MGB Biopharma
Innovative Development Company

Bringing True Novelty to the Anti-Infective Space

New Class of Antibacterials Based on a Unique Mechanism of Action

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Superbugs & Superdrugs
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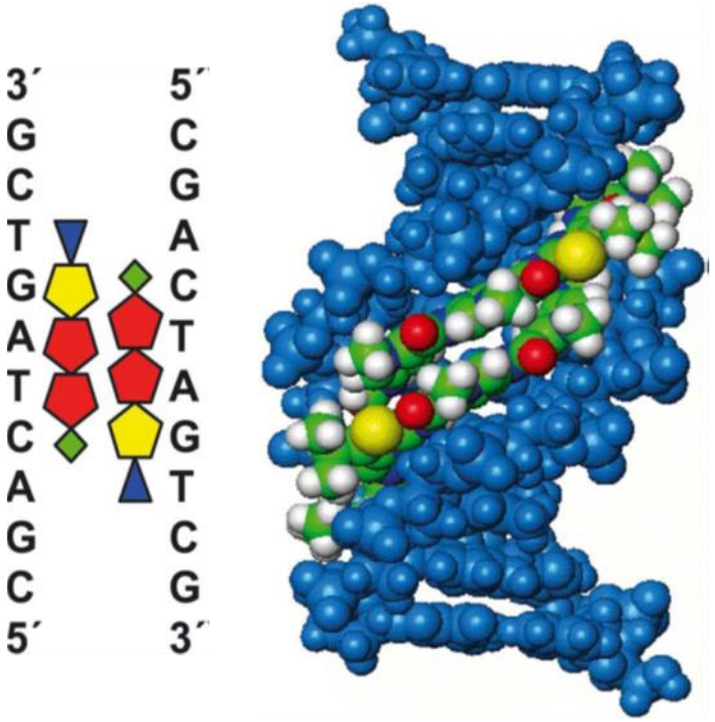
MGB Biopharma Limited

- Founded in Glasgow April 2010
- Based on the University of Strathclydes DNA **M**inor **G**roove **B**inders
- Platform hosts a novel class of anti-infectives
- Completely new mechanism of action distinct from current antimicrobial drugs
- MGB Biopharma's anti-infective platform provides development opportunities for managing Gram-positive, Gram-negative, viral, fungal & parasitic infections
- Lead compound, **MGB-BP-3**, is being developed for oral, intravenous and topical preparations

MGBs Novel Mode of Action

- MGB-BP-3 binds *A-T* rich sequences in the minor groove of bacterial DNA via a sequential & conformational process that interferes with transcription and alters genetic regulation
- MGB-BP-3 does not inhibit bacterial DNA replication
- MGB-BP-3 acts at multiple points and affects numerous genes

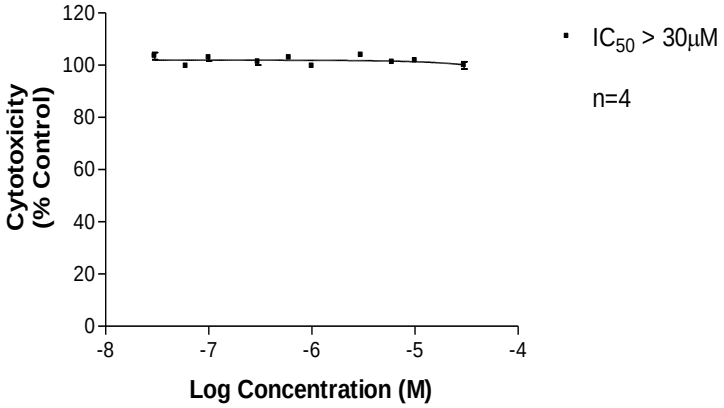


Binding of MGB-BP ligand to the DNA minor groove; NMR-derived structure

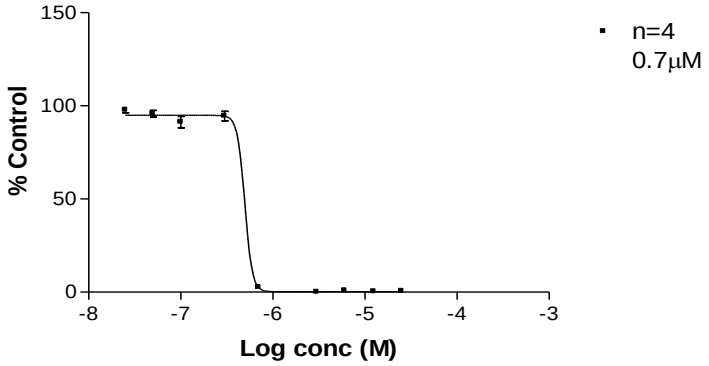
MGBs Selective Toxicity Against Bacteria

- No toxicity observed in mammalian cells at concentration tested
- Selective toxicity of MGB-BP-3 in bacterial cells e.g. *S. aureus*

Mammalian Cells



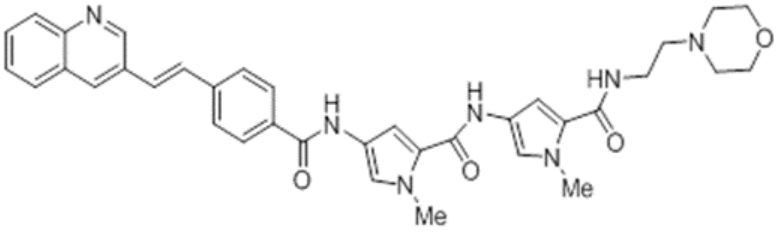
Bacterial Cells



MGB-BP-3 Development

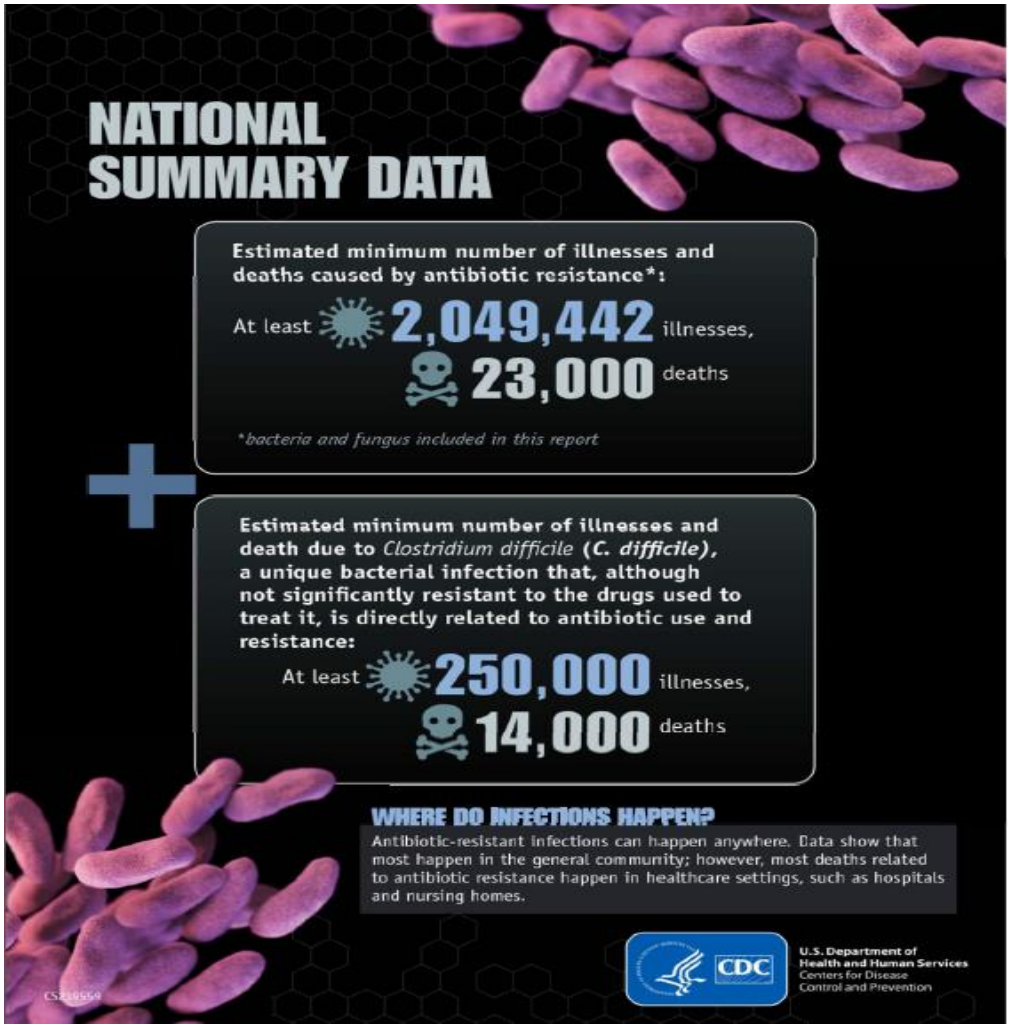
MGB Biopharma's current programmes:

1. Oral MGB-BP-3 for treating *C. difficile* infections (CDI)
2. Intravenous MGB-BP-3 for treating Gram-positive infection
3. Topical MGB-BP-3 for eradication of Gram-positive carrier states



- MGB-BP-3 is the first compound from the MGB platform, with strong activity against Gram-positive pathogens
- Oral MGB-BP-3, aimed at CDI, is about to start clinical development

Clostridium difficile
CDC Statistics



Statistics from the most recent CDC Drug Resistance Threat Report (2013)[1] highlights the number of illnesses and deaths caused by antibiotic resistant bacteria, and how many of these are attributed to *Clostridium difficile*

2014 statistics for the UK were reported as approximately 6,500 *Clostridium difficile* cases[2&3]

1. www.cdc.gov/drugresistance/threat-report-2013

2 & 3. www.hps.scot.nhs.uk & www.gov.uk/government/organisations/public-health-england

Clostridium difficile
Current Treatment

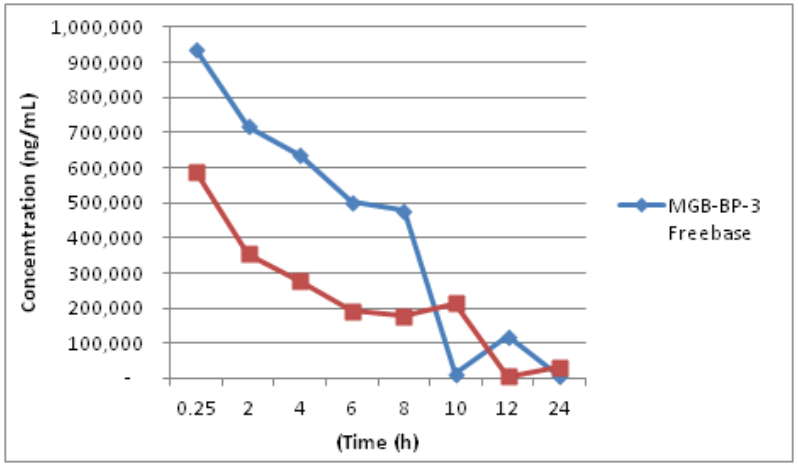
Current treatment options are limited

- Until 2010 launch of DIFICID (fidaxomycin – Optimer/Cubist/ Astellas) oral metronidazole & vancomycin were the only options for treating CDI
- Oral metronidazole is generally used first in mild cases as it is generic; in addition it does not encourage appearance of vancomycin-resistant enterococci (VRE). Vancomycin is only used in severe cases or non-responders
- Utility of these antibiotics is limited due to recurrence; either re-infection with same pathogen or new infection

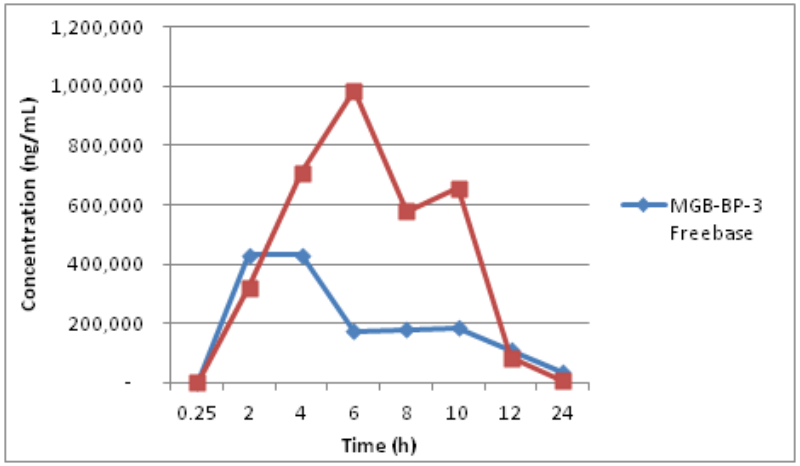
MGB-BP-3 Activity Against *C. difficile*

MGB-BP-3 concentrations

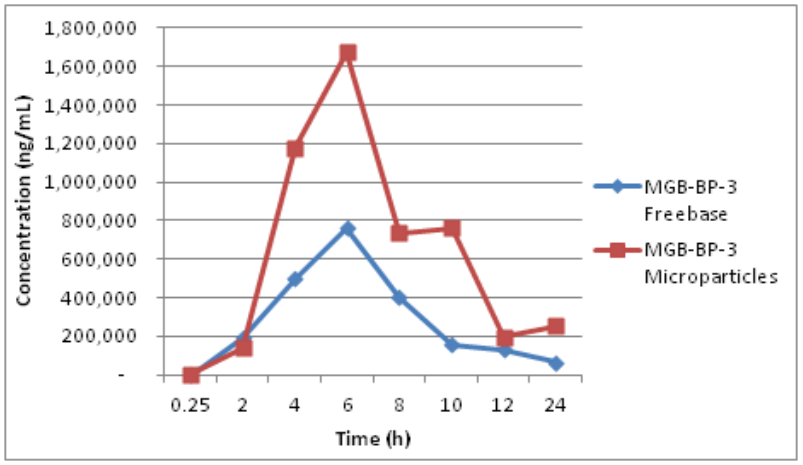
Single oral dose 100mg/kg MGB-BP-3 20h post *C. diff* infection



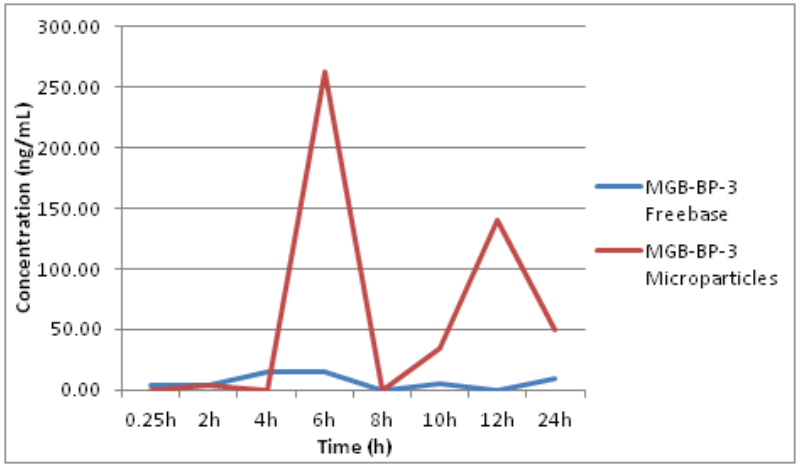
Small Intestine



Caecum



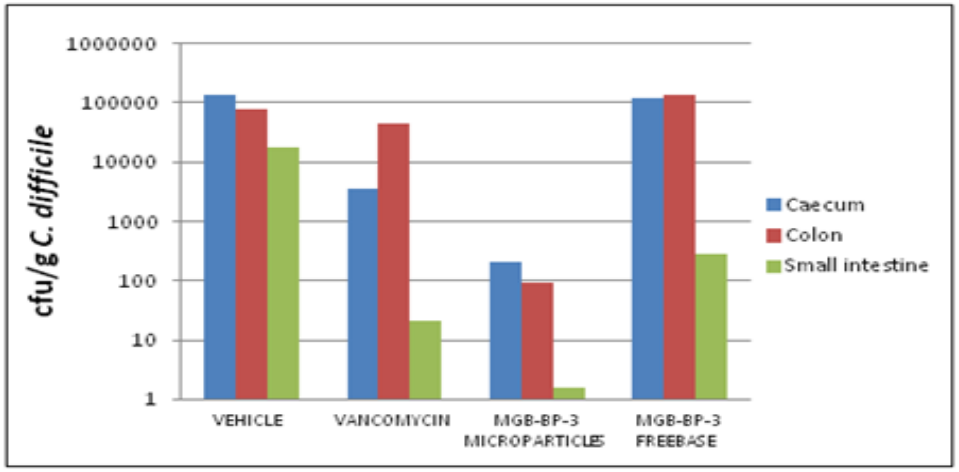
Colon



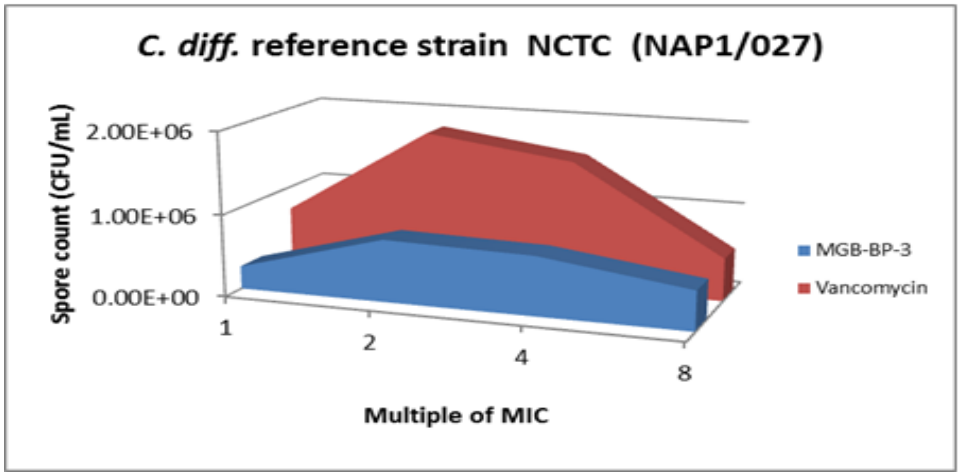
Plasma

MGB-BP-3 Activity Against *C. difficile*

Activity of MGB-BP-3 against *C. difficile* compared with vancomycin



Hamster model of CDI showed that MGB-BP-3 reduced *C. difficile* CFU/g in the gut and was superior to vancomycin



Sporulation studies showed MGB-BP-3 was superior to vancomycin in reducing *C. difficile* spores CFU/mL

MGB-BP-3 Safety Profiles

Species/Cell line	*Dose*	*Route*	*Findings*
CHO-hERG	10^{-6} to 10^{-5}M	*In vitro*	**No abnormalities observed from direct drug effects**
Rat	Oral: 90 mg/kg, 180mg/kg, and 360mg/kg	Oral	
Rat	Oral: 90 mg/kg, 180 mg/kg, and 360 mg/kg	Oral	
Dog	Oral: 44 mg/kg 111 mg/kg 211 mg/kg	Oral	

Species	*Dose*	*Route*	*Duration*	*Findings*
Rat	180mg/kg/day, 360mg/kg/day and 720mg/kg/day	Oral	14 days	**No toxic effects** **NOAEL 720mg/kg/day**
Dog	76mg/kg/day	Oral	14 days	**NOAEL (male dogs)** **59mg/kg/day**

MGB-BP-3 Clinical Development Programme

- Single Ascending Dose (SAD)

Cohort	Study session	n=2	n=2	n=2	n=2
1	1	DL 1	DL 1	DL 1	Placebo
	2	DL 2	DL 2	Placebo	DL 2
	3	DL 3	Placebo	DL 3	DL 3
2	1	DL 4	DL 4	DL 4	Placebo
	2	DL 5	DL 5	Placebo	DL 5
	3	DL 6	Placebo	DL 6	DL 6

- Multiple Ascending Dose (MAD)

Cohort	n=6	n=2
1	DL 1	Placebo
2	DL 2	Placebo
3	DL 3	Placebo

- Phase I completion End 2015

MGB-BP-3 Summary

- New class and novel Mode of Action
- Potent activity to *Clostridium difficile* and a range of aerobic Gram-positive bacteria
- Superior activity to vancomycin
- Oral programme for the treatment of *Clostridium difficile* infections about to enter Phase I
- Development of intravenous formulation for the treatment of systemic Gram-positive disease is near POC completion
- Development of topical formulation for managing carriage – feasibility testing

Acknowledgements

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Supporters & Agency Involvement

Thank you for your attention!