327 or involved in any RECCE clinical trials.

Patents

Four families across all major markets

Country	Title	Case_Status	Grant_Date	Applicant	Family
Australia	ANTI-MICROBIAL POLYMERS AND THEIR COMPOSITIONS	Granted	25/08/2011	Recce Pharmaceuticals Ltd	Family 1
China	ANTI-MICROBIAL POLYMERS AND THEIR COMPOSITIONS	Granted	25/11/2015	Recce Pharmaceuticals Ltd	Family 1
France	ANTI-MICROBIAL POLYMERS AND THEIR COMPOSITIONS	Granted	7/10/2015	Recce Pharmaceuticals Ltd	Family 1
Germany	ANTI-MICROBIAL POLYMERS AND THEIR COMPOSITIONS	Granted	7/10/2015	Recce Pharmaceuticals Ltd	Family 1
Italy	ANTI-MICROBIAL POLYMERS AND THEIR COMPOSITIONS	Granted	7/10/2015	Recce Pharmaceuticals Ltd	Family 1
Japan	ANTI-MICROBIAL POLYMERS AND THEIR COMPOSITIONS	Granted	3/10/2014	Recce Pharmaceuticals Ltd	Family 1
Spain	ANTI-MICROBIAL POLYMERS AND THEIR COMPOSITIONS	Granted	7/10/2015	Recce Pharmaceuticals Ltd	Family 1
Sweden	ANTI-MICROBIAL POLYMERS AND THEIR COMPOSITIONS	Granted	7/10/2015	Recce Pharmaceuticals Ltd	Family 1
United Kingdom	ANTI-MICROBIAL POLYMERS AND THEIR COMPOSITIONS	Granted	7/10/2015	Recce Pharmaceuticals Ltd	Family 1
USA	ANTI-MICROBIAL POLYMERS AND THEIR COMPOSITIONS	Granted	1/09/2015	Recce Pharmaceuticals Ltd	Family 1
Australia	COPOLYMER AND METHOD FOR TREATMENT OF BACTERIAL INFECTION	Granted	8/11/2018	Recce Pharmaceuticals Ltd	Family 2
China	COPOLYMER AND METHOD FOR TREATMENT OF BACTERIAL INFECTION	Response Lodged		Recce Pharmaceuticals Ltd	Family 2
France	COPOLYMER AND METHOD FOR TREATMENT OF BACTERIAL INFECTION	Granted	28/08/2019	Recce Pharmaceuticals Ltd	Family 2
Germany	COPOLYMER AND METHOD FOR TREATMENT OF BACTERIAL INFECTION	Granted	28/08/2019	Recce Pharmaceuticals Ltd	Family 2
Italy	COPOLYMER AND METHOD FOR TREATMENT OF BACTERIAL INFECTION	Granted	28/08/2019	Recce Pharmaceuticals Ltd	Family 2
Japan	COPOLYMER AND METHOD FOR TREATMENT OF BACTERIAL INFECTION	Granted	25/10/2019	Recce Limited	Family 2
Spain	COPOLYMER AND METHOD FOR TREATMENT OF BACTERIAL INFECTION	Granted	28/08/2019	Recce Pharmaceuticals Ltd	Family 2
Sweden	COPOLYMER AND METHOD FOR TREATMENT OF BACTERIAL INFECTION	Granted	28/08/2019	Recce Pharmaceuticals Ltd	Family 2
United Kingdom	COPOLYMER AND METHOD FOR TREATMENT OF BACTERIAL INFECTION	Granted	28/08/2019	Recce Pharmaceuticals Ltd	Family 2
USA	COPOLYMER AND METHOD FOR TREATMENT OF BACTERIAL INFECTION	Granted	12/03/2019	Recce Pharmaceuticals Ltd	Family 2
Australia	ANTI-VIRUS AGENT AND METHOD FOR TREATMENT OF VIRAL INFECTION	Report Received		Recce Pharmaceuticals Ltd	Family 3
China	ANTI-VIRUS AGENT AND METHOD FOR TREATMENT OF VIRAL INFECTION	Granted	22/06/2021	Recce Pharmaceuticals Ltd	Family 3
France	ANTI-VIRUS AGENT AND METHOD FOR TREATMENT OF VIRAL INFECTION	Granted	21/04/2021	Recce Pharmaceuticals Ltd	Family 3
Germany	ANTI-VIRUS AGENT AND METHOD FOR TREATMENT OF VIRAL INFECTION	Granted	21/04/2021	Recce Pharmaceuticals Ltd	Family 3
Hong Kong	ANTI-VIRUS AGENT AND METHOD FOR TREATMENT OF VIRAL INFECTION	Granted	25/02/2022	Recce Pharmaceuticals Ltd	Family 3
Italy	ANTI-VIRUS AGENT AND METHOD FOR TREATMENT OF VIRAL INFECTION	Granted	21/04/2021	Recce Pharmaceuticals Ltd	Family 3
Japan	ANTI-VIRUS AGENT AND METHOD FOR TREATMENT OF VIRAL INFECTION	Granted	18/12/2020	Recce Pharmaceuticals Ltd	Family 3
Spain	ANTI-VIRUS AGENT AND METHOD FOR TREATMENT OF VIRAL INFECTION	Granted	21/04/2021	Recce Pharmaceuticals Ltd	Family 3
Sweden	ANTI-VIRUS AGENT AND METHOD FOR TREATMENT OF VIRAL INFECTION	Granted	21/04/2021	Recce Pharmaceuticals Ltd	Family 3
United Kingdom	ANTI-VIRUS AGENT AND METHOD FOR TREATMENT OF VIRAL INFECTION	Granted	21/04/2021	Recce Pharmaceuticals Ltd	Family 3
USA	ANTI-VIRUS AGENT AND METHOD FOR TREATMENT OF VIRAL INFECTION	Granted	29/06/2021	Recce Pharmaceuticals Ltd	Family 3
USA	ANTI-VIRUS AGENT AND METHOD FOR TREATMENT OF VIRAL INFECTION	Filed		Recce Pharmaceuticals Ltd	Family 3
Australia	PROCESS FOR PREPARATION OF BIOLOGICALLY ACTIVE COPOLYMER	Exam Requested		Recce Pharmaceuticals Ltd	Family 4
Brazil	PROCESS FOR PREPARATION OF BIOLOGICALLY ACTIVE COPOLYMER	Filed		Recce Pharmaceuticals Ltd	Family 4
Canada	PROCESS FOR PREPARATION OF BIOLOGICALLY ACTIVE COPOLYMER	Filed		Recce Pharmaceuticals Ltd	Family 4
China	PROCESS FOR PREPARATION OF BIOLOGICALLY ACTIVE COPOLYMER	Filing Sent		Recce Pharmaceuticals Ltd	Family 4
Europe	PROCESS FOR PREPARATION OF BIOLOGICALLY ACTIVE COPOLYMER	Filing Sent		Recce Pharmaceuticals Ltd	Family 4
Hong Kong	PROCESS FOR PREPARATION OF BIOLOGICALLY ACTIVE COPOLYMER	To be Filed		Recce Pharmaceuticals Ltd	Family 4
India	PROCESS FOR PREPARATION OF BIOLOGICALLY ACTIVE COPOLYMER	Filed		Recce Pharmaceuticals Ltd	Family 4
Japan	PROCESS FOR PREPARATION OF BIOLOGICALLY ACTIVE COPOLYMER	Filing Sent		Recce Pharmaceuticals Ltd	Family 4
PCT	PROCESS FOR PREPARATION OF BIOLOGICALLY ACTIVE COPOLYMER	PCT Filed		Recce Pharmaceuticals Ltd	Family 4
USA	PROCESS FOR PREPARATION OF BIOLOGICALLY ACTIVE COPOLYMER	Filed		Recce Pharmaceuticals Ltd	Family 4
Vietnam	PROCESS FOR PREPARATION OF BIOLOGICALLY ACTIVE COPOLYMER	Filing Sent		Recce Pharmaceuticals Ltd	Family 4
Israel	PROCESS FOR PREPARATION OF BIOLOGICALLY ACTIVE COPOLYMER COMPRISING AN ACROLEIN DERIVATIVE AND A POLYALKYLENE GLYCOL OLIGOMER	Direction Issued		Recce Pharmaceuticals Ltd	Family 4

Recce's patent portfolio includes more than 40 patents and patent applications in the world's major markets.

The Way Forward

- **New Class of Anti-Infectives**
- **Universal Mechanism of Action**
- **Unmet medical needs**
- What can we look forward to?
  - Exploring **multiple clinical-stage therapeutic indications**
  - **Multiple** pre-clinical programs
  - **Market** and **commercial opportunities**

Thank you

recce.com.au

ASX:RCE FSE:R9Q

References

Pre-clinical Update

- https://www.cdc.gov/nchs/fastats/sinuses.htm
- Brook I. Microbiology of sinusitis. Proc Am Thorac Soc. 2011 Mar;8(1):90-100. doi: 10.1513/pats.201006-038RN. PMID: 21364226.
- Cingi. Nature Public Health Emergency Collection. 2019; UpToDate; Physician Interviews; ClearView Analysis
- Physician Interviews; ClearView Analysis.
- https://www.racgp.org.au/afp/2014/may/helicobacter-pylori-eradication
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6632043/#:~:text=To%20this%20date%2C%204.4%20billion,have%20shown%20the%20highest%20H
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6928860/
- Lee MR, Sheng WH, Hung CC, Yu CJ, Lee LN, Hsueh PR. Mycobacterium abscessus Complex Infections in Humans. Emerg Infect Dis. 2015 Sep;21(9):1638-46. doi: 10.3201/2109.141634. PMID: 26295364; PMCID: PMC4550155.
- Cowman. European Respiratory Journal. 2019; https://erj.ersjournals.com/content/54/1/1900250.long
- Spaulding. Ann Am Thorac Soc. 2017; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5711271/pdf/AnnalsATS.201611-860OC.pdf
- Kwon. J Korean Med Sci. 2016; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4835588/pdf/jkms-31-649.pdf
- Winthrop. Ann Am Thorac Soc. 2020; https://www.atsjournals.org/doi/10.1513/AnnalsATS.201804-236OC?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed
- Adjemian. Am J Respir Crit Care Med. 2012 https://www.atsjournals.org/doi/full/10.1164/rccm.201111-2016OC
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5192163/

Market and Commercial Opportunities

- https://www.health.harvard.edu/blog/antibiotic-resistant-urinary-tract-infections-are-on-the-rise-2019101417982
- https://www.ncbi.nlm.nih.gov/books/NBK482344/
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5414046/
- https://assets.researchsquare.com/files/rs-829349/v1/79b047d9-8a26-4888-ada2-e07f28cb5164.pdf?c=1642898772
- https://pmj.bmj.com/content/81/952/83
- https://www.globenewswire.com/en/news-release/2022/02/02/2377803/0/en/Global-Urinary-Tract-Infection-Therapeutics-Market-Size-Will-Touch-USD-11-652-Million-Mark-by-2027-at-a-4-56-CAGR-Study-by-Facts-Factors.html
- https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-019-4303-y
- https://outbreakproject.com.au/2020/11/17/australias-multi-billion-dollar-superbug-crisis/#:~:text=%E2%80%9CWe%20found%20that%20UTIs%20already,costs%20such%20as%20lost%20productivity
- https://www.gsk.com/en-gb/media/press-releases/gsk-and-spero-therapeutics-announce-exclusive-licence-agreement-for-tebipenem-hbr-a-late-stage-antibiotic-that-may-treat-complicated-urinary-tract-infections/

Scientific Strategy

- https://www.independent.co.uk/life-style/health-and-families/sepsis-uti-symptoms-amputation-transplant-b2195975.html
- https://www.ncbi.nlm.nih.gov/books/NBK482344/