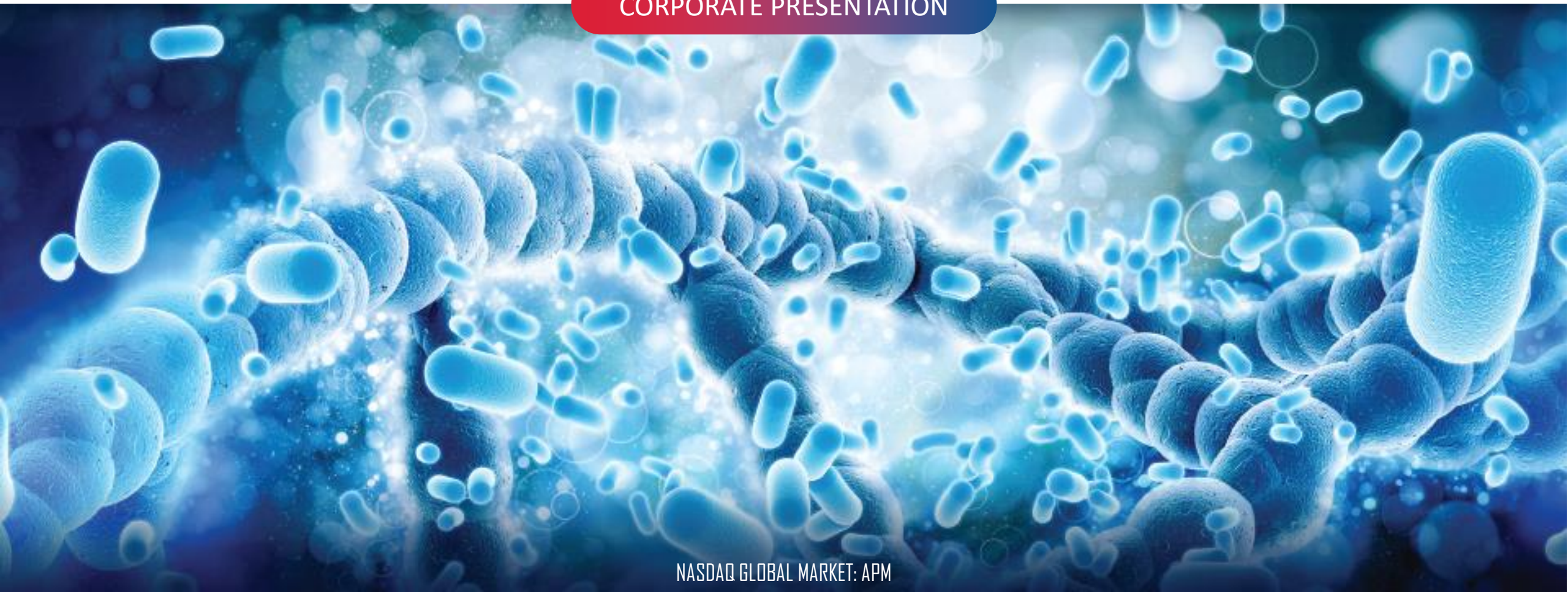
APTORUM

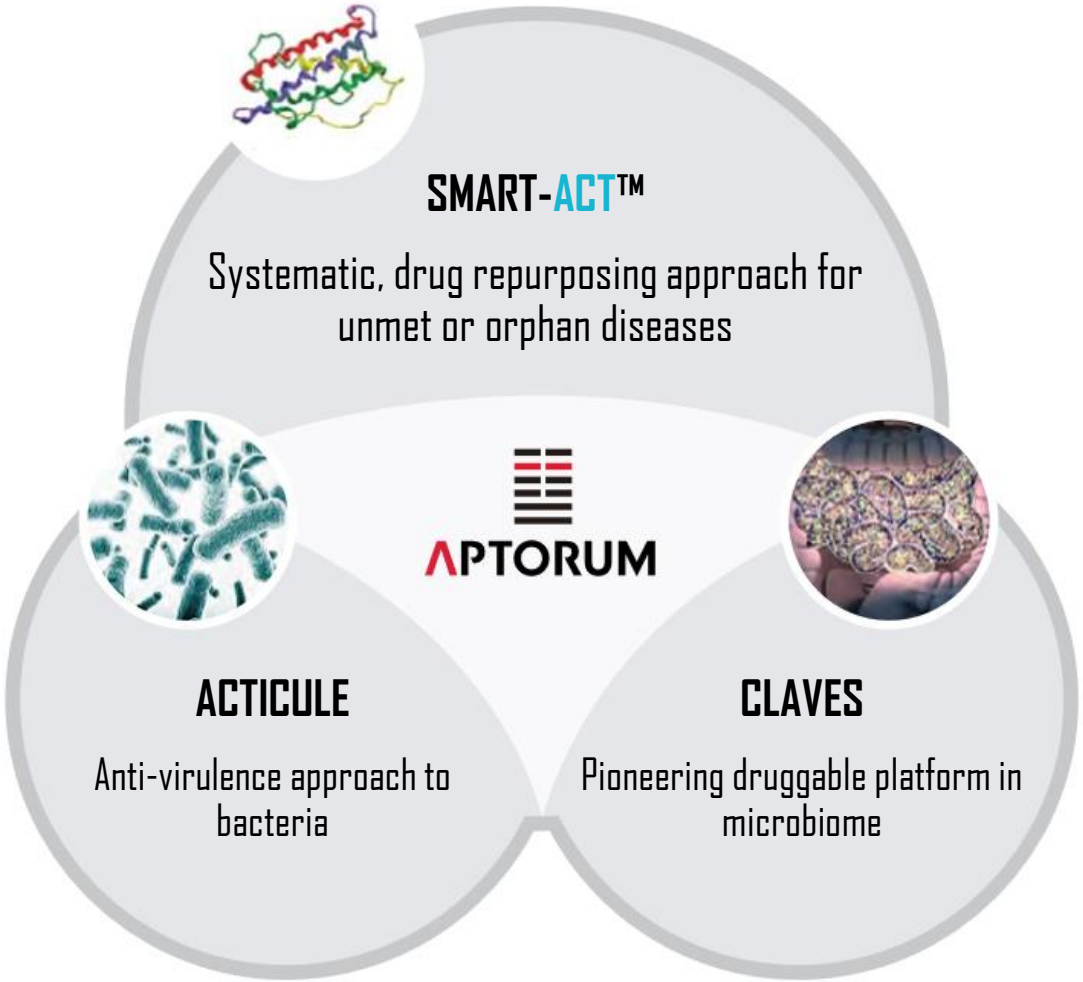
Facilitating Life Science Innovations to Serve Unmet Medical Needs

CORPORATE PRESENTATION



NASDAQ GLOBAL MARKET: APM

Aptorum's 3 Core Pillars



- Aptorum's 3 core pillars of therapeutic discovery and development, focused on novel therapeutics for unmet medical needs
- Ever expanding universe of proprietary intellectual property in relation to our pipeline products

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SMART-ACT™: Executive Summary

SMART-ACT™

Unmet or Orphan Diseases

- FDA-approved small molecules
- Expedited Phase I through existing safety data on the approved drug
- Greatly reduces duration of drug development from 12 years to 4 years
- Patent protection through indication, reformulation and combination patents

+

Drug Repurposing

- FDA fast track procedures
- Small scale clinical trials
- 7 years of market exclusivity in parallel to patent protections
- 10% combined incidence in the US
- 95% orphan diseases without treatment
- 7000 orphan diseases & rising

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Rapid generation of late-stage clinical candidates

Systematic approach to rare disease

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SMART-ACT™: Pipeline Workflow

1 New drug indication

- Life threatening disease
- Lack of effective treatment
- Large market size

2 Drug target selection

- Computational mining from literature
- Up to 5 disease drug targets selected

3 2,600 approved small molecule drugs

Computational

4 *In silico* generated hits

Wet lab

5 *In vitro* validation

- Cell line model
- IC_{50}
- Combo treatment standard therapy

6 *In vivo* validation

- Animal model
- *In vivo* efficacy

7 IP protection

- Indication patent
- Reformulation
- Combination patent
- Dosage patent

8 Development / out-licensing

- US FDA 505(b)(2) filing
- In-house development or out-licensing with co-development partners

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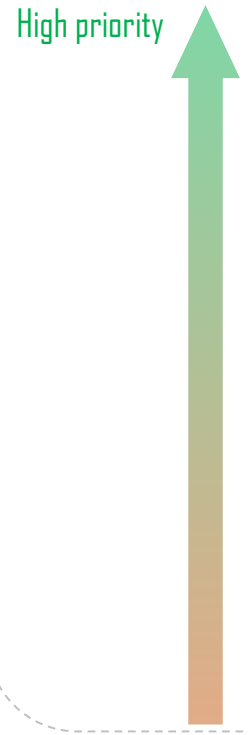
Orphan Disease Selection

7000+ Orphan Diseases + Unmet

Patient population definition:

- US: <200,000 patients
- EU: <5 in 10,000
- Japan: <50,000 patients
- China: defined list of 121 rare diseases
- Coronavius

Disease selection criteria



Life threatening disease

High unmet need

IP protection

Market size

Competitive landscape

Clinical trial design

Paediatric disease

By region

Target selection

Disease knowledge

SMART-ACT™

High Priority
Unmet/Orphan Diseases

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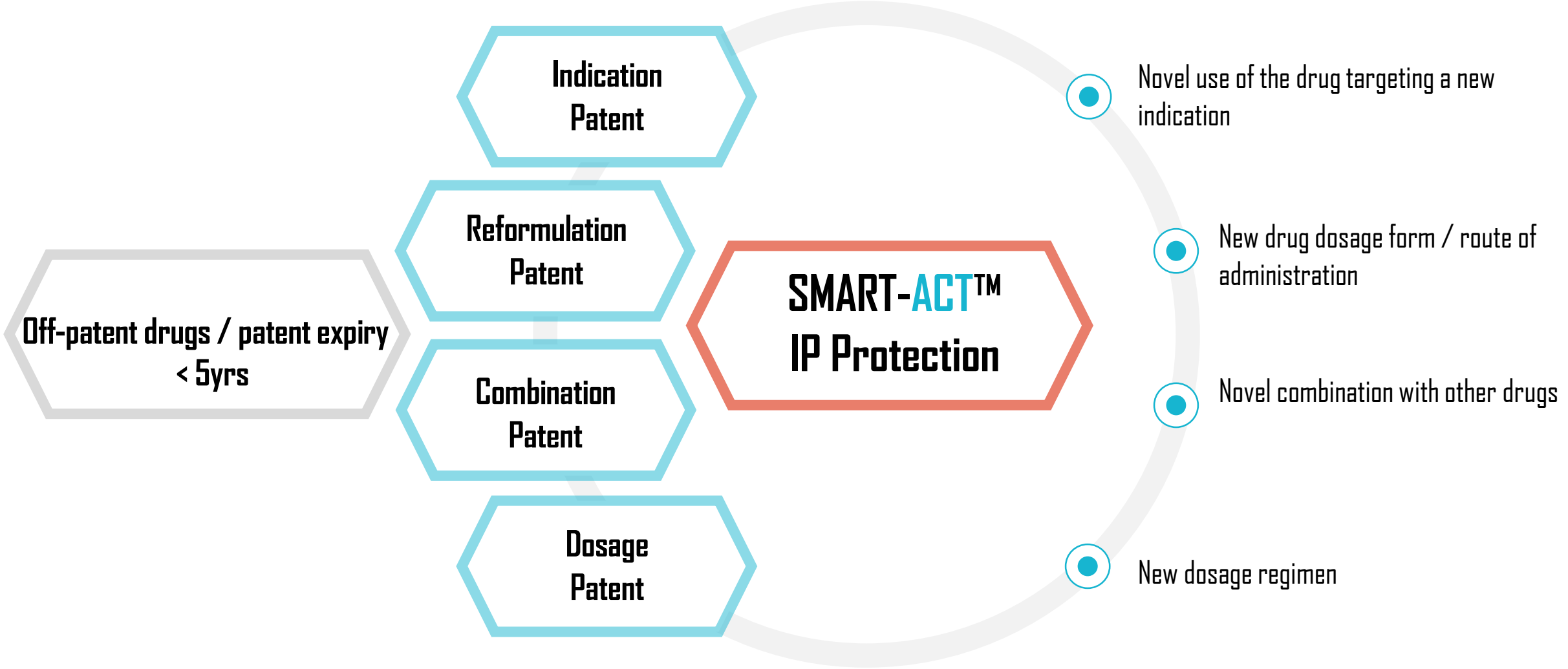
SMART-ACT™: Patent Strategy



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SMART-ACT™: pipeline overview

Current progress of pipeline programs: → Lead Projects → Other Candidates → Projected timeline[1]

Note: all projected timelines refer to the estimated commencement time of the indicated stages

Pillar 1: SMART-ACT™ (SACT series) - Orphan disease drug repurposing platform

Over 7,000 orphan diseases to be screened in the next 5 years

Program	Indication	Mechanism	Computational Discovery	*In vitro* validation	Existing PhI/II clinical safety data[1]	*In vivo* validation	Bridging studies	PhII / III with limited population[3]
SACT-1	Neuroblastoma	Drug Repurposing				IND 505(b)(2) filing[2] Q4 2019		ready for clinical trial in 2H 2020
SACT-COV19	COVID-19	Drug Repurposing						
SACT-2	To be disclosed	Drug Repurposing						
SACT-3	To be disclosed	Drug Repurposing						

1. All projected timelines refer to the estimated commencement time of the indicated stages 2. Refers to the drug's existing Phase I/II safety data previously conducted by a third party. Does not refer to clinical trials conducted by Aptorum 3. Subject to FDA's approval on a case-by-case basis, a 505(b)(2) can rely in part on existing information from approved products (such as FDA's previous finding on safety and efficacy) or data in the public

- IP rights filed for all 3 programs
- Subject to the FDA's approval, IND-enabling studies and Phase I for repurposing approved drugs may be expedited

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SACT-COVID19

- Severe Acute Respiratory Syndrome Coronavirus 2 ("SARS-COV-2") is highly infectious and WHO has declared COVID-19 disease as a global pandemic;
- Mortality rates: SARS-COV-2 (4.1%) vs 2003 SARS-COV-1 (9.6%) vs 2012 MERS-COV (37%)[Ref A]
- Multi-dimensional approach needed: Therapeutic + Vaccine + Diagnostics
- Aptorum Group initiates new strategic initiative targeting coronavirus, such as SARS-COV-2
- Deploying both a combination of drug repurposing (Smart-ACT™ Platform) and our infectious disease expertise (Acticule Platform)
- In collaboration with University of Hong Kong's Microbiology team – who identified and subsequently sequenced the 2003 SARS-COV-1 virus

Ref A:

www.worldometers.info. Archived from the original on 31 January 2020 and retrieved 2 February 2020.:

Smith, Richard D. (2006). "Responding to global infectious disease outbreaks: Lessons from SARS on the role of risk perception, communication and management". Social Science & Medicine. 63 (12): 3113–3123.

https://www.mdpi.com/2076-0817/9/3/231/htm

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SACT-COV19: Targets and Candidates

2 Protein Targets

- 3CL-Protease:
  - 6LU7 the crystal structure of SARS-COV-2 main protease in complex with an inhibitor N3

  - 3CL-Protease plays pivotal role in mediating viral replication and transcription functions through extensive proteolytic processing

- RNA dependent RNA Polymerase (RDRP)
  - Homolog (https://swissmodel.expasy.org/interactive/JDUya4/models/01)

  - An enzyme that catalyzes the replication of RNA from the RNA template

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SACT-COV19: Methodology and Candidates

Methodology

- It is proposed that inhibition of 3CL-protease or RDRP can slow down/terminate the replication of coronavirus.
- There is an inhibitor/co-crystal ligand in 6LU7 protein structure that may imply the potential binding site of 3CL-protease, therefore can be considered as the binding site of 3CL-protease.
- On the other hand, it is reported that Gilead's remdesivir (nucleotide analog) showed positive effect to patients infected by SARS-COV-2. It will be considered as the positive control in our study.

Candidates

- Based on our Smart-ACT™ selection process so far out of 2600+ approved small molecule library, at least 3 small molecule candidates have shown potential interference against the enzyme targets. Investigation to commence preclinical validation.
- Selected candidates have established safety, toxicity and PK profiles in prior human clinical trials – potential to efficiently enter into human clinical trials subject to regulatory clearance.
- Patent applications have been submitted.

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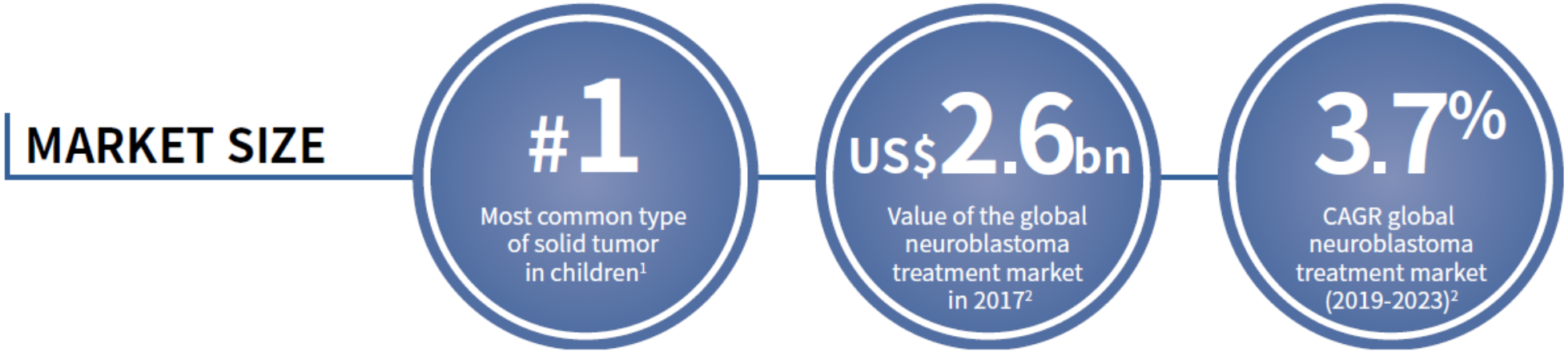
SACT-1 (neuroblastoma): market overview

SACT-1 targets neuroblastoma, a cancer that develops from nerve cells



Prevalence

- ~800 new cases every year and ~650 cases of neuroblastoma in children each year in the US averagely diagnosed between birth and 14 months[3]
- Accounts for ~15% of all cancer-related deaths in the pediatric population[4]
- Neuroblastoma 5 year survival rate: 40-50%[3]

Orphan drug designation[5]

- Neuroblastoma is a rare disease and drugs are qualified for orphan designation by the FDA
- Designated orphan drugs receive 7 years of market exclusivity
- Patents on reformulation, if granted, will provide up to 20 years of patent exclusivity from the application date in parallel to the 7-year market exclusivity

1. Pediatr Rev. 2018 Feb;39(2):57-67; 2. "Neuroblastoma Market Global Industry Perspective, Comprehensive Analysis, Size, Share, Growth, Trends, and Forecast 2019 – 2023"(2019). MRFR Research. 3. Curr Oncol Rep. 2009 Nov;11(6):431-8; https://www.cancer.net/cancer-types/neuroblastoma-childhood/statistics 4. Paediatr Drugs. 2011 Aug 1;13(4):245-55 5. https://www.fda.gov/about-fda/office-special-medical-programs/office-orphan-products-development.

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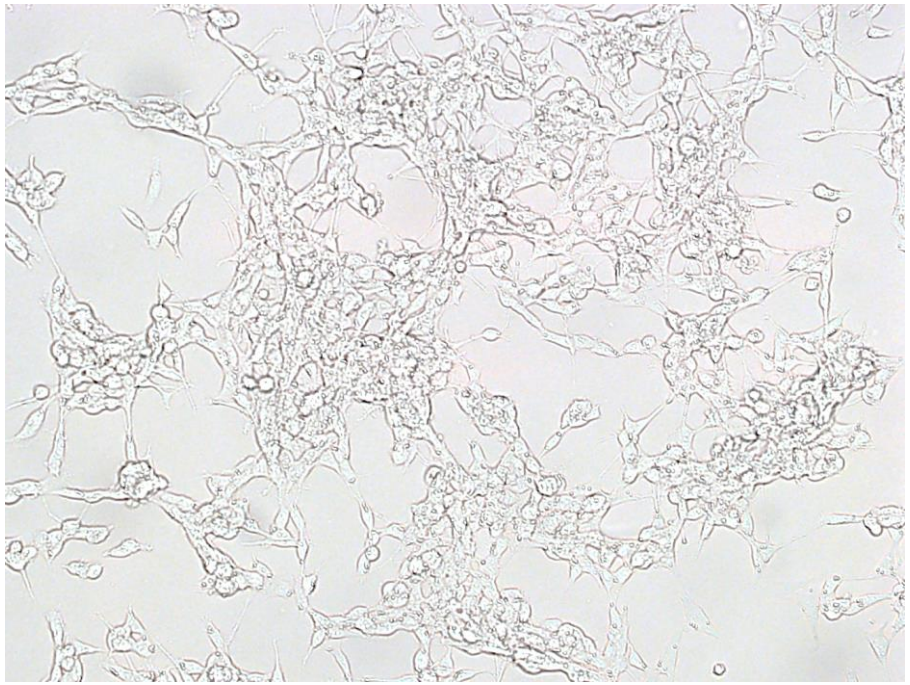
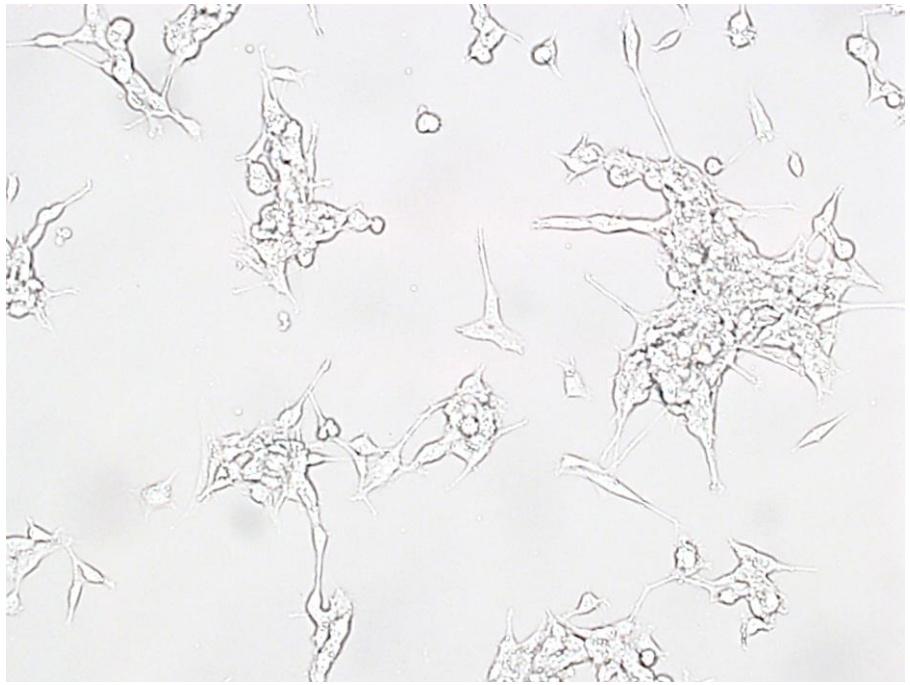
SACT-1 : In vitro drug activity against neuroblastoma cell lines

- 48 drug candidate hits from the computational screen were evaluated *in vitro* for activity validation
- 1 candidate, SP055, was found to provide favorable anticancer activities in 4 different neuroblastoma cell lines

Control treatment on neuroblastoma cells



SP055 treatment on neuroblastoma cells



Drug candidates under SACT-1	IC_{50} [µM]
SP055	**2.97**

The results shown in this slide are based on Aptorum's internal (in vitro/in vivo) tests/experiments that have not been verified in clinical trials and/or third party testing

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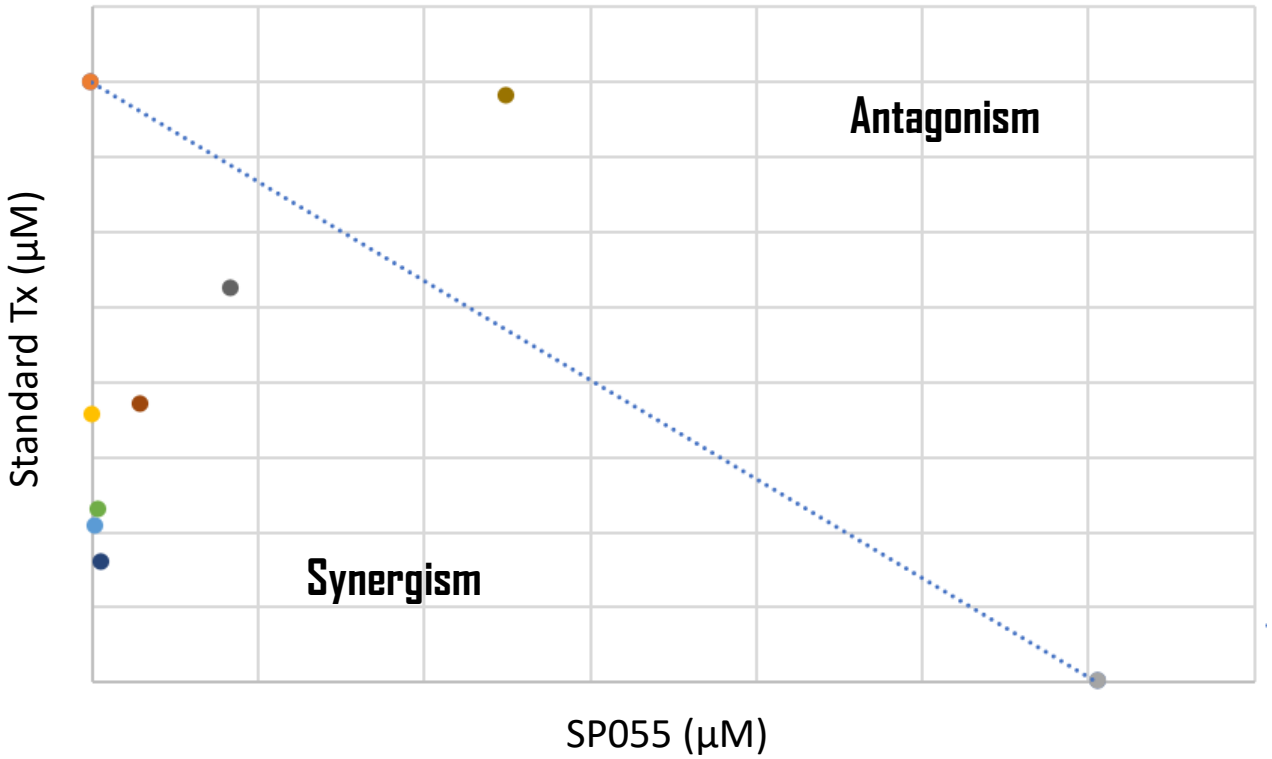
SACT-1: Synergistic effect of SP055 in combination with standard treatment

- Synergistic effect observed for SP055 in combination with standard treatment in 2 different neuroblastoma cell lines, as seen in the isobologram (left) and the Excess over Bliss (right)



Neuroblastoma cell line #1

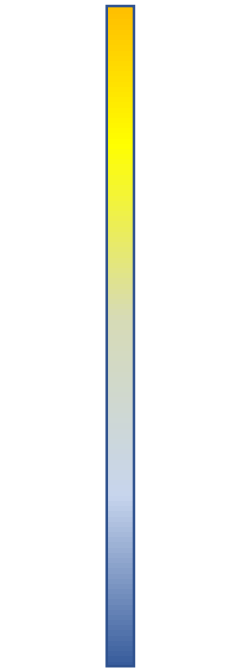
Excess over Bliss

Standard Tx (µM) \ SP055 (µM)	0.37	1.11	3.33	10
0.2	14	13	1	1
0.4	18	21	2	0

Neuroblastoma cell line #2

Excess over Bliss

Standard Tx (µM) \ SP055 (µM)	0.37	1.11	3.33	10
0.2	10	13	5	0
0.4	11	9	2	-7



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SACT-1: SP055 safety & tolerability

FDA approved safety profile

- Did not show genotoxic potential even at the highest feasible concentration dose (*in vitro* and *in vivo*)
- In a phase IIb study over 2 years, all SP055 doses were safe and well tolerated
- No dose relationship between SP055 and adverse events (AE)

SP055	25mg/day (N=93)	75mg/day (N=95)	150mg/day (N=91)
Median treatment duration, weeks	101	100	100
Adverse events (AE)			
Any grade 2-4 AE at least possibly related to SP055	20%	20%	21%
AEs leading to discontinuation	9%	12%	14%
Any serious AE	13%	14%	10%
Deaths	0%	2%	0%

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SACT-1: SP055 pharmacokinetics

FDA approved pharmacokinetics profile

- Data package can be potentially accepted by the FDA in our 505(b)(2) new drug application
- Relatively long half-life ($t_{1/2}$ = 43-55h). Frequent dosing may not be required

SP055 pharmacokinetic parameter in humans	(N=19)
t_{max}, h	5
C_{max}, ng/ml	~300
AUC_{last}, ng·h/ml	~10,000
AUC_{inf}, ng·h/ml	~11,000
$t_{1/2,term}$, h	~48

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SMART-ACT™: Priority Focus

Deep, prioritised pipeline of orphan diseases to be screened

- 3-5 drugs to reach ph2/3 confirmation study per year

Orphan cancers		
Carcinoma of esophagus	Familial colorectal cancer	Malignant peripheral nerve sheath tumor
Carcinoma of gallbladder and extrahepatic biliary tract	Familial Melanoma	Neuroblastoma
Cholangiocarcinoma	Gastrointestinal stromal tumor	Non-Hodgkin Lymphoma
Epstein-Barr virus-associated gastric carcinoma	Glioblastoma	Rare carcinoma of pancreas
Erdheim-Chester Disease	Hereditary breast and ovarian cancer syndrome	Squamous cell carcinoma of the esophagus/lip
Ewing Sarcoma	Langerhans Cell Histiocytosis	Thyroid carcinoma

Genetic, Immune, Metabolic & Neurological Disorders		
Cystic fibrosis	Mastocytosis	Primary hyperoxaluria type 1
Duchenne Muscular Dystrophy	Primary biliary cholangitis	Autosomal dominant familial amyotrophic lateral sclerosis
Sickle cell disease	Glycogen storage disease type II	Chronic Inflammatory Demyelination Polyneuropathy
Atypical hemolytic uremic syndrome	Mucopolysaccharidosis II	Primary erythromelalgia
Hereditary angioedema	Mucopolysaccharidosis III	Idiopathic arthritis

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ALS pipeline overview

Current progress of pipeline programs: → Lead Projects → Other Candidates → Projected timeline

Note: all projected timelines refer to the estimated commencement time of the indicated stages

Pillar 2: Acticule (ALS series) – Infectious diseases[4]

Small molecule, anti-virulence and non-bactericidal approach

IND NDA

Program	Indication	Discovery	Lead Optimization	IND enabling	Phase I	PhII/III based on LPAD pathway[1]
ALS-4	Anti *S. aureus* (incl. MRSA)	+ oral formulation		Q3 2019	2H 2020	
ALS-1	Anti Influenza A			Q4 2020		
ALS-2	Gram+ bacteria					
ALS-3	Gram+ bacteria					

Hybrid study
-volunteers + patients
-initial efficacy readout

1. ALS-4's eligibility for the LPAD pathway is subject to the FDA's approval. Targeting other indications in Phase II may affect our valuation. QIDP status can be applied once we identify an indication

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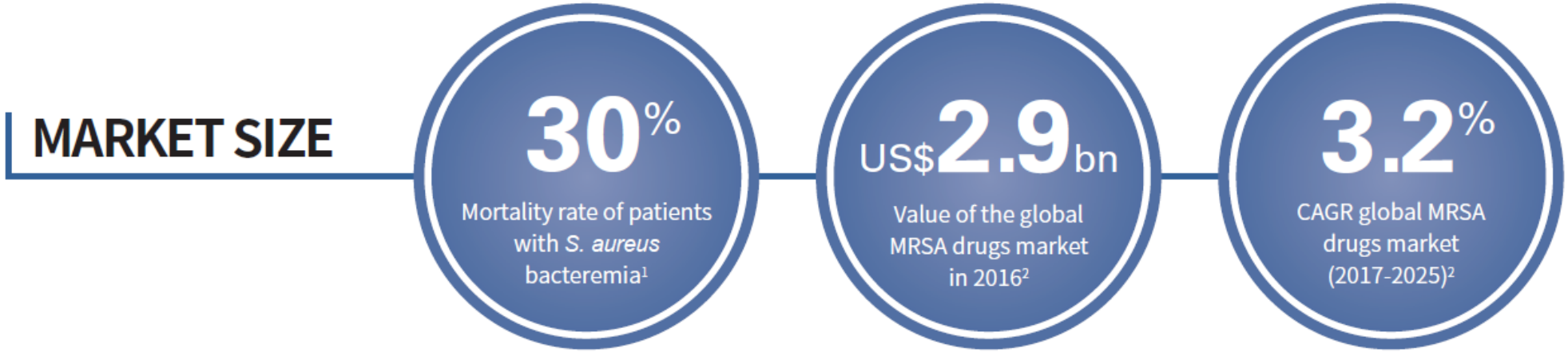
ALS4: Staph. Aureus Market Overview

ALS-4 is an anti-virulent, non-bactericidal drug candidate for *Staphylococcus aureus* infections including MRSA



Key Statistics of S. aureus

- Estimated 2 billion people carry S.aureus worldwide; 53 million people carry MRSA[5]
- c. 150,000+ S. aureus infections in US per year[6] and up to 30% mortality rate[7] and MRSA sepsis mortality rate maybe up to 55%[8]

Recent deals in infectious disease

- In 2014, Merck's acquisition of Cubist Pharmaceuticals, a large developer of antibiotics, for USD 8.4bn[3]
- In 2018, Roivant's licensing of Intron's Phase II asset for USD 667.5m in upfront and milestone payments[4]

1. Clin Microbiol Rev. 2012 Apr;25(2):362-86; 2. "Methicillin-resistant Staphylococcus Aureus (MRSA) Drugs Market - Global Industry Analysis, Size, Share, Growth, Trends, and Forecast, 2017-2025" (2018). Transparency market research; 3. https://dealbook.nytimes.com/2014/12/08/merck-agrees-to-acquire-drug-maker-cubist-for-9-5-billion/; 4. https://www.prnewswire.com/news-releases/roivant-sciences-and-intron-bio-sign-licensing-dealfornovel-anti-superbugs-biologic-sal200-300753307.html. 5. *"MRSA Infections"*. *Keep Kids Healthy. Archived from the original on December 9, 2007.* 6. https://www.uptodate.com/contents/epidemiology-of-staphylococcus-aureus-bacteremia-in-adults. 7. https://www.ncbi.nlm.nih.gov/pubmed/22491776. 8. Gurusamy, Kurinchi Selvan; Koti, Rahul; Toon, Clare D.; Wilson, Peter; Davidson, Brian R. (2013-08-20). "Antibiotic therapy for the treatment of methicillin-resistant Staphylococcus aureus (MRSA) infections in surgical wounds". *The Cochrane Database of Systematic Reviews* (8): CD009726.

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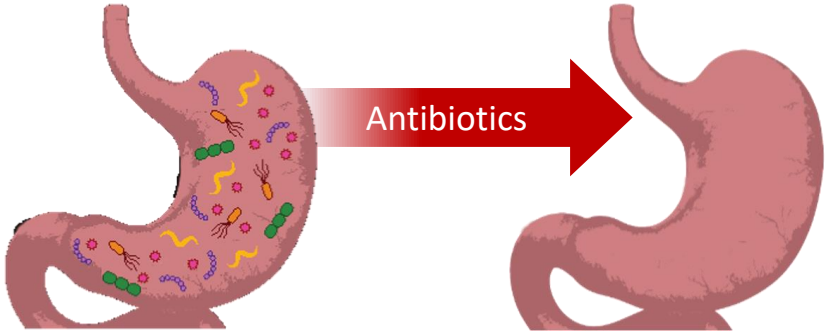
ALS-4: Value Proposition

Antibiotic

- Antibiotic resistance in S. aureus has been discovered in most prescribed antibiotics for MRSA[1]
- Broad spectrum and indiscriminate[2]
- Commonly affect normal flora, may lead to superinfection in case of drug resistance[3]

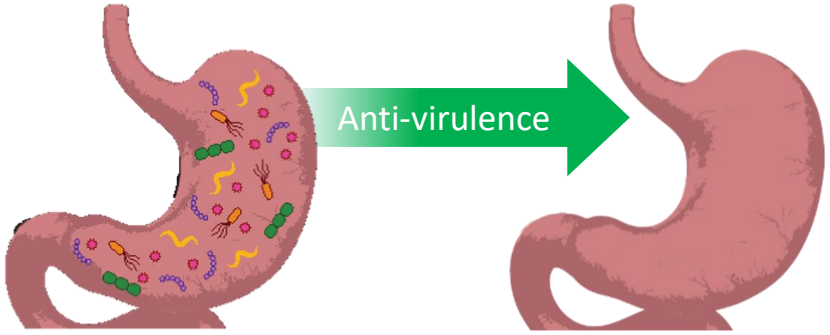
Indiscriminate clearance



Anti-virulence (ALS-4)

- ✓ Not bactericidal, potentially less selective pressure and much less likely for bacteria to develop resistance[4,5]
- ✓ "Disarms" the bacteria by reducing pathogenicity[4,5,6]
- ✓ Bacterial clearing is mediated by host immunity[4,5]

Directed against pathogen



1. Refer to "ALS-4: Approved Drugs for MRSA Infections" for complete set of sources; 2. P T. 2016 Feb; 41(2): 126–128; 3. J Infect Dis. 2018 Jan 30;217(4):628-636; 4. Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing; 5. MBio. 2017 Sep 5;8(5). pii: e01224-17; 6. J Exp Med. 2005 Jul 18;202(2):209-15.

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ALS-4: Approved Drugs for MRSA Infections

Frequently prescribed antibiotics for MRSA infections[1]

Product (Company)	Antibiotic Class	Indication(s)	RoA	Dose	Cost of Treatment (duration)	Notes
Vancomycin (Generic)	Glycopeptide	Severe infections caused by MRSA	IV / oral*	2g/day	USD 101-144 (7-10 days)	• **Currently, the most frequently prescribed** antibiotic for MRSA suspected infections[1,2] • In clinical use for >60 years[3], **vancomycin-resistant *S. aureus* (VRSA) was first discovered in 2002[4]**
Daptomycin (Merck)	Lipopeptide	ABSSSI, *S. aureus* bacteremia	IV	4-6mg/kg/day	USD 6,736-23,710[5] (14-42 days)	• In clinical use since 2003[6] • **Daptomycin resistance described in S. aureus as early as 2006[7]**
Linezolid (Pfizer)	Oxazolidinone	ABSSSI, CABP, HABP, uSSSI	IV / oral	0.8-1.2g/day	IV: USD 1,920-5,376 Oral: USD 2,978-11,429 (10-14 days)	• In clinical use since 2003[8]. Entirely synthetic, not expected to develop clinical resistance[9], however • **Linezolid resistance encountered clinically since 2010[9]**
Ceftaroline fosamil (Actavis)	Cephalosporin	ABSSSI, CABP	IV	1.2g/day	USD 1,831-5,127 (5-14 days)	• In clinical use since 2010[10] • **Ceftaroline resistance encountered clinically since 2016[11]**
Tigecycline (Pfizer)	Glycycycline	ABSSSI, CABP, CIAI	IV	0.1-0.2mg/day	USD 1,888-4,977 (5-14 days)	• In clinical use since 2005[12] • **Tigecycline resistance encountered clinically in developing countries since 2017[13,14]**
Televancin (Theravance Biopharma)	Lipoglycopeptide	ABSSSI, HABP, VABP	IV	10mg/kg/day	USD 3,002-10,568 (7-21 days)	• In clinical use since 2009[15] • **Vancomycin resistance leads to a 4-8x increase in telavancin MIC** (minimum inhibitory concentration)[16]

ABSSSI: acute bacterial skin and skin structure infection; CABP: community-acquired bacterial pneumonia; HABP: hospital-acquired bacterial pneumonia; CIAI: complicated intra-abdominal infection; VABP: ventilator-associated bacterial pneumonia; * Only for intestinal infections; 1. Reproduced from" Companies Take Aim at MRSA Infections" P T. 2016 Feb; 41(2): 126–128; 2. Clin Infect Dis. 2011 Feb 1;52(3):e18-55; 3. Clin Infect Dis. 2006 Jan 1;42 Suppl 1:S5-12; 4. Centers for Disease Control and Prevention. https://www.cdc.gov/hai/settings/lab/vrsa_lab_search_containment.html; 5. Cost of treatment of Daptomycin for S. aureus bacteremia at a dosage of 6mg/kg; 6. FDA. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2003/21-572_Cubicin.cfm; 7. Int J Antimicrob Agents. 2006 Oct;28(4):280-7; 8. FDA. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2002/21-130s003_2131s003_21132s003_ZyvoxTOC.cfm; 9. Pharmaceuticals (Basel). 2010 Jul; 3(7): 1988–2006; 10. FDA. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2010/200327origIs000toc.cfm; 11. J Antimicrob Chemother. 2016 Jun; 71(6): 1736–1738; 12. FDA. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2005/21-821_Tygacil.cfm; 13. New Microbes New Infect. 2017 Sep; 19: 8–12; 14. Journal of Microbiology and Infectious Diseases 2017; 7 (4):173-177; 15.FDA. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2009/022110s000TOC.cfm; 16. Clin Infect Dis. 2015 Sep 15;61 Suppl 2:S58-68.

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ALS-4: Addressing the Shortfall of Vancomycin

Vancomycin

- Generic antibiotic that is the most frequently prescribed for MRSA-suspected infections[1,2]
- After >60 years[3] of clinical use, its use against *S. aureus* is becoming limited. Vancomycin has been shown to have slow bactericidal activity, poor anti-staphylococcal activity, poor tissue penetration, and high rates of infection relapse[4,5,6,7,8,9]
- The shortcomings of Vancomycin has been compounded since the discovery of vancomycin-resistant S. aureus (VRSA) in 2002 and studies shown VRSA strain may exceed that 50% of the strain population[10];
- Vancomycin is not orally bioavailable and must be administered intravenously in order to treat systemic infections[11,12]. Oral vancomycin is only effective for treating local intestinal infections. Therefore, for MRSA-suspected infections oral vancomycin is only indicated for the treatment of pseudomembranous colitis

ALS-4: Potentially a complementary therapeutic to vancomycin

- Phase I clinical trials planned in N.America for 2020
- Clinical trials based on as a combination therapy to overcome the shortcomings of vancomycin
- ALS-4 can potentially complement other bactericidal antibiotics as well, therefore ALS-4 is not a direct competitor of antibiotics
- Synergistic effects of other drugs with vancomycin against MRSA has been demonstrated previously with β-lactam antibiotics and vancomycin[13]

1. "Companies Take Aim at MRSA Infections" P T. 2016 Feb; 41(2): 126–128; 2. Clin Infect Dis. 2011 Feb 1;52(3):e18-55; 3. Clin Infect Dis. 2006 Jan 1;42 Suppl 1:S5-12; 4. Antimicrob Agents Chemother. 2008 Jan;52(1):192-7; 5. Clin Infect Dis. 2007 Jan 15;44(2):190-6; 6. Clin Infect Dis. 2007 Sep 1;45(5):601-8; 7. J Clin Microbiol. 2011 Oct;49(10):3669-72; 8. Clin Infect Dis. 2007 Sep 15;45 Suppl 3:S191-5; 9. J Clin Microbiol. 2004 Jun;42(6):2398-402; 10. Centers for Disease Control and Prevention. https://www.cdc.gov/hai/settings/lab/vrsa_lab_search_containment.html; and https://aricjournal.biomedcentral.com/articles/10.1186/s13756-019-0585-4 11. J Infect. 2018 Dec;77(6):489-495; 12. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019-2018 Nov 18; 13. J Clin Microbiol. 2016 Mar; 54(3): 565–568

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ALS-4: mechanism of action

ALS-4

inhibits a key enzyme in the biosynthesis of staphyloxanthin[1]

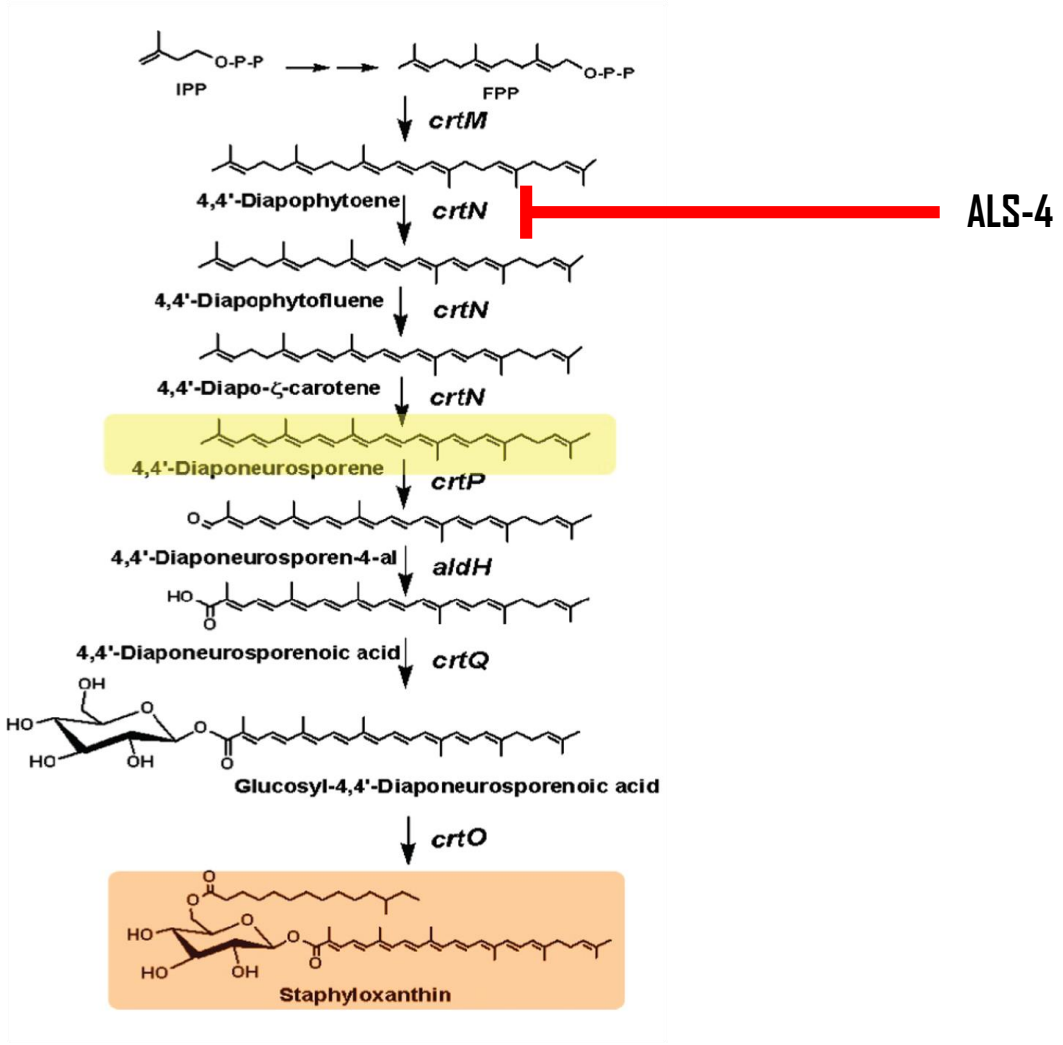

Figure adapted from MBio. 2017 Sep 5;8(5). pii: e01224-17.

The description of ALS-4 and related conclusory statements on ALS-4 on this slide are based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing.

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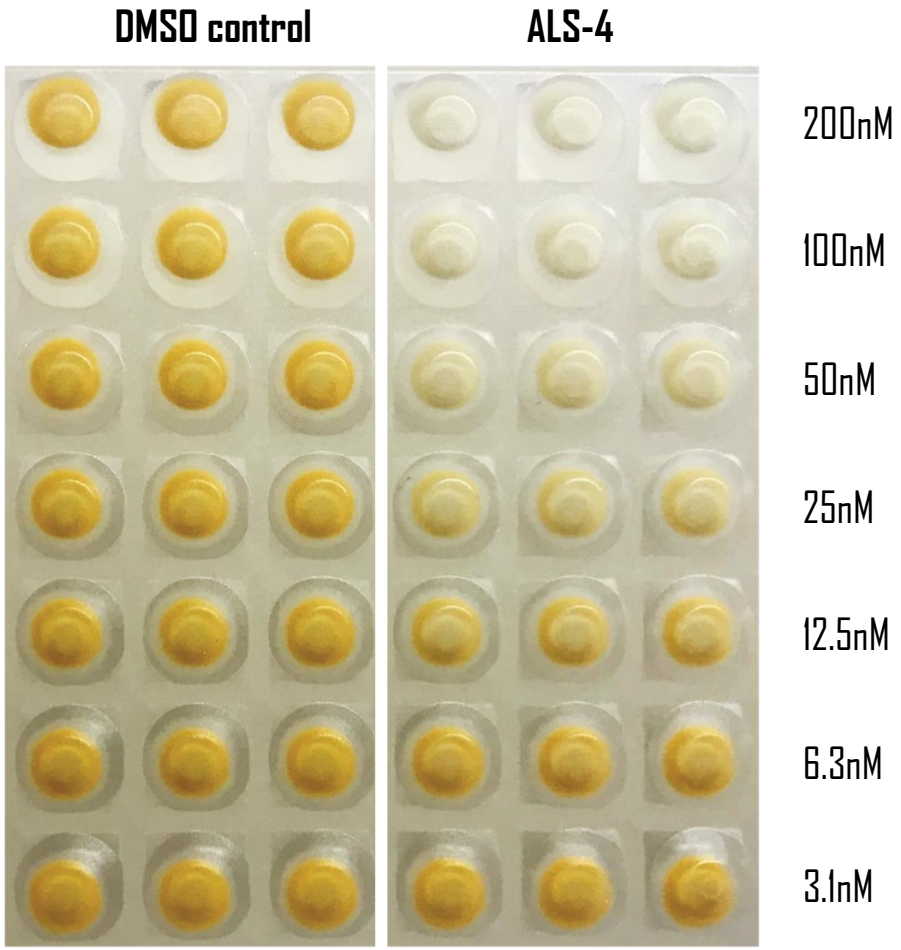
ALS-4: mechanism of action

ALS-4

inhibits S. aureus pigment production with an IC_{50} = 20nM



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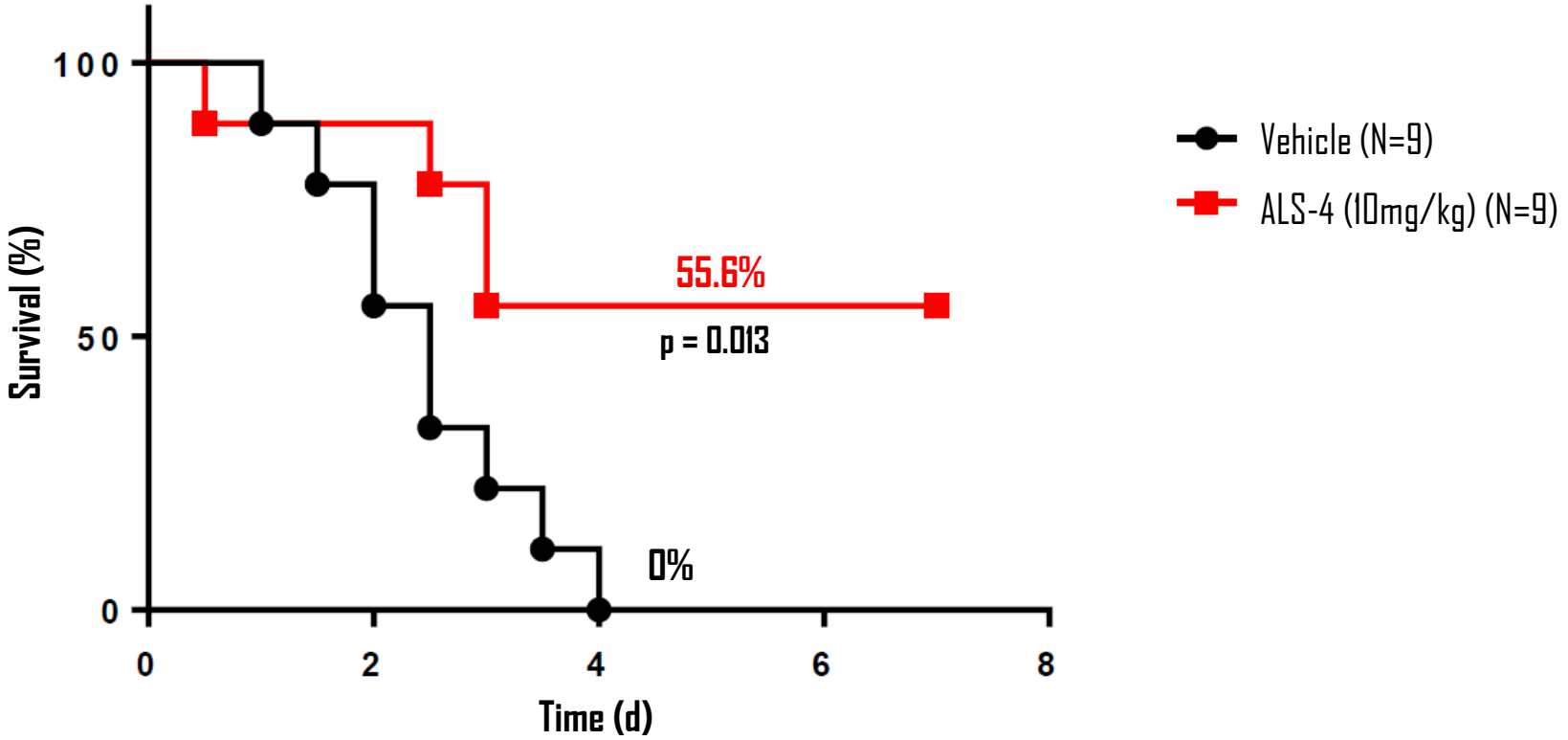
ALS-4: oral formulation treatment in an MRSA survival study

ALS-4 rescues rats infected with a lethal dose of MRSA USA300 in a bacteremia model



- A lethal dose (10^9 CFU) of MRSA was introduced through the tail vein
- ALS-4 was administered **orally** 30 minutes after infection for twice a day thereafter

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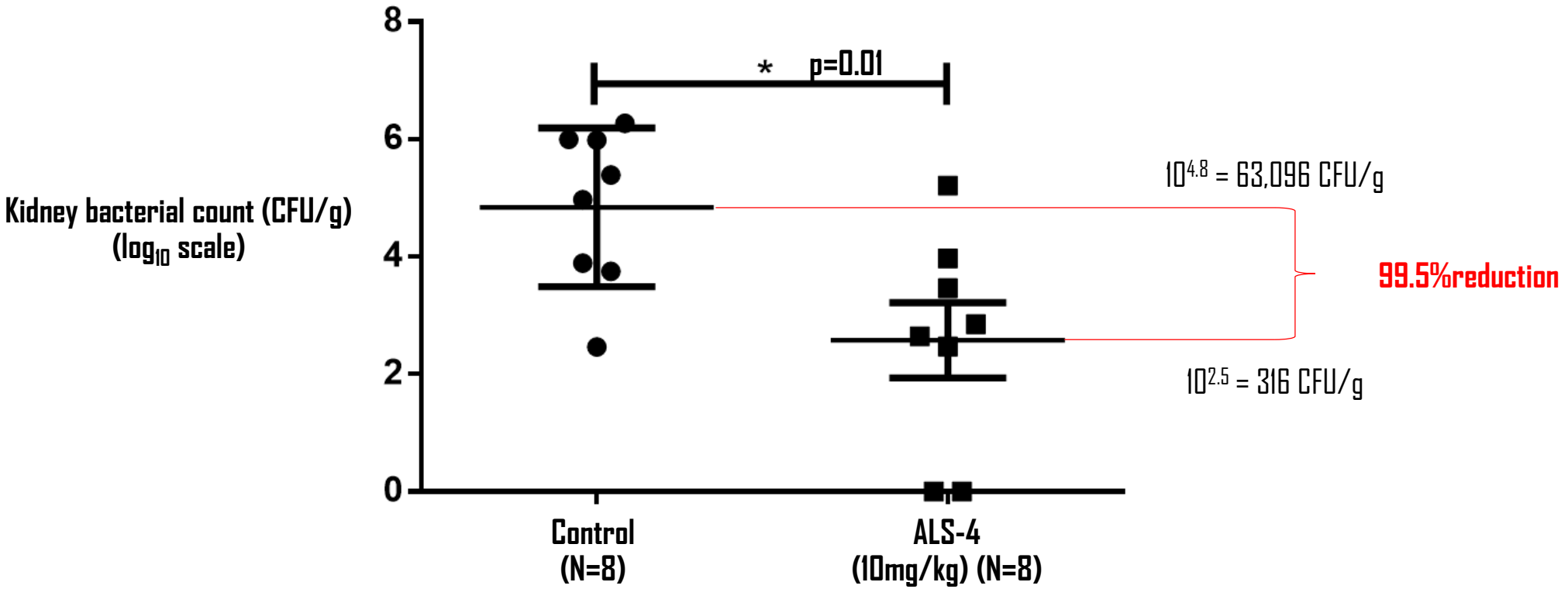
ALS-4: oral formulation treatment in a non-lethal bacteremia model

ALS-4 is shown to greatly reduce organ bacterial count in a bacteremia animal model



- Rats were challenged with a non-lethal dose (10^7 CFU) of MRSA through the tail vein
- In order to simulate a more realistic clinical scenario, treatment was introduced 14-days after infection, where ALS-4 was administered orally twice a day at 10mg/kg per animal

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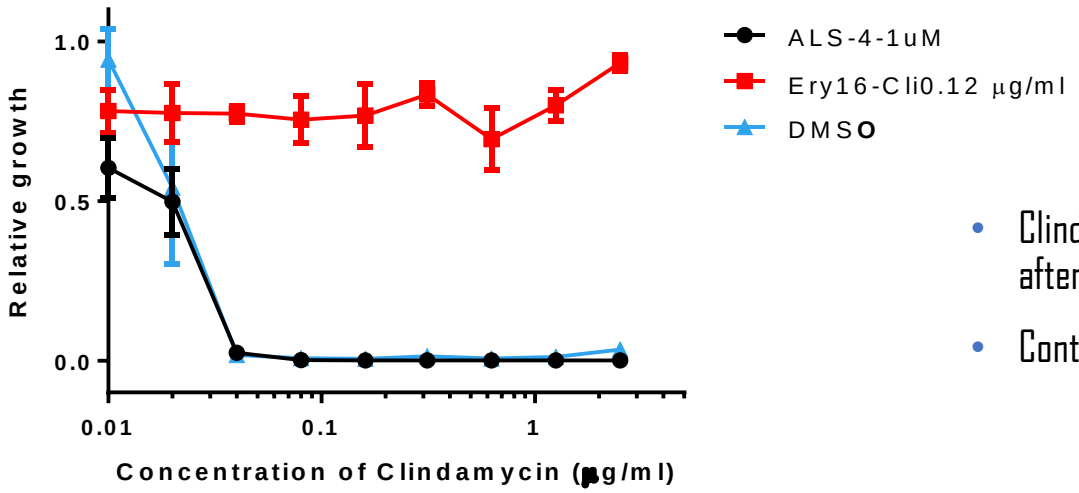
Resistance of *S. aureus* USA 300(lac) to clindamycin after various treatment conditions

Pre-treatment

Tubes	Day 1-4	Day 6-10
1	DMSO	DMSO
2	Ery 16 + CLI 0.12 µg/ml	Ery 16
3	ALS-4 1µM	ALS-4 1µM

(Clindamycin withdrawn between day 5-10)

Clindamycin resistance test after pre-treatment (BHI medium with 5 x 10^4/well bacterial inoculum)



- Clindamycin resistance (MIC from 0.12 µg/ml to >5 µg/ml) appeared rapidly after a 10-day intermittent treatment
- Controls without the addition of antibiotics showed no resistance to clindamycin

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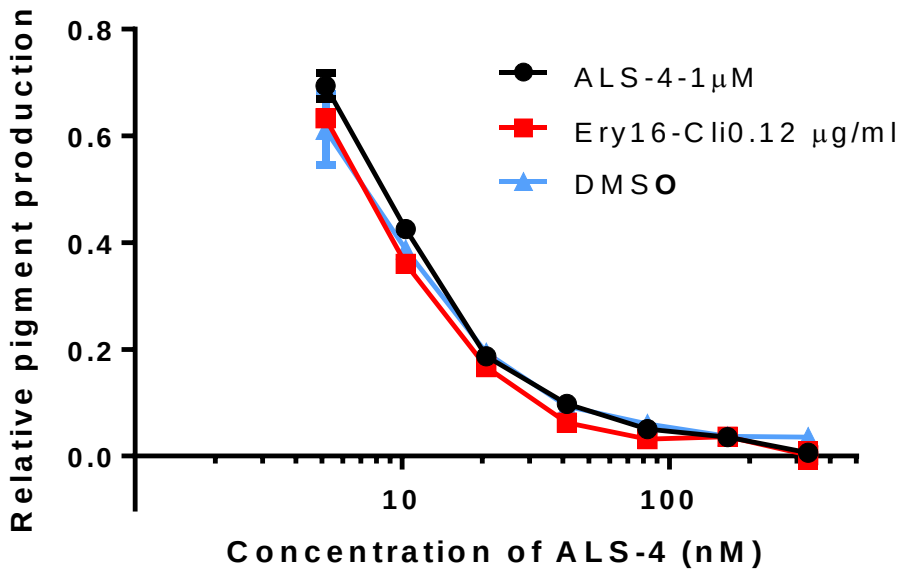
Resistance of *S. aureus* USA 300(lac) to clindamycin after various treatment conditions

ALS-4 efficacy test

(Bacterial inoculum: 4 x 10^7/ml)



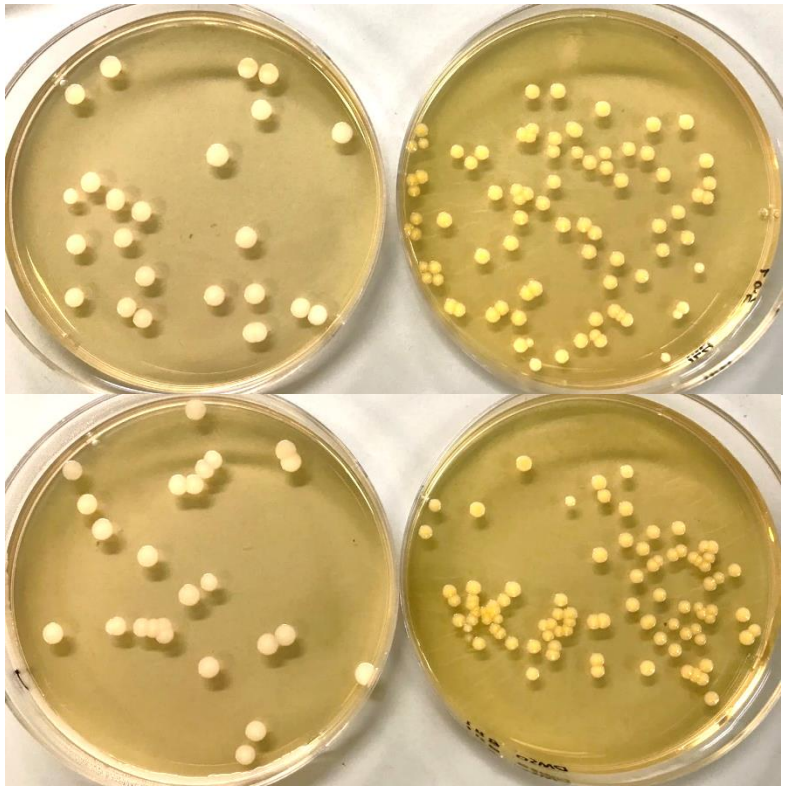
BHI agar plates

Recovered bacteria after 11-day resistance-raising with 1μM ALS-4

Recovered bacteria after 11-day resistance-raising with DMSO as control

100nM ALS-4
(all colonies turned white)

No ALS-4
(all colonies remained yellow)



No bacterial resistance to ALS-4 detected after continuous incubation of the bacteria in the presence of 1μM ALS-4 for 11 days

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Landscape Overview: The Human Gut Microbiota

- Contains **100s of species of microbes**
- Constantly producing **1000s of active metabolites**
- Some metabolites provides immunological and metabolic benefits
- **Dysbiosis (microbial imbalance) is a significant factor in disease**

Source: Lancet. 2003 Feb 8;361(9356):512-9; 2. Science. 2012 Jun 8;336(6086):1268-73; 3. Gastroenterology. 2014 May;146(6):1547-53

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Claves pipeline overview

Current progress of pipeline programs: → Lead Projects → Other Candidates → Projected timeline

Note: all projected timelines refer to the estimated commencement time of the indicated stages

Pillar 3: Claves (CLS series) - Microbiota

Large molecule approach. Over 70 targets / indications

IND NDA

Program	Indication	Discovery	Lead Optimization	IND enabling	Phase I	Phase II / III
CLS-1	Obesity	→	Q4 2019 →	Q2 2020 →	Q4 2020 →	
CLS-2	To be disclosed	→				
CLS-3	To be disclosed	→				

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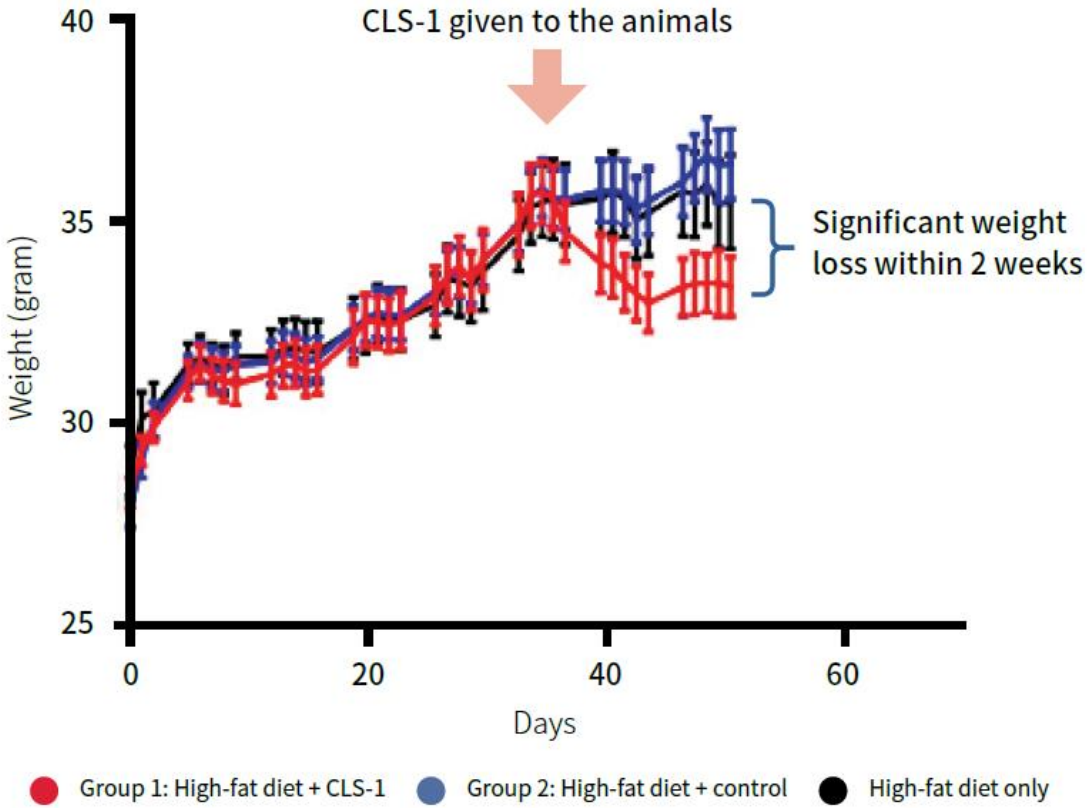
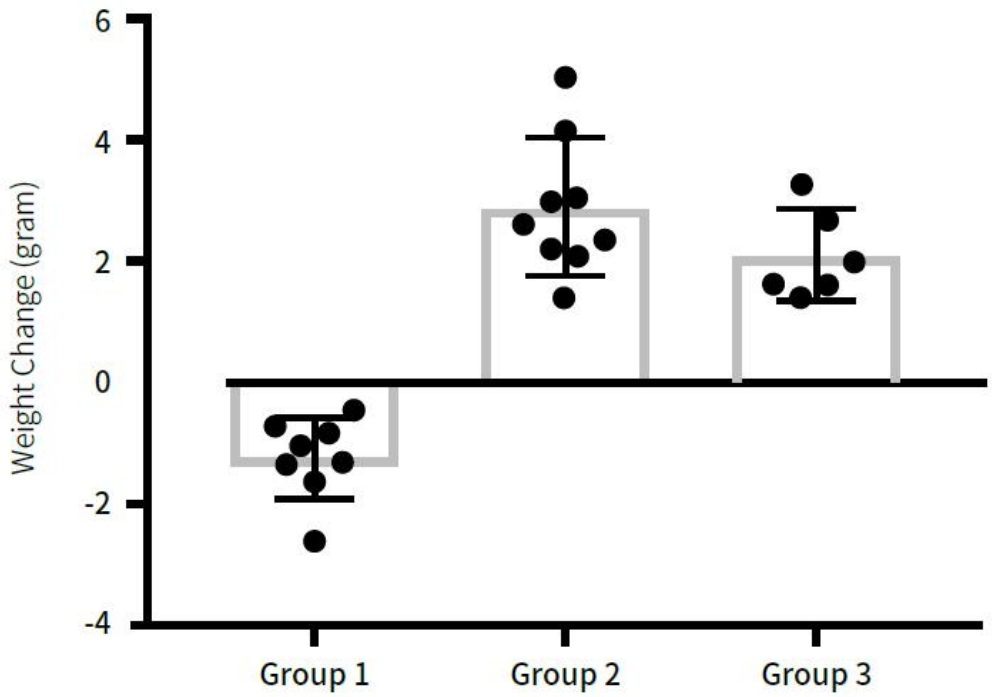
CLS-1: efficacy in a mouse model

CLS-1 treatment significantly reduces body weight in mice





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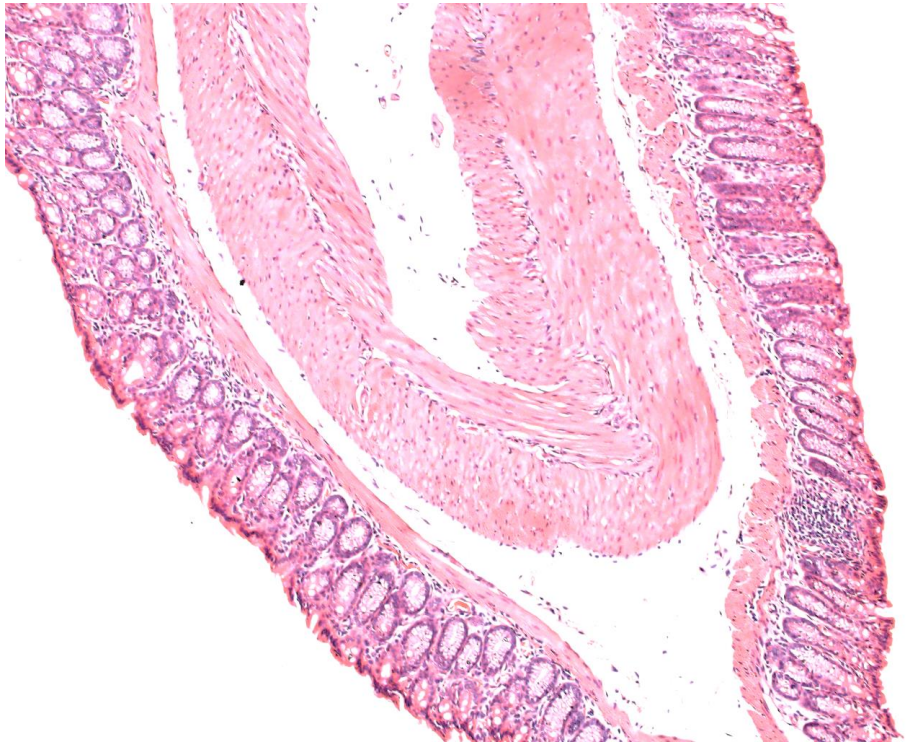
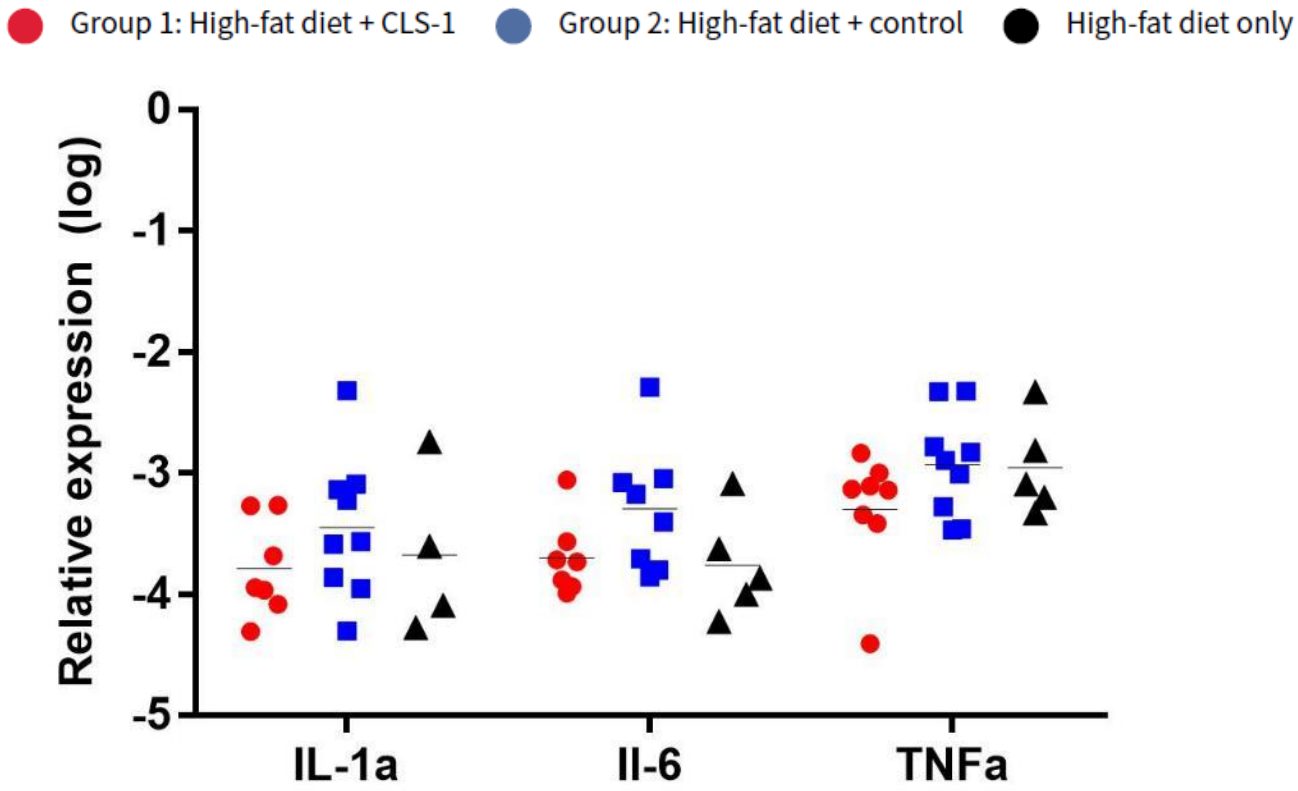
CLS-1: toxicology (gut histology and inflammatory markers)

Mucosa and Inflammatory Markers





CLS-1 does not upregulate inflammatory markers

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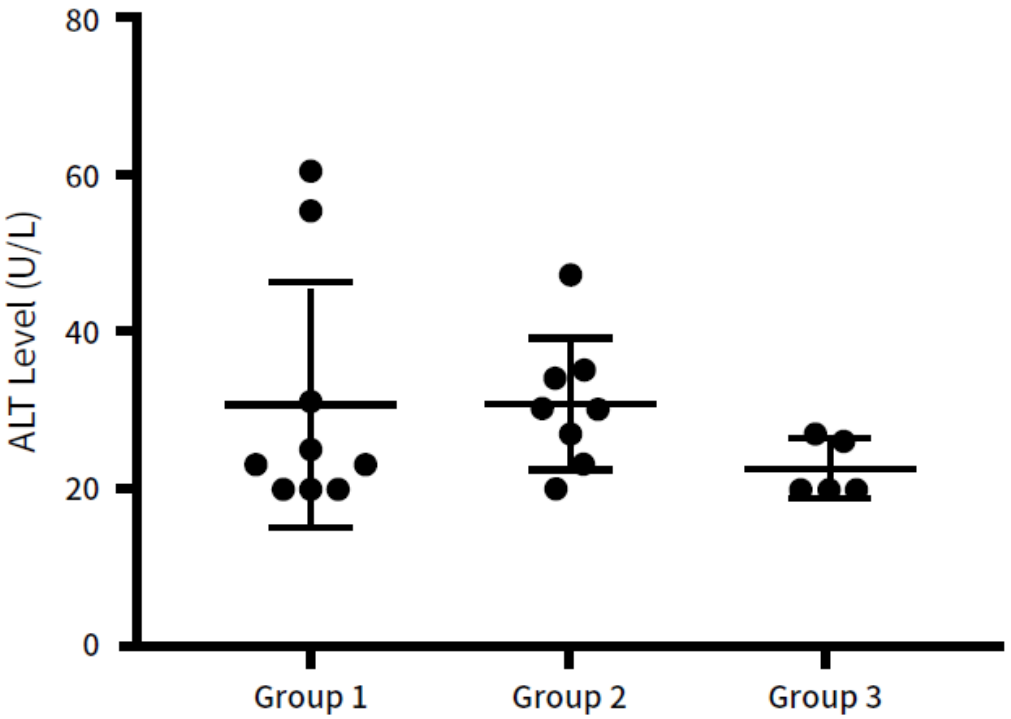
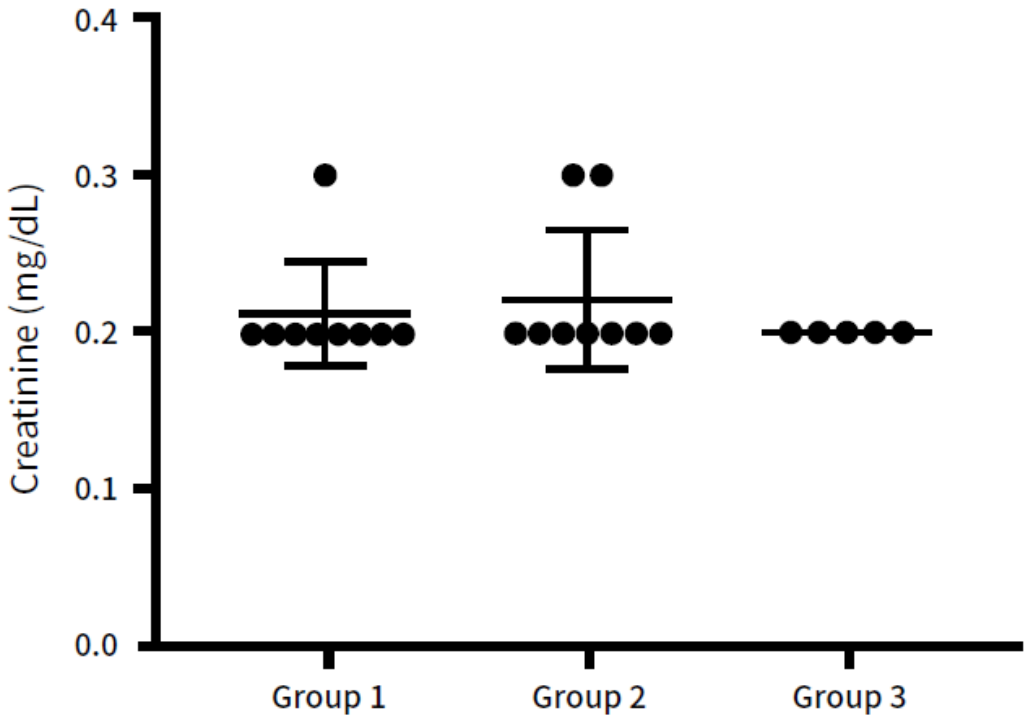
CLS-1: toxicology (liver and renal functions)

Liver and Renal Functions





CLS-1 does not interfere with liver and renal functions

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NLS-2 Woman's Health Supplement: Market Overview

1.2bn

- postmenopausal women projected by the year 2030[1]
- **85%** of postmenopausal women experience menopause-related symptoms in their lifetime[2]

USD 2.5 bn

Value of the global menopause treatment market in 2019[3]

USD 17.1 bn

Value of the global isoflavone supplement market in 2019[4]

4.2%

CAGR global menopause treatment market (2017-2023)[3]

1. World Health Technical Report Series . Research on the Menopause in the 1990's, https://apps.who.int/iris/bitstream/handle/10665/41841/WHO_TRS_866.pdf?sequence=1&isAllowed=y; 2. Symptoms during the perimenopause: prevalence, severity, trajectory, and significance in women's lives, https://www.amjmed.com/article/S0002-9343(05)00885-5/fulltext; 3. Calculated based on the forecasted market size of USD 3bn by 2023 and a forecasted CAGR of 4.2% between 2017-2023. Menopause Treatment Market 2019: https://www.reuters.com/brandfeatures/venture-capital/article?id=119980; 4. Isoflavones Market Size To Reach USD 50.06 Billion By 2025. https://www.grandviewresearch.com/press-release/global-isoflavones-market. (Isoflavones are naturally occurring compounds found in a wide variety of plants. The isoflavones supplement market is the main menopausal supplement market.)

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NLS-2: Executive Summary

NLS-2[1]

- NLS-2 is a dietary supplement for the relief of menopausal symptoms.
- The bioactive component of NLS-2 is DOI, a novel non-hormonal compound extracted from Chinese Yam
- DOI significantly increased estradiol biosynthesis and aromatase expression in granulosa cells *in vitro* and *in vivo* (rat animal model)
- Osteoporosis is frequently associated with menopause. DOI increases the apparent bone mineral density, bone volume fraction and trabecular thickness in an *in vivo* rat model
- DOI acts in a tissue-specific manner. Upregulation of aromatase, an enzyme involved in the production of estrogen, by DOI was found in ovary but not in other tissue
- DOI does not cause toxicity in vitro based on cell viability in the MTT assay
- Targeting to launch as a dietary supplement in Q1 2020

Timeline

- NLS-2 supplement is commercialised in Hong Kong 2020 as announced in Q1 2020
- Manufacturing has commenced in Canada
- Additional Target markets for 2020 will include China, UK, Europe, Canada and US (subject to registration)

1. Lancet. 2003 Feb 8;361(9356):512-9; 2. Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing; 3. Data available in this presentation

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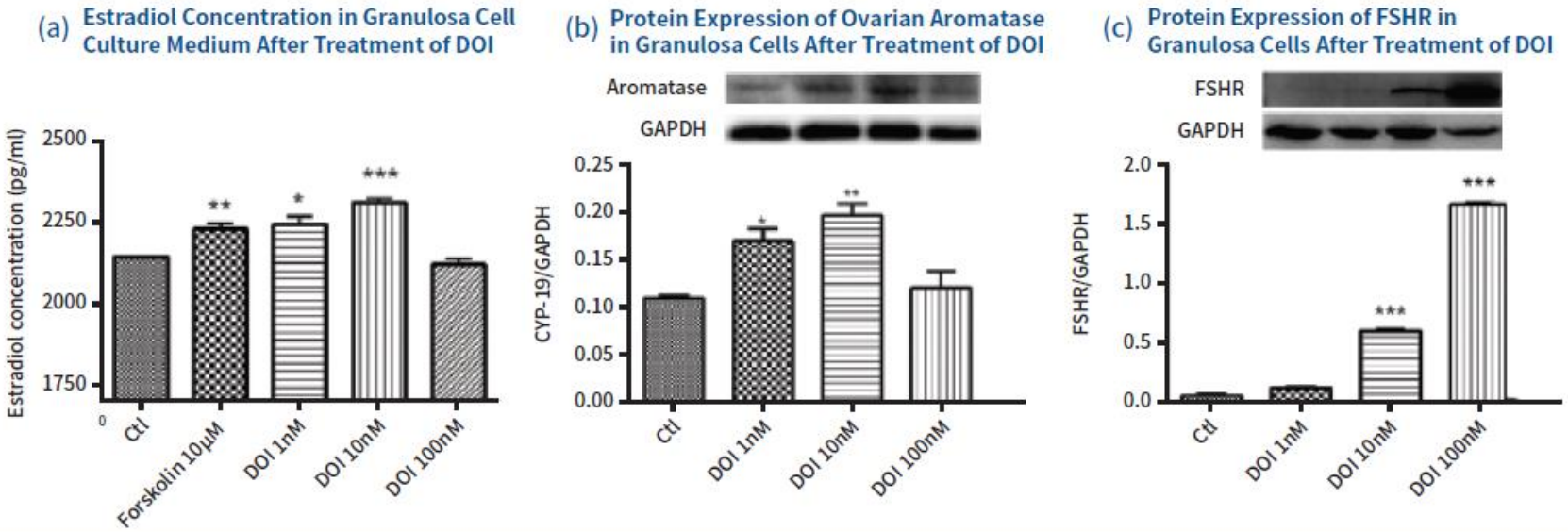
DOI- A Chinese Yam Extract To Address Menopausal Syndrome

DOI, a novel bioactive peptide with estrogen-stimulating activity[1]

- Discovered an estrogen-stimulating activity from an extract obtained from the Chinese yam, Dioscorea opposita Thunb
- Identified and isolated a novel bioactive component, DOI, which conferred the estrogen-stimulating activity[1]
- DOI significantly increased estradiol biosynthesis and aromatase expression in granulosa cells
- The upregulation of aromatase, an enzyme involved in the production of estrogen, by DOI was found in ovary but not in other cells/tissues

In vitro **studies show that DOI stimulated estradiol level in rat ovarian granulosa within a specified concentration range.**



(a) Stimulatory activity of DOI on estrogen biosynthesis in granulosa cells. Protein expression of (b) aromatase and (c) follicle-stimulating hormone receptor (FSHR) in ovarian granulosa cells. Results are expressed as means ± SEM (n = 3). *P < 0.05, **P < 0.01, ***P < 0.001 compared with the control group (unpaired t-test). (Adopted from Science Report (5:10179, 2015))

1. Sci. Rep. 5, 10179; doi: 10.1038/srep10179 (2015). This source applies to all the content on this slide.

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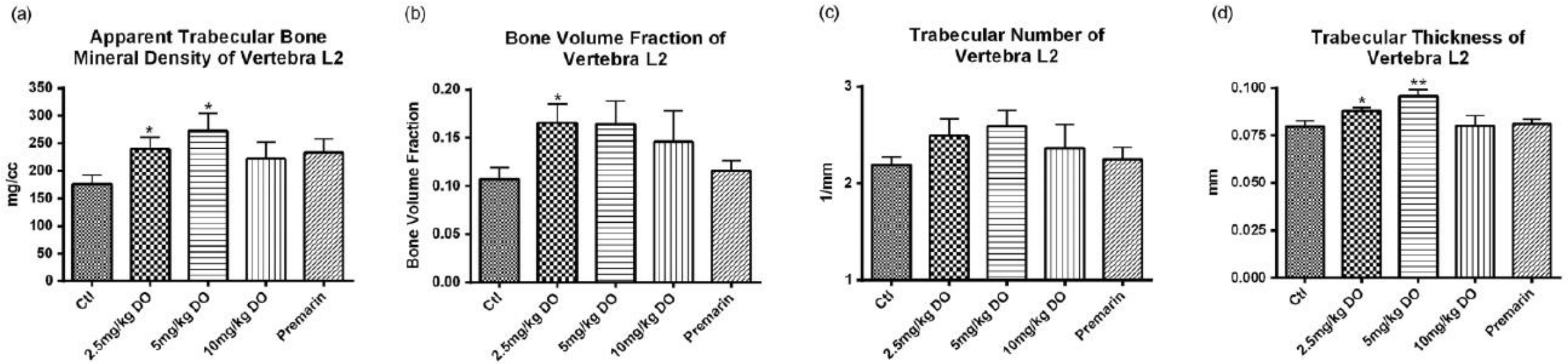
DOI- A Chinese Yam Extract To Address Menopausal Syndrome

DOI and bone density[1]

- DOI in old female SD rats demonstrated an increase in the apparent bone mineral density, bone volume fraction and trabecular thickness by microCT scanning



(a) Serum estradiol, (b) apparent trabecular bone mineral density, (c) bone volume fraction of Sprague Dawley rats after treatment with DOI for 2, 4, and 6 weeks. Results are expressed as means ± SEM (n = 6; except Premarin group, where n = 3). *p < 0.05, **p < 0.01 compared with the control group (unpaired t-test).

1. Sci. Rep. 5, 10179; doi: 10.1038/srep10179 (2015). This source applies to all the content on this slide.

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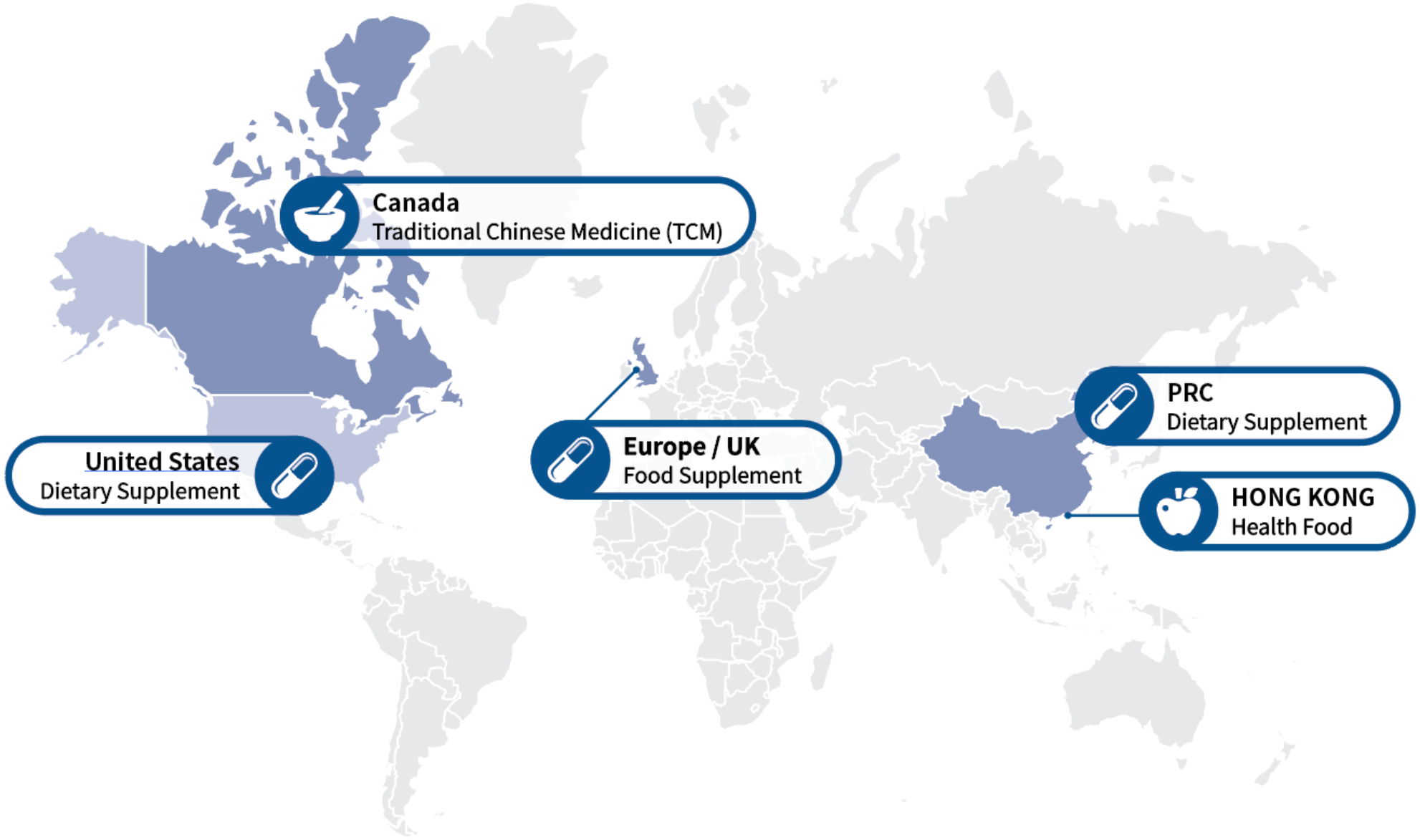
Regulatory Information



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Financials

Timeline	Figures
Pre-IPO 2016 – 2018 - Capital Raised	US$ 37m
IPO Dec 2018 – Capital Raised	US$ 12m
Feb 2020 Registered Direct Offering	US$ 10m
As at mid-March 2020 Cash + Undrawn Credit Facility	US$ 20m+
Total Shares Issued	30,386,466
% of Company owned by Insiders and Founders	~69%

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