



Facilitating Life Science Innovations to Serve Unmet Medical Needs

CORPORATE PRESENTATION



NASDAQ GLOBAL MARKET: APM

Disclaimer

This document includes statements concerning Aptorum Group Limited and its future expectations, plans and prospects that constitute “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. For this purpose, any statements contained herein that are not statements of historical fact may be deemed to be forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “may,” “should,” “expects,” “plans,” “anticipates,” “could,” “intends,” “target,” “projects,” “contemplates,” “believes,” “estimates,” “predicts,” “potential,” or “continue,” or the negative of these terms or other similar expressions. Aptorum Group has based these forward-looking statements, which include statements regarding projected timelines for application submissions, trials and commercialization and market potential of related products, largely on its current expectations and projections about future events and trends that it believes may affect its business, financial condition and results of operations. These forward-looking statements speak only as of the date of this document and are subject to a number of risks, uncertainties and assumptions including, without limitation, risks related to its announced management and organizational changes, the continued service and availability of key personnel, its ability to expand its product assortments by offering additional products for additional consumer segments, development results, the company’s anticipated growth strategies, anticipated trends and challenges in its business, and its expectations regarding, and the stability of, its supply chain, and the risks more fully described in Aptorum Group’s Form 20-F and other filings that Aptorum Group may make with the SEC in the future. As a result, the projections included in such forward-looking statements are subject to change. Aptorum Group assumes no obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

About Aptorum Group

Company information

- Established in 2010, focused on current unmet medical needs, including orphan diseases, infectious diseases, metabolic diseases and women's health, over 15 therapeutic candidates
- **Business Strategy:** From Discovery to Ph2 Proof-of-Concept (PoC)
- **Markets and Regulatory:** Targeted for US FDA clinical, China NMPA and Europe EMA approval and other major countries
- **IPO:** Listed on NASDAQ Global Market (ticker symbol: APM) on December 18, 2018 and cross-listed on Euronext Paris (ticker symbol: APM) on July 24, 2020
- Company's principal office based in London, United Kingdom
- Core development site based in Toronto (GLP, GMP, clinical trial coordination)
- ~40 full time staff and ~45 scientists, advisors and consultants with vast experience in drug development and clinical studies

Directors, Management and Significant Employees

Leadership



MR. IAN HUEN

Founder, Chief Executive Officer and Executive Director

- Over 15 years in global asset management;
- US healthcare equity research analyst at Janus Henderson Group;
- Trustee board member of Dr. Stanley Ho Medical Development Foundation;
- CFA, Princeton University, U.S. (Econ)



MR. DARREN LUI

President and Executive Director

- Over 13 years in global capital market;
- Extensive experience in Investment in UK, Singapore, US, etc.;
- ICAS, CFA & Associate of Chartered Institute of Securities & Investments (UK);
- First-Class Honors from Imperial College (Biochemistry)



DR. CLARK CHENG

Chief Medical Officer and Executive Director

- Almost 10 years working in Raffles Medical Group as Operations Director and Deputy General Manager;
- Received medical training at the University College London in 2005 & obtained membership of the Royal College of Surgeons of Edinburgh in 2009;
- MBA, University of Iowa, U.S.



MISS SABRINA KHAN

Chief Financial Officer

- Almost 10 years serving US & Asian healthcare companies;
- Extensive experience in business development, restructuring, US & Asian IPO, and M&A deals;
- Solid accounting experience gained from Big 4;
- Advanced China Certified Taxation Consultant;
- CPA, University of Hong Kong (BBA(Acc & Fin))



DR. THOMAS LEE WAI YIP

Head of Research and Development

- Former Assistant Professor at The Chinese University of Hong Kong (CUHK) specialized in drug delivery and formulation development;
- 10 years from Novartis & Celgene;
- B.Pharm.(Hons), CUHK; Ph.D. in Pharmaceutical Sciences (Drug Delivery), the University of Wisconsin-Madison



DR. HERMAN WEISS

*CEO of Claves Life Sciences
Senior Medical Advisor of
Aptorum Group*

- Over 20 years of experience in medical field;
- Chairman of the Board of Directors of Todos Medical;
- Former Head of Clinical Development and Medical Affairs at Juniper Pharmaceuticals;
- MBA, George Washington University; M.D., Ohio State University



DR. ANGEL NG SIU YAN

Chief Operating Officer

- Research Officer cum Project Manager at The University of Hong Kong (HKU) towards cadaveric trial for a novel soft robotics medical device;
- Former Project Manager at Hong Kong Science & Technology Parks Corporation and CUHK;
- B.Sc (Hons), HKU; M.Sc in Composite Materials, Imperial College London; Ph.D. in Mechanical Engineering, HKU

Independent Non-Executive Directors



PROFESSOR DOUGLAS ARNER

Kerry Holdings Professor in Law, HKU



DR. JUSTIN WU

COO of CUHK Medical Centre



DR. MIRKO SCHERER

CEO of CoFeS China and
Ex Head of TVM Asia



MR. CHARLES BATHURST

Founder of Summerhill Advisors Limited

Aptorum Team

Consultants and Advisors to Aptorum Group and Subsidiaries



DR. KEITH CHAN

Consultant

- Adjunct professor and advisor at the Research Center for Drug Discovery, National Yang Ming University in Taipei;
- Former Division Director of Office of Generic Drugs, US FDA;
- Co-founder of Globomax LLC;
- Formerly employed at Ciba-Geigy



DR. NISHANT AGRAWAL

Senior Clinical Advisor

- Professor of Surgery, School of Medicine, University of Chicago;
- Former Asso. Professor at Johns Hopkins University;
- M.D., Johns Hopkins University School of Medicine



DR. LAWRENCE BAUM

Senior Scientific Advisor

- Asso. Professor, School of Pharmacy, The Chinese University of Hong Kong;
- Research Officer, Faculty of Medicine, The University of Hong Kong;
- Ph.D. in Neurosciences, UC San Diego



DR. FRANCIS SZELE

Senior Scientific Advisor

- Asso. Professor, Department of Physiology, Anatomy & Genetics, University of Oxford;
- Asst. Professor, Subventricular Zone, Northwestern University;
- Ph.D. in Biology, The University of Pennsylvania, U.S.



MR. WILLIAM WEISS

Consultant

- Currently Director of Preclinical Service and Instructor of Pharmaceutical Sciences, College of Pharmacy, University of North Texas;
- 38 years of experience in drug discovery and development of antimicrobials including antibiotics, antivirals and antifungals;
- Former Director of Cumbre Pharmaceuticals Inc;
- Former Group Leader at Wyeth for 17 years;
- Formerly employed at Schering-Plough for 7 years;
- BSc in Microbiology from Rutgers University; MSc in Microbiology from Penn State University and Fairleigh Dickinson University



DR. KIRA SHEINERMAN

Senior Strategic Consultant

- Co-Founder, CEO and Executive Director of DiamIR Biosciences;
- Serves as a Managing Director, Healthcare Investment Banking at H.C. Wainwright & Co.;
- Ph.D. in Biomedical Sciences from Mount Sinai School of Medicine in New York;
- Honors MBA from Zicklin School of Business, Baruch College, City University of New York



DR. ROBBIE MAJZNER

Advisor

- Assistant professor of Pediatrics (Hematology/Oncology) at the Stanford University Medical Center;
- Completed residency training in pediatrics and fellowship training in pediatric hematology-oncology;
- Board certified in pediatrics and pediatric hematology-oncology;
- M.D., Harvard Medical School

Current progress of leading pipeline programs and discovery

→ Lead Projects → Other Candidates → Non-therapeutics Candidates

Projects	Candidate / Modality	Indication	Computational Discovery	In Vitro Validation	Existing PhI/II Clinical Safety Data ¹	In Vivo Validation	IND Preparation & Submission	PhI/III w/ Limited Population ²	
SACT's Series									
SACT-1	Repurposed Drug Molecule	Neuroblastoma	→						
SACT-2	Repurposed Drug Molecule	To be disclosed	→						
SACT-3	Repurposed Drug Molecule	To be disclosed	→						
SACT-COV19	Repurposed Drug Molecule	Coronavirus Disease 2019 (COVID-19)	→						
Projects	Candidate / Modality	Indication	Development Stage					NDA	
			Target Identification & Selection	Lead Discovery	Lead Optimization	IND-Enabling	Phase 1	Phase 2	Phase 3
Acticule's Series									
ALS-4	Small molecule	Treatment of bacterial infections caused by Staphylococcus aureus including MRSA	→						
ALS-1	Small molecule	Treatment of viral infections caused by influenza virus A	→						
ALS-2	Small molecule	Treatment of bacterial infections caused by Staphylococcus aureus including MRSA	→						
ALS-3	Small molecule	Reviving existing antibiotics to overcome drug resistance	→						
Claves' Series									
CLS-1	Macromolecule	Treatment of Obesity	→						
CLS-2	To be disclosed	To be disclosed	→						
CLS-3	To be disclosed	To be disclosed	→						

1. 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 2. Subject to FDA's approval

Current progress of leading pipeline programs and discovery

Projects	Candidate / Modality	Indication	Development Stage					
			Target Identification & Selection	Lead Discovery	Lead Optimization	IND-Enabling	Phase 1	Phase 2
Nativus' Series								
NLS-1	Small molecule	Treatment of Endometriosis						
Scipio's Series								
SPLS-1	83b-1 Novel Quinoline Derivative	Treatment of Liver Cancer						
Videns' Series								
VLS-2	MITA	Treatment of Alzheimer's & Parkinson's Disease						
VLS-4	Imaging Agent for MRI Diagnosis	Diagnosis of Alzheimer's Disease						

Projects	Modality	Target Customer	Formulation	Commercialization
NativusWell [®] DOI (NLS-2)	Supplement	Women undergoing menopause		

Projects	Candidate / Modality	Indication	Development Stage				
			Lab-based Phantom Trial	Animal Trial	IDE Application Approval	Safety/ Feasibility Clinical Study	Pivotal Clinical Study
Signate's Series							
SLS-1	Robotic Catheter Platform for Intra-Operative MRI-Guided Cardiac Catheterization	Heart Rhythm Disorders by Cardiac Electrophysiology Intervention					

7000+ Orphan Diseases

Patient population definition:

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

Disease selection criteria

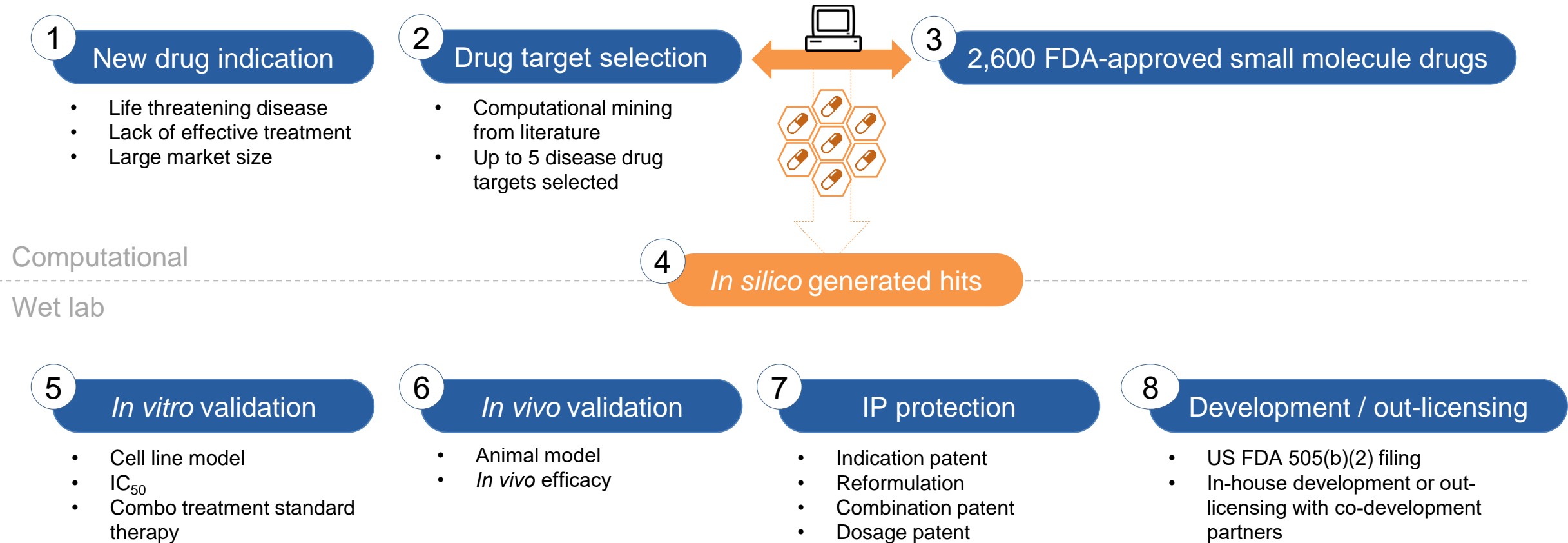
High
priority



- Life threatening disease
- High unmet need
- IP protection
- Market size
- Competitive landscape
- Clinical trial design
- Paediatric disease
- By region
- Target selection
- Disease knowledge

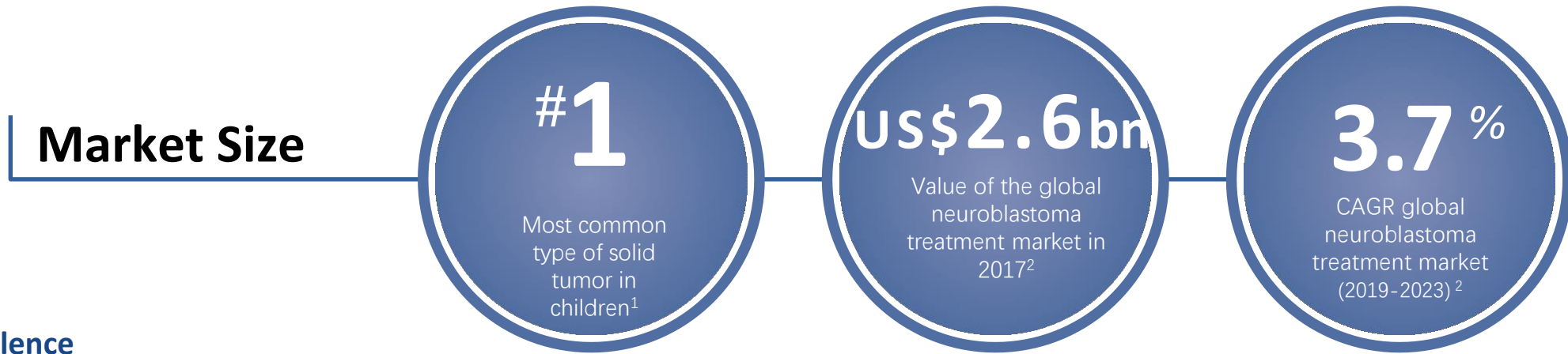
SMART-ACT[®]
High Priority
Orphan Diseases

SMART-ACT[®] : Pipeline Workflow



SACT-1 (neuroblastoma): market overview

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



Prevalence

- ~700 cases of high risk neuroblastoma (NB) patients each year in the US³ and we estimated EU has 1.5x those cases, c. 1050 high risk NB patients per year.
- Accounts for ~15% of all cancer-related deaths in the pediatric population⁴

Orphan drug designation⁵

- Neuroblastoma is a rare disease and drugs are qualified for orphan designation by the FDA
- Designated orphan drugs receive 7 years of market exclusivity in US and 10 years of marketing exclusivity in EU
- Patents on reformulation, if granted, will provide up to 20 years of patent exclusivity from the application date in parallel to the market exclusivity

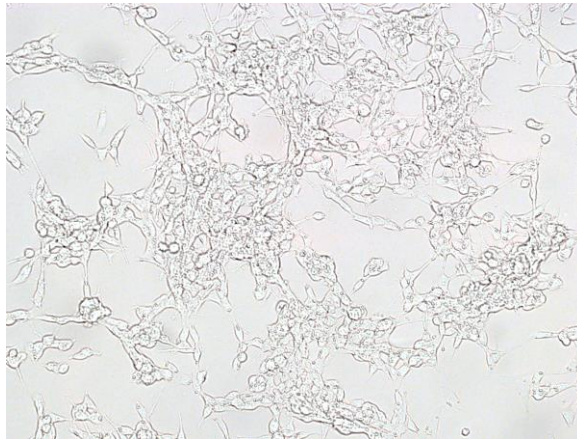
1. *Pediatr Rev.* 2018 Feb;39(2):57-67; 2. "Neuroblastoma Market Global Industry Perspective, Comprehensive Analysis, Size, Share, Growth, Trends, and Forecast 2019 – 2023" (2019). MRFR Research. 3. *Curr Oncol Rep.* 2009 Nov;11(6):431-8 4. *Paediatr Drugs.* 2011 Aug 1;13(4):245-55 5. <https://www.fda.gov/about-fda/office-special-medical-programs/office-orphan-p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

All conclusory statements on this slide are based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing.

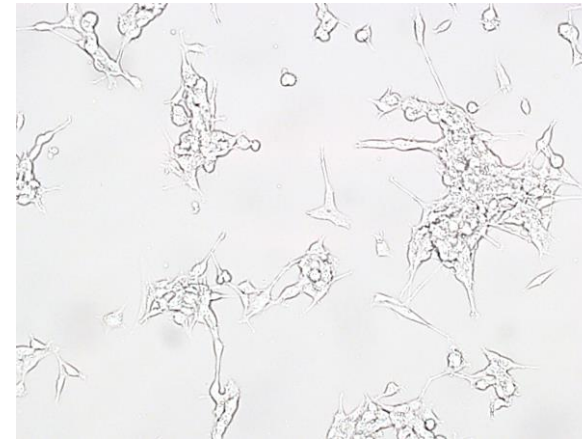
In vitro drug activity against neuroblastoma cell lines

- SACT-1's potential action against neuroblastoma might be patentable
- We find that its action against neuroblastoma could be patentable

Control treatment on neuroblastoma cells



SACT-1 treatment on neuroblastoma cells

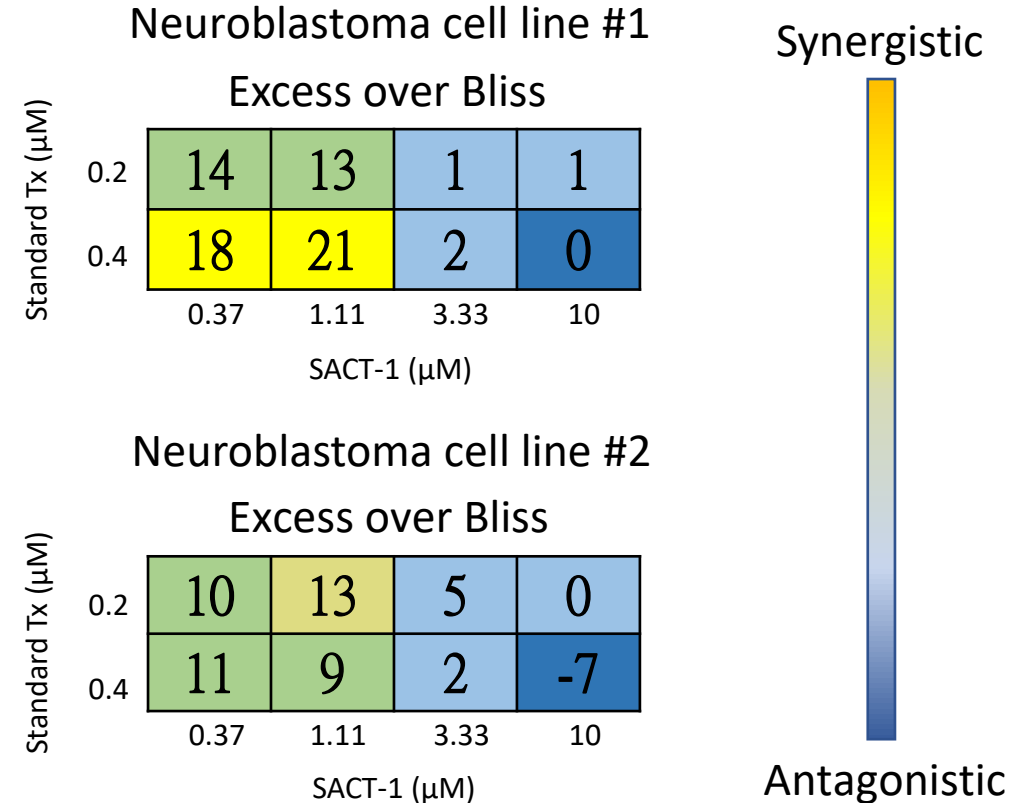
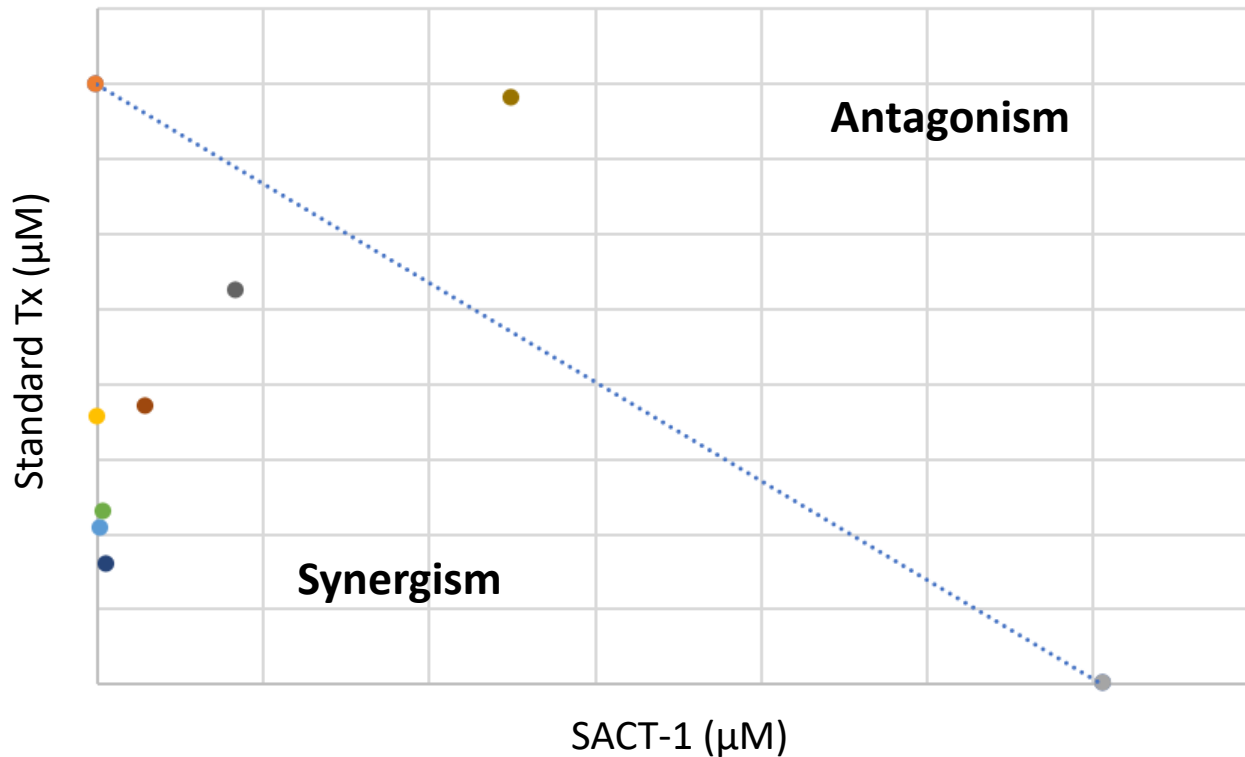


	IC₅₀ [μM] For IMR-32	IC₅₀ [μM] For SK-N-BE(2)	IC₅₀ [μM] For SK-N-SH	IC₅₀ [μM] For SH-SY5Y
SACT-1	2.97	3.37	2.75	3.12

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

Synergistic effect of SACT-1 in combination with standard treatment

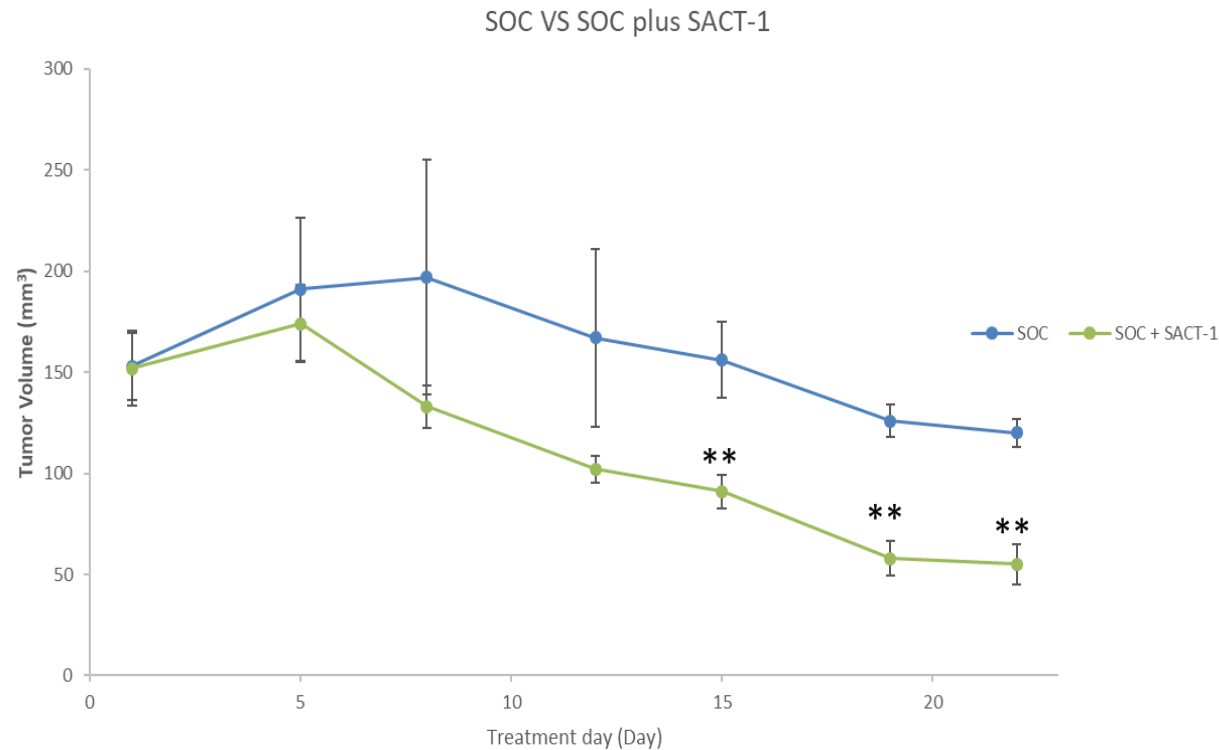
- Synergistic effect observed for SACT-1 in combination with standard treatment in 2 different neuroblastoma cell lines, as seen in the isobologram (left) and the Excess over Bliss (right)



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

SACT-1: Combination study with standard chemotherapy *in vivo* model

SACT-1 when combined with standard of care chemotherapy showed a statistically significant reduction in tumour volume in a xenograft mouse model.



** Unpaired Student's T-test, $p < 0.01$, $n = 8$ (based on data observed over initial 22 day period of the study, with SOC applied from day 1 to day 15 and SACT-1 applied from day 1 to day 21)

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

SACT-1: safety & tolerability

Well-established Safety profile based on a FDA approved product

- 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 SACT-1 doses were safe and well tolerated
- No dose relationship between RPV and adverse events (AE)

RPV	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 RPV	20%	20%	21%
AEs leading to discontinuation	9%	12%	14%
Any serious AE	13%	14%	10%
Deaths	0%	2%	0%

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

Ref: doi: 10.1089/AID.2011.0050

Executive summary: Acticule projects

ALS-4

- Aptorum's lead program ALS-4 is an anti-virulent, non-bactericidal drug candidate for *Staphylococcus aureus* infections including MRSA¹
- Unlike all major treatments on the market, ALS-4 is an orally administered anti-virulent molecule using a non-bactericidal approach¹, potentially reducing significant risks of developing *S. aureus* resistance
- Targeting IND submission by H2 2020
- Upon IND approval, a Phase I clinical study to commence in H2 2020 in North America
- Targeting to submit written request for approval under the newly established LPAD regulatory pathway (Limited Population Pathway for Antibacterial and Antifungal Drugs), to expedite marketing approval and commercialization

ALS-1

- A unique antiviral therapeutic against Influenza A that has a more upstream target than Tamiflu[®] which is shown to be more effective in vitro¹
- Viral resistance to Tamiflu and other neuraminidase inhibitors has risen rapidly in recent years²
- ALS-1 has a distinct mechanism of action compared with Tamiflu[®] and Xofluza^{TM1,3}

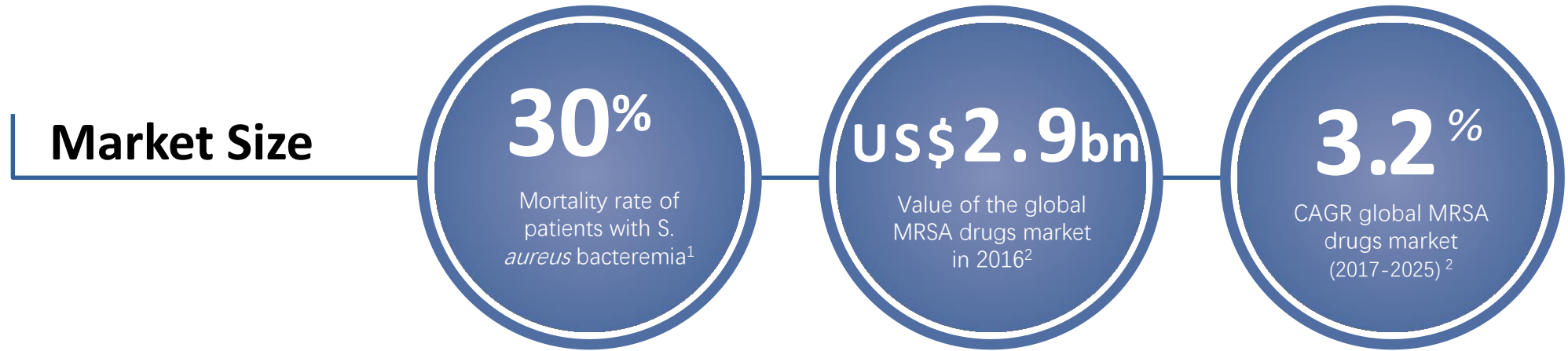
ALS-2/ALS-3

- Additional novel anti-virulent, non-bactericidal approach therapeutics targeting Gram-positive bacteria¹
- In discovery/lead optimization stage and generating good traction towards doing IND-enabling studies¹

1. Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing; 2. Influenza Antiviral Medications: Summary for Clinicians. CDC. <https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>; 3. Nat Biotechnol. 2010 Jun;28(6):600-5

ALS-4: Market Overview

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



Third-party infectious disease drugs or company-related mergers and acquisitions

- In 2014, Merck's acquisition of Cubist Pharmaceuticals, a large developer of antibiotics, for USD 8.4bn³
- In 2018, Roivant's licensing of Intron's Phase II asset for USD 667.5m in upfront and milestone payments⁴

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-deal-for-novel-anti-superbugs-biologic-sal200-300753307.html>

Market Approved Drugs for MRSA Infections

Frequently prescribed antibiotics for MRSA infections¹

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)	<ul style="list-style-type: none"> Currently, the most frequently prescribed antibiotic for MRSA suspected infections^{1,2} In clinical use for >60 years³, vancomycin-resistant <i>S. aureus</i> (VRSA) was first discovered in 2002⁴
Daptomycin (Merck)	Lipopeptide	ABSSSI, <i>S. aureus</i> bacteremia	IV	4-6mg/kg/day	USD 6,736-23,710 ⁵ (14-42 days)	<ul style="list-style-type: none"> In clinical use since 2003⁶ Daptomycin resistance described in <i>S. aureus</i> as early as 2006⁷
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)	<ul style="list-style-type: none"> In clinical use since 2003⁸. Entirely synthetic, not expected to develop clinical resistance⁹, however Linezolid resistance encountered clinically since 2010⁹
Ceftaroline fosamil (Actavis)	Cephalosporin	ABSSSI, CABP	IV	1.2g/day	USD 1,831-5,127 (5-14 days)	<ul style="list-style-type: none"> In clinical use since 2010¹⁰ Ceftaroline resistance encountered clinically since 2016¹¹
Tigecycline (Pfizer)	Glycycycline	ABSSSI, CABP, CIAI	IV	0.1-0.2mg/day	USD 1,888-4,977 (5-14 days)	<ul style="list-style-type: none"> In clinical use since 2005¹² 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)	<ul style="list-style-type: none"> In clinical use since 2009¹⁵ Vancomycin resistance leads to a 4-8x increase in televancin 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_21131s003_21132s003_ZyvoxTOC.cfm; 9. Pharmaceuticals (Basel). 2010 Jul; 3(7): 1988-2006; 10. FDA. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2010/200327orig1s000toc.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.

ALS-4: Addressing the Shortfall of Vancomycin

Vancomycin

- Generic antibiotic that is the most frequently prescribed for MRSA-suspected infections^{1,2}
- After >60 years³ 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 2002¹⁰
- 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 infections¹³. Therefore, for MRSA-suspected infections oral vancomycin is only indicated for the treatment of pseudomembranous colitis¹⁴

ALS-4: Stand Alone or as Combination Therapy with Antibiotics (e.g. Vancomycin)

- As a combination therapy believed to overcome the shortcomings of vancomycin¹⁵
- 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 vancomycin¹⁶

1st place, Innovation Academy Category, ICPI 2017



- Awarded to the Company's Hong Kong team, led by Dr. Richard KAO
- For the revolutionary concept of applying chemical genetics to tackle MRSA infection, which forms the scientific basis of ALS-2, ALS-3 and ALS-4

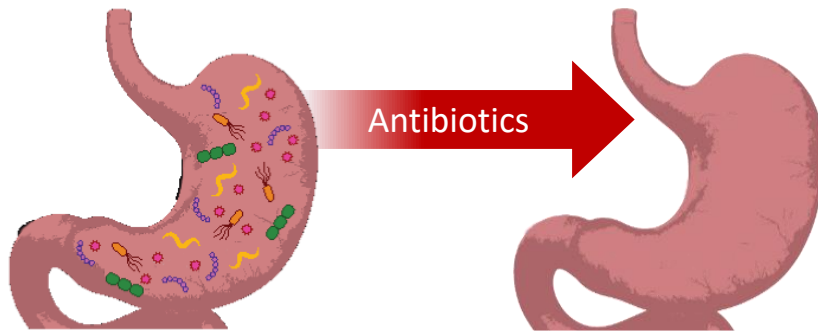
1. "Companies Take Aim at MRSA Infections" P T. 2016 Feb; 41(2): 126–128; 2. Clin Infect Dis. 2011 Feb 1;52(3):e18-55; 3. Clin Infect Dis. 2006 Jan 1;42 Suppl 1:S5-12; 4. Antimicrob Agents Chemother. 2008 Jan;52(1):192-7; 5. Clin Infect Dis. 2007 Jan 15;44(2):190-6; 6. Clin Infect Dis. 2007 Sep 1;45(5):601-8; 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; 11. J Infect. 2018 Dec;77(6):489-495; 12. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019-2018 Nov 18; 13. HealthJade, <https://healthjade.net/vancomycin/>; 14. Medscape, <https://reference.medscape.com/drug/firvanq-vancocin-vancomycin-342573>; 15. Combination Antibiotic Treatment of Serious Methicillin-Resistant Staphylococcus aureus Infections, <https://www.thieme-connect.com/products/ejournals/pdf/10.1055/s-0034-1396906.pdf>; 16. J Clin Microbiol. 2016 Mar; 54(3): 565–568

ALS-4: Value Proposition

Antibiotic

- Antibiotic resistance in *S. aureus* has been discovered in most prescribed antibiotics for MRSA¹
- Broad spectrum and indiscriminate²
- Commonly affect normal flora, may lead to superinfection in case of drug resistance³

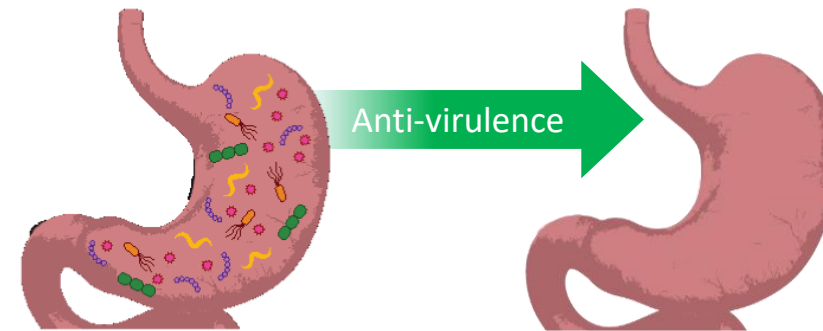
Indiscriminate clearance



Anti-virulence (ALS-4)

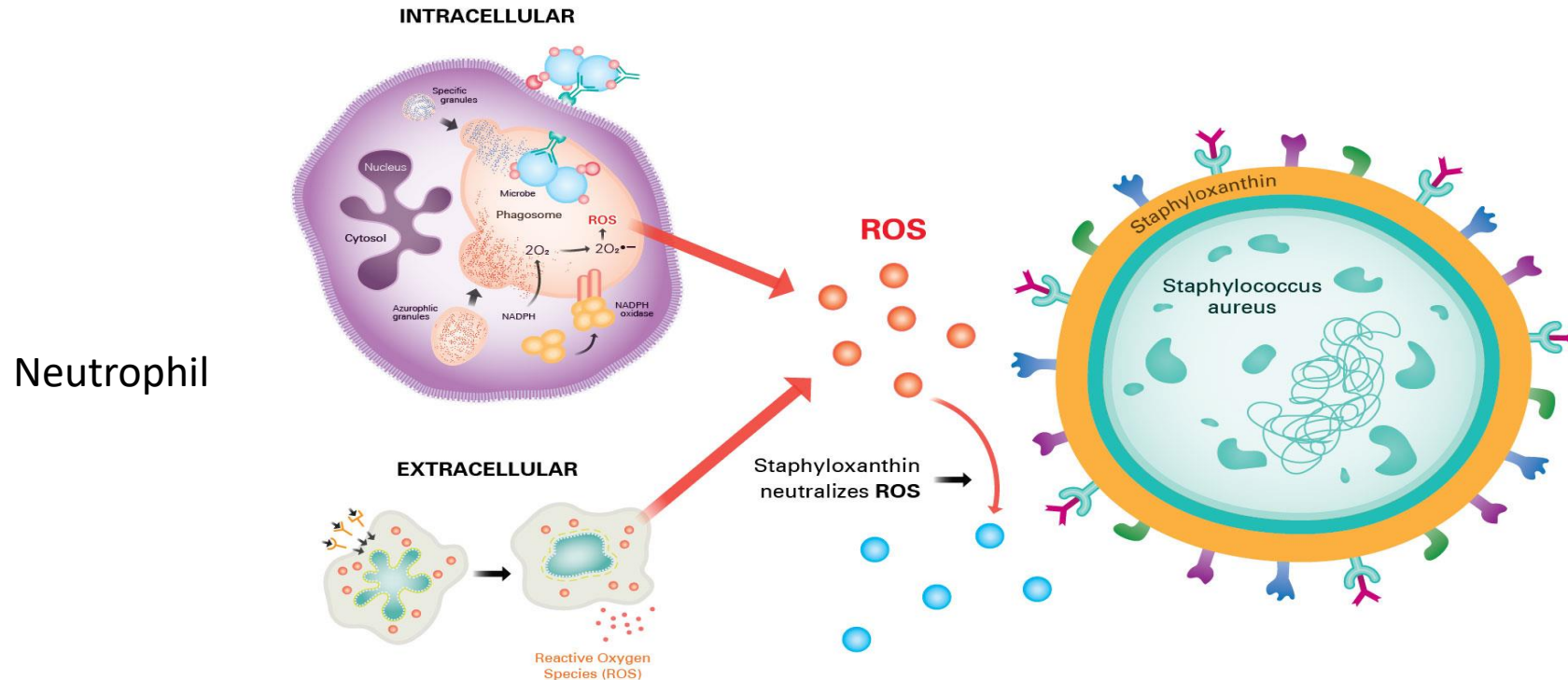
- ✓ Not bactericidal, potentially less selective pressure and much less likely for bacteria to develop resistance^{4,5}
- ✓ "Disarms" the bacteria by reducing pathogenicity^{4,5,6}
- ✓ Bacterial clearing is mediated by host immunity^{4,5}

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.

Mechanism of Action: Staphyloxanthin of Staphylococcus aureus

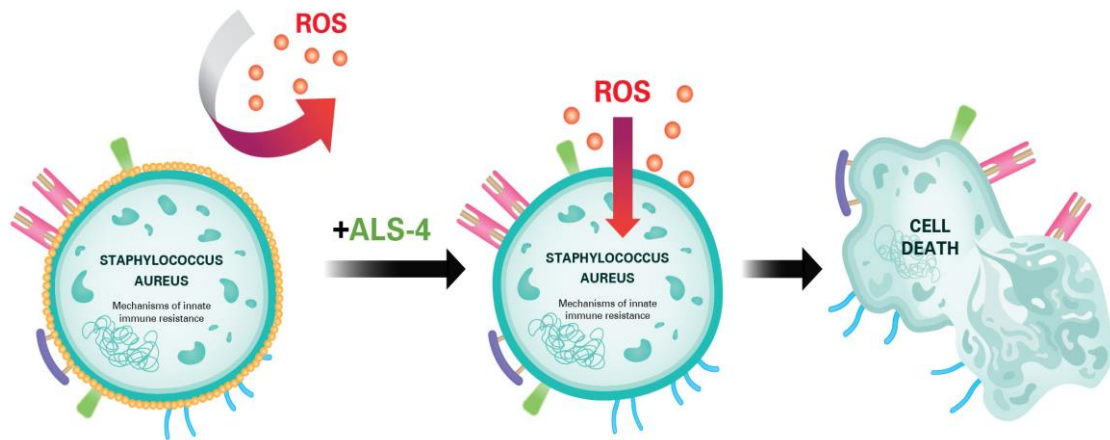


The above diagram summarizes the mechanism of action by Staphyloxanthin of Staphylococcus aureus:

- Neutrophils kill bacteria including Staphylococcus aureus intracellularly or extracellularly via Reactive Oxygen Species “ROS-oxygen radicals released by neutrophils trigger the subsequent bacterial damage processes”¹.
- To counteract, Staphyloxanthin protects the bacteria by serving as an anti-oxidant to neutralize the ROS secreted by neutrophils².

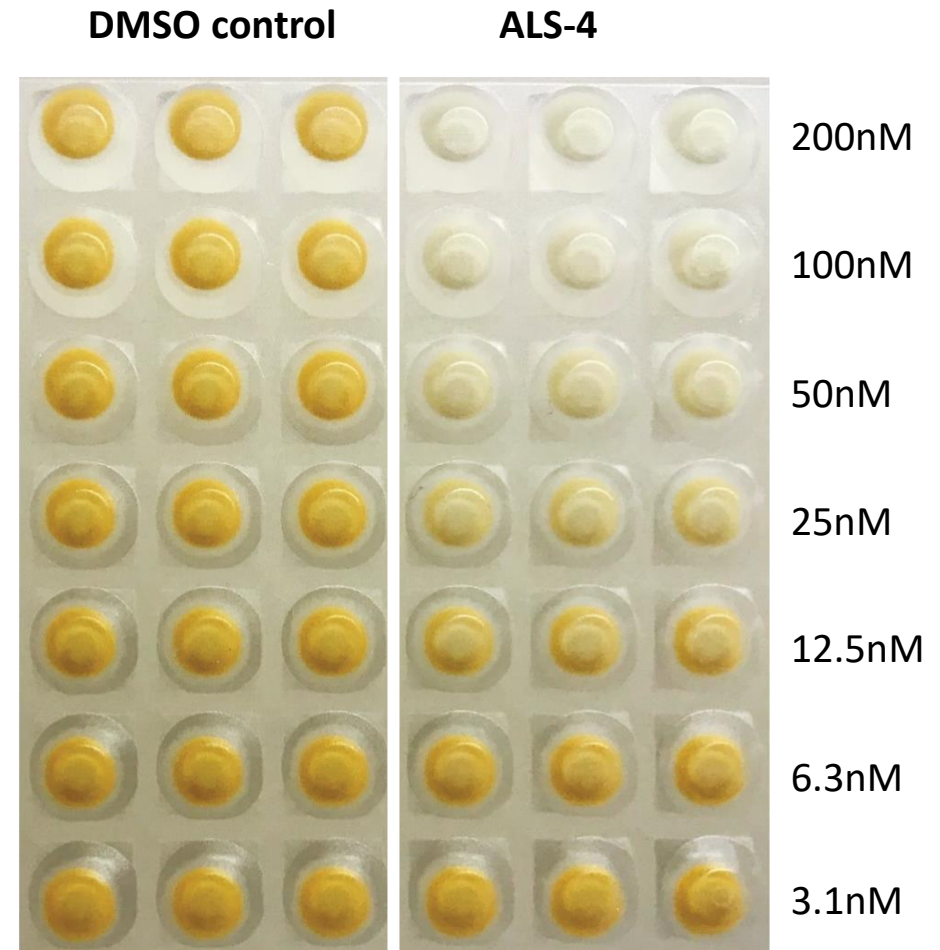
¹Annu Rev Immunol. 2005;23:197-223; ²mBio. 2017 Sep 5;8(5). pii: e01224-17

Mechanism of Action-ALS-4 on Staphyloxathin Synthesis



The above diagram summarizes our findings about how ALS-4 inhibits Staphyloxathin synthesis:

- ALS-4 inhibits a key enzyme in the biosynthesis of Staphyloxanthin with an $IC_{50} = 20nM$.
- In the absence of Staphyloxanthin, the bacteria become susceptible to damage by ROS, triggering the usual series of mechanisms by neutrophils that ultimately leads bacterial cell death.

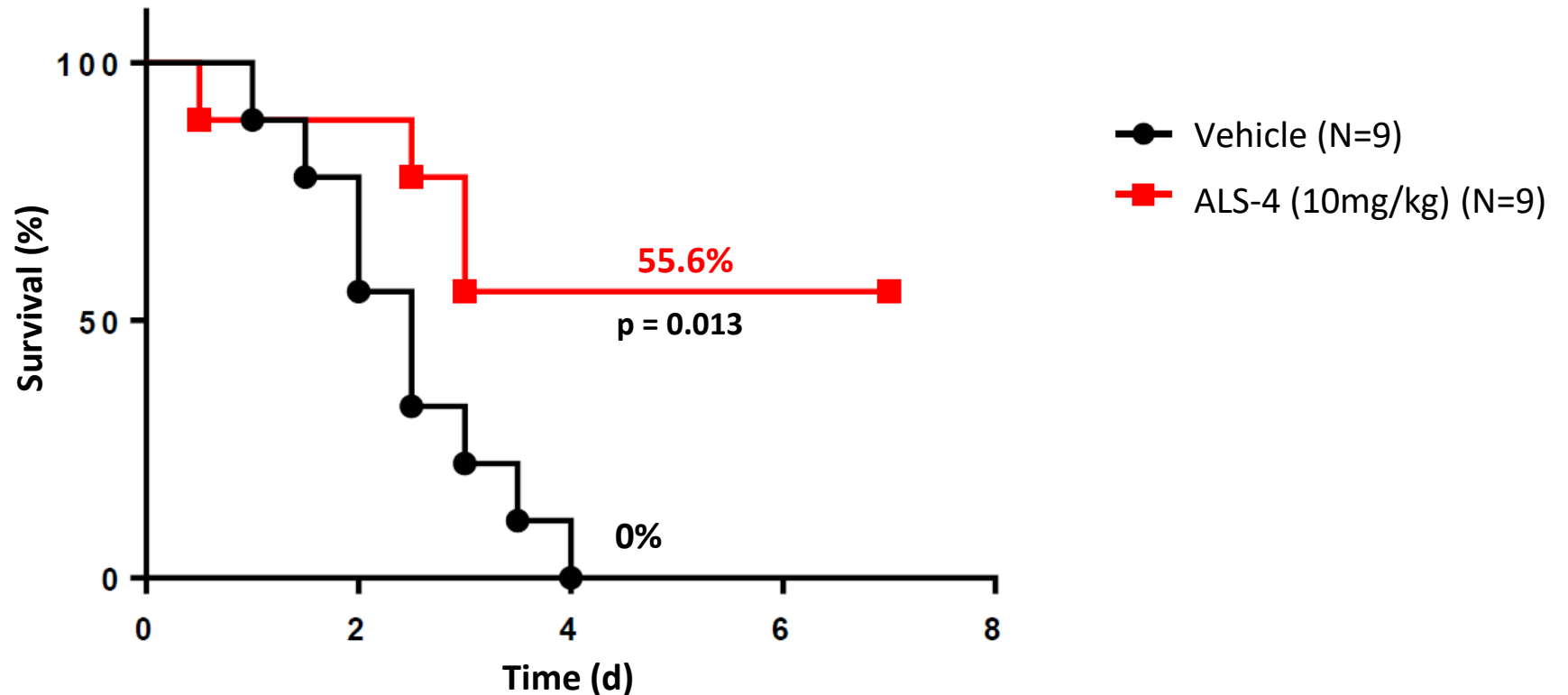


The description of ALS-4 and related conclusory statements on ALS-4 on this slide are based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing.

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

The combination of ALS-4's anti-virulence properties together with host immune system, efficacy is still superior.

The below in-vivo data includes rats infected with a lethal dose of MRSA USA300 in a bacteremia model.

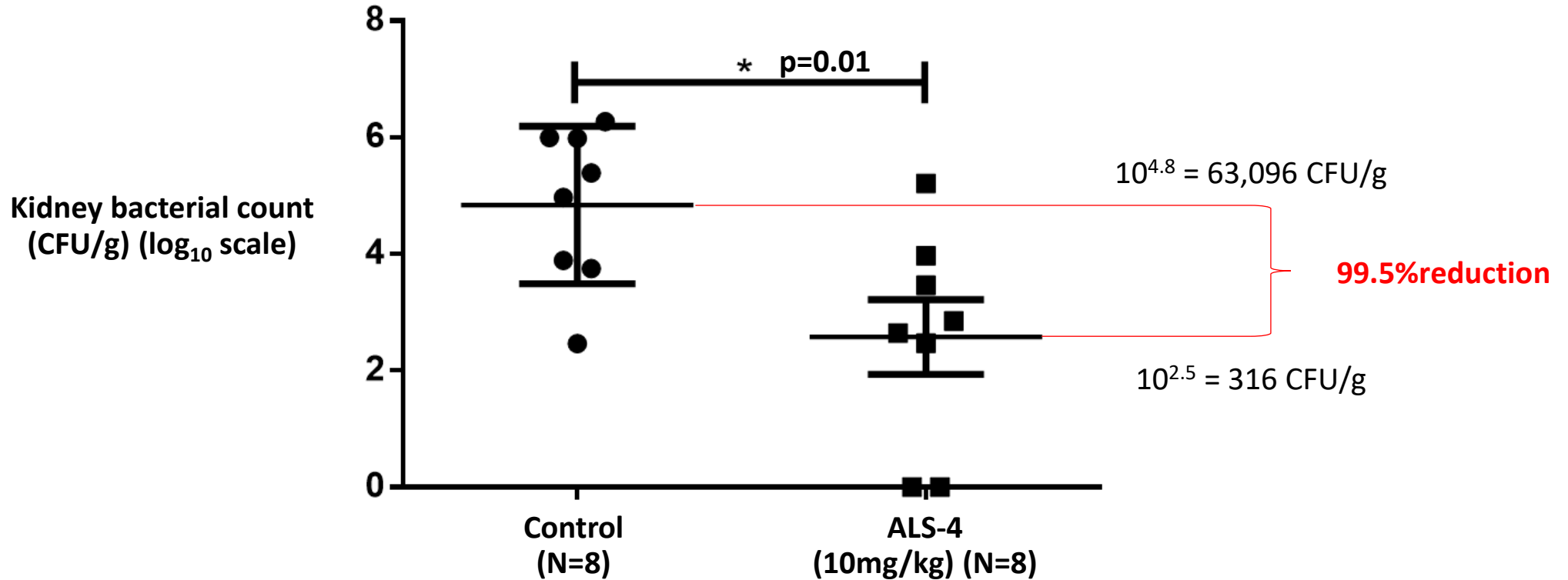


- A lethal dose (10^9 CFU) of MRSA was introduced through the tail vein
- ALS-4 was administered **orally** 30 minutes after infection for twice a day thereafter

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

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

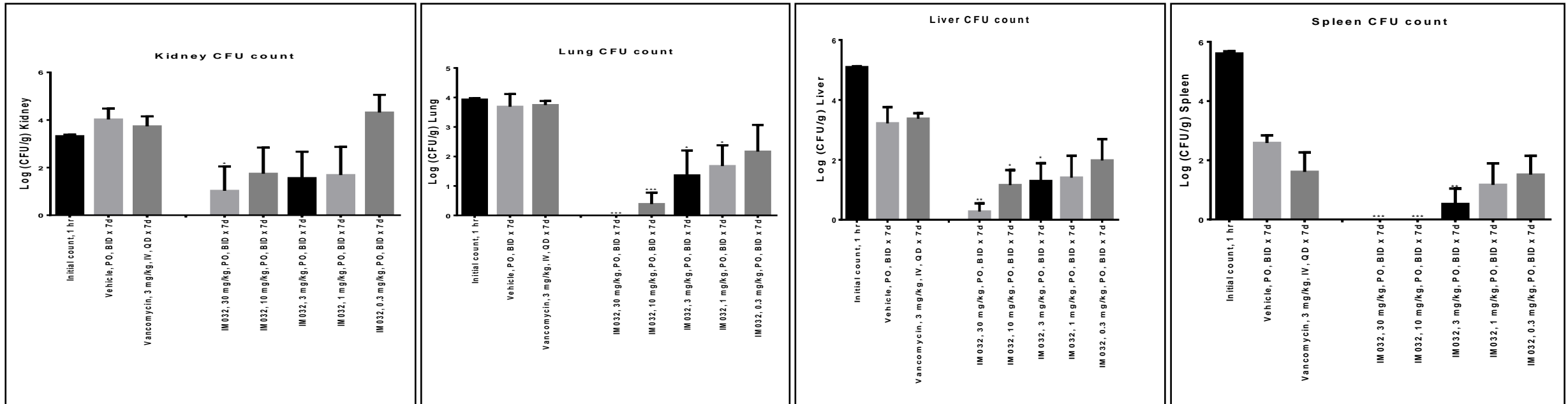


- Rats were challenged with a non-lethal dose (10^7 CFU) of MRSA through the tail vein
- In order to simulate a more realistic clinical scenario, treatment was introduced 14-days after infection, where ALS-4 was administered orally twice a day at 10mg/kg per animal

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

ALS-4: Oral administration in a MRSA non-lethal bacteraemia mouse model

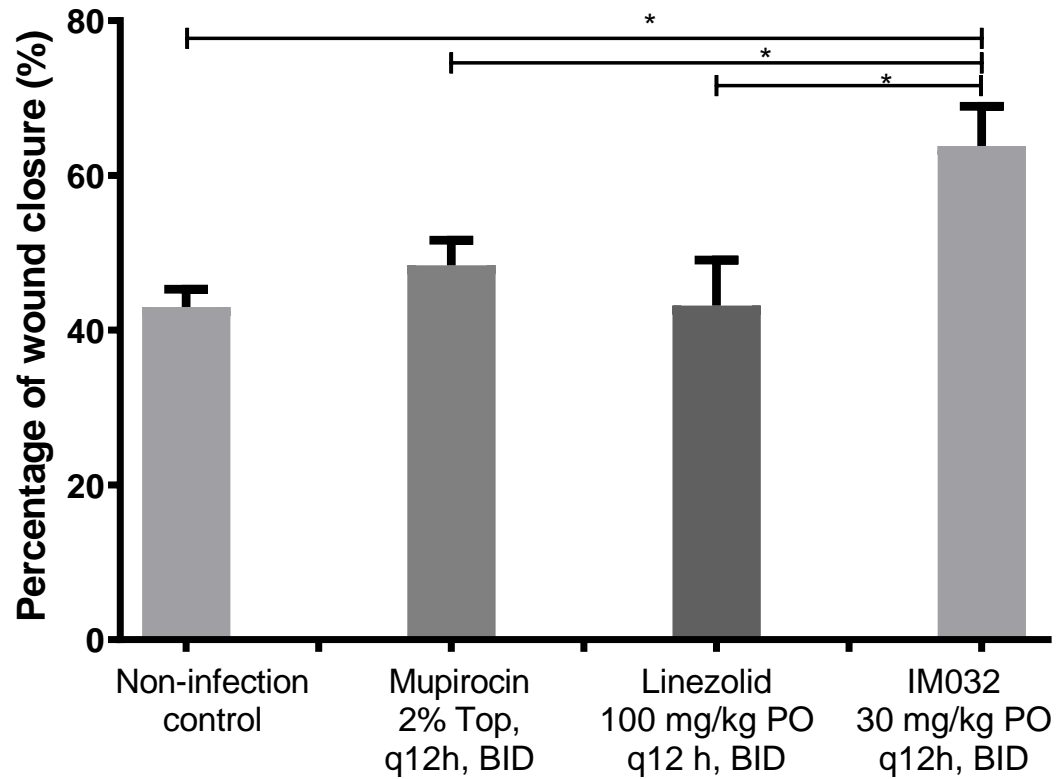
ALS-4 (Compound IM032) with increasing dose range shows a statistically significant reduction in bacteria count across major organs relative to vancomycin as a control.



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

ALS-4: Oral administration in a MRSA mouse skin wound infection model

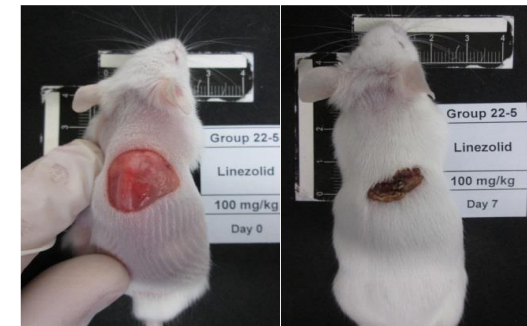
ALS-4 (Compound IM032) shows a statistically significant improvement in skin wound closure / healing.



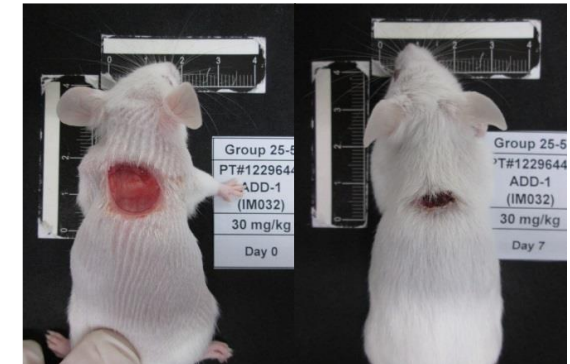
*unpaired t-test: $p < 0.05$



Day 0 Day 7
2% Mupirocin Topical BID x 7 Days



Day 0 Day 7
Linezolid 100mg/kg PO BID x 7 Days



Day 0 Day 7
ALS-4 30mg/kg PO BID x 7 Days

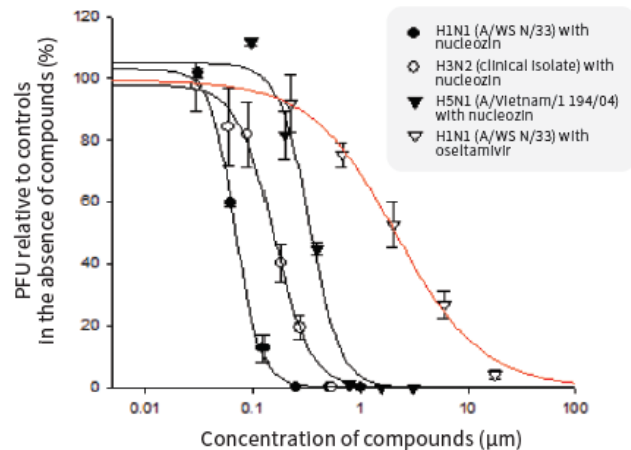
The results shown in this slide are based on Aptorum's internal (in vitro/in vivo) tests/experiments that have not been verified in clinical trials and/or third party testing

ALS-1: Targeting a Novel Druggable Target for Influenza A

ALS-1 inhibits influenza A nucleoprotein (NP)

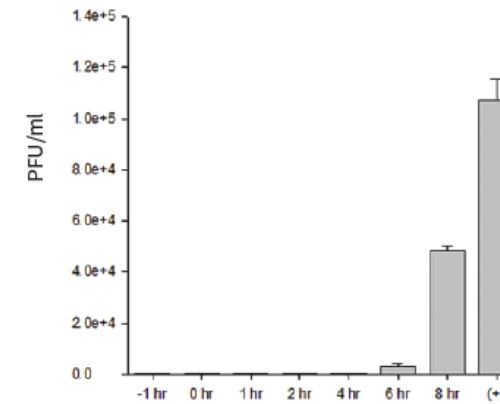
- NP is the most abundantly expressed protein during the course of an infection¹. Its primary function is to encapsidate the virus genome for RNA transcription, replication and packaging. It is also a key adapter molecule between virus and host processes¹
- ALS-1, by targeting NPs, acts upstream of Neuraminidase inhibitors such as Tamiflu, which target the last stage (budding) of the viral life cycle². This novel mechanism distinguishes ALS-1 from all other currently marketed antiviral drugs³

ALS-1 outperforms Tamiflu® (oseltamivir, in red) in vitro with a lower IC₅₀²



This figure shows the concentration dependence of ALS-1 in reducing the plaque-forming unit (pfu, a measure of number of infectious virus particulates) of human H1N1, H3N2 and H5N1 influenza viruses. The IC₅₀ for these viruses is between 0.1-1μM

ALS-1 inhibited viral growth up to 6 hours after infection, indicating antiviral activities reside on post-entry and post-nuclear events²



This figure shows that MDCK cells were infected and ALS-1 (1 μM) was added before infection (-1 h), at the time of infection (0 h) and at 1, 2, 4, 6 and 8 hour after infection as indicated. (+) control without ALS-1

1. J Gen Virol. 2002 Apr;83(Pt 4):723-34; 2. Nat Biotechnol. 2010 Jun;28(6):600-5; 3. Refer to the next slide "ALS-1: A Unique Antiviral Therapeutic Against Influenza A".

Claves Executive Summary

Human Microbiota

- We live in constant symbiosis with our gut bacteria, and dysbiosis can be the cause to numerous diseases¹

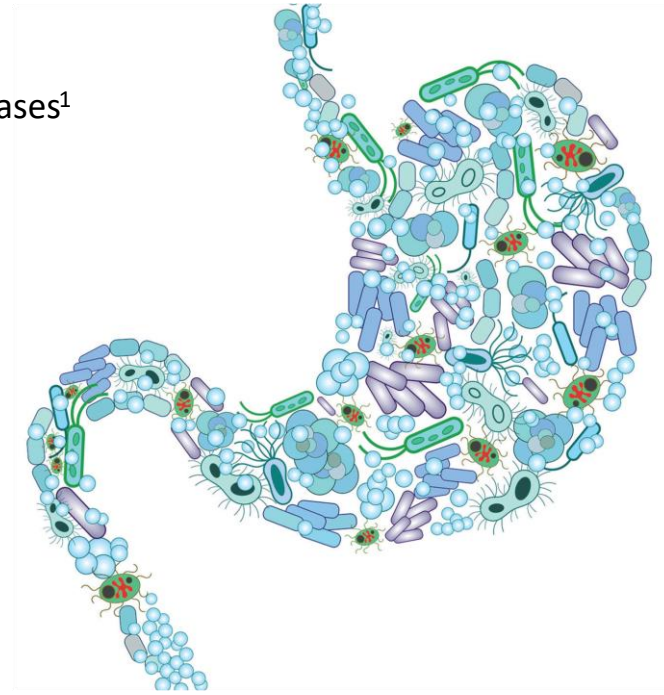
Claves Technology

- The Claves technology is designed to physically modulate the chemical signaling of diseases-causing microbiota²
- Highly scalable large molecule technology with over 70 potential therapeutic targets possible for development²
- Claves therapeutics bind target chemicals with high affinity and specificity, they are non-absorbable and expected to be free from any systemic toxicity^{2,3}
- Multiple candidates under development for various indications²

CLS-1: Lead Program Targeting Obesity

- CLS-1 is the lead program in the Claves projects, intended to target metabolites secreted by the microbiota linked to obesity²
- CLS-1 is also shown to modulate gut microbiota population linked to obesity^{2,3}
- CLS-1 achieves significant weight loss in a mouse model without affecting the gut mucosa, inflammation, and the functions of the liver and kidneys^{2,3}
- Non-absorbable nature of the Claves therapeutics may expedite traditional toxicological studies²

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; 4. Current understanding of dysbiosis in disease in human and animal models, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4838534/>



- 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 disease⁴**

Claves Platform and CLS-1: Value Proposition

CLS-1

- Identified specific microbiota metabolite linked to obesity
- Novel therapeutic that physically modulates microbiota metabolite
- Acts locally in the gut with high affinity and specificity
- Non-absorbable and is expected to be free from any systemic toxicity
- Significant weight loss in an animal study

Claves Platform

- Novel platform technology that can be customized to bind a wide variety of microbiota metabolites with high affinity and specificity
- Sustainable pipeline of drug candidates for treatment of multiple indications (see next page)

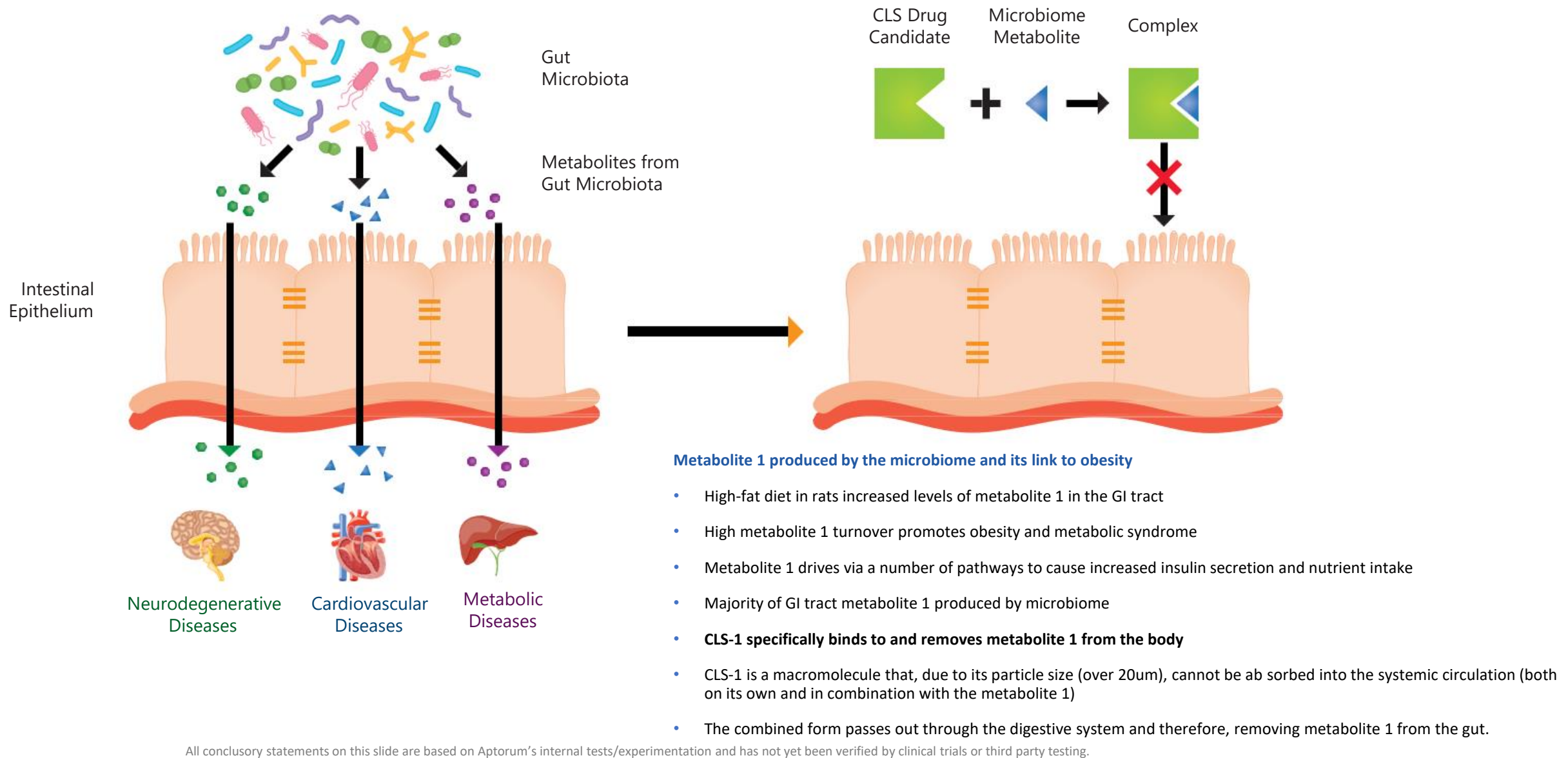


POSSIBLE INDICATIONS

SYSTEMIC DISEASES		DIGESTIVE DISEASES
Obesity	Renal failure	C. difficile infection
Diabetes	Depression	Colorectal cancer
Fatty liver	Parkinsonism	Inflammatory bowel disease
Cardiovascular diseases	Autistic spectrum disorder	Irritable bowel syndrome

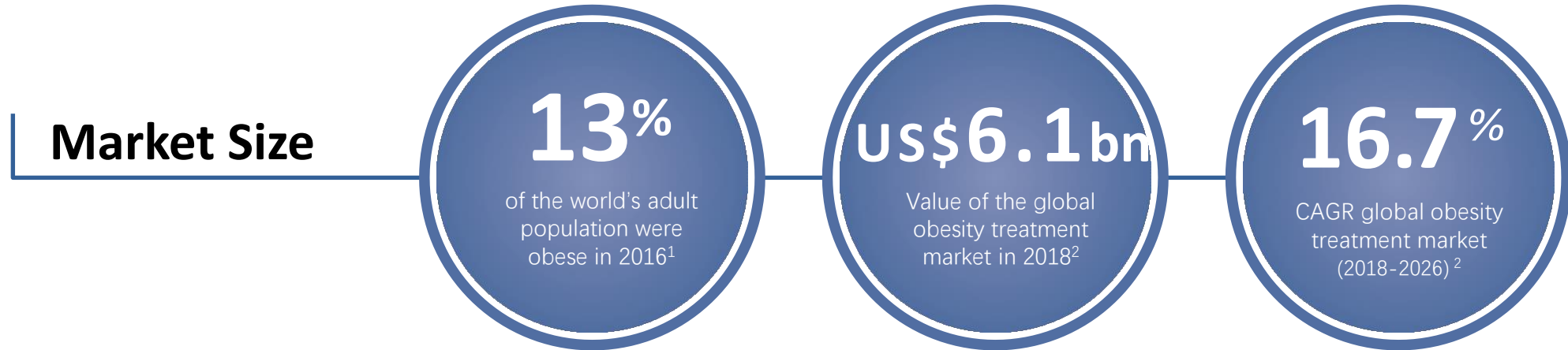
All conclusory statements on this slide are based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing.

Mechanism of Action



CLS-1: Market Overview

CLS-1: the lead program in the Claves projects, targeting obesity



Recent Deals in Obesity Treatment

- Boehringer Ingelheim committed up to USD 300m to work with Gubra on obesity treatments

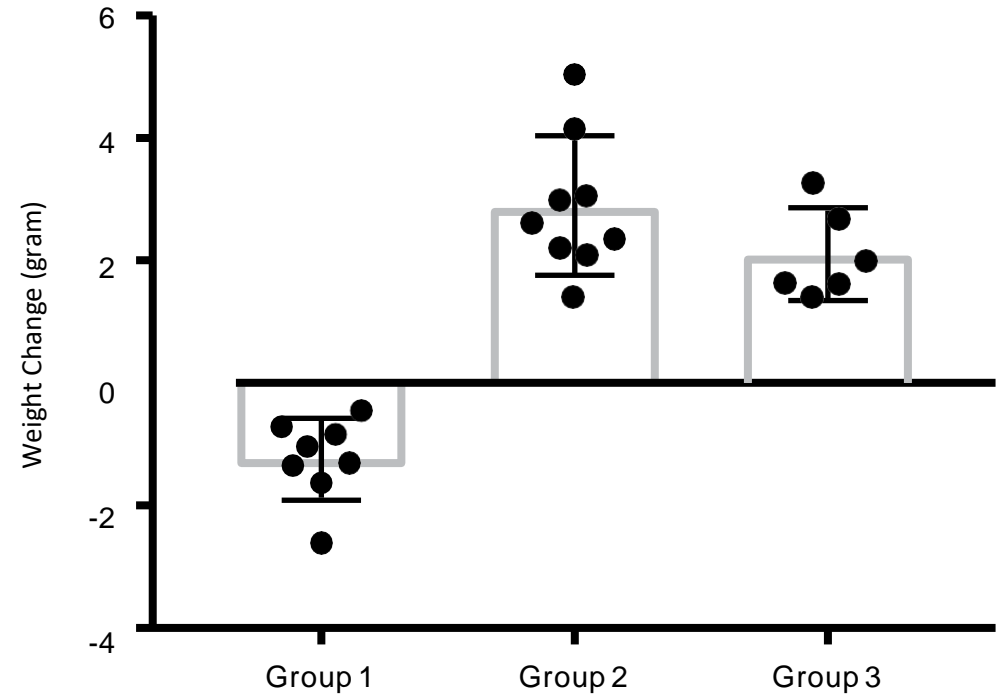
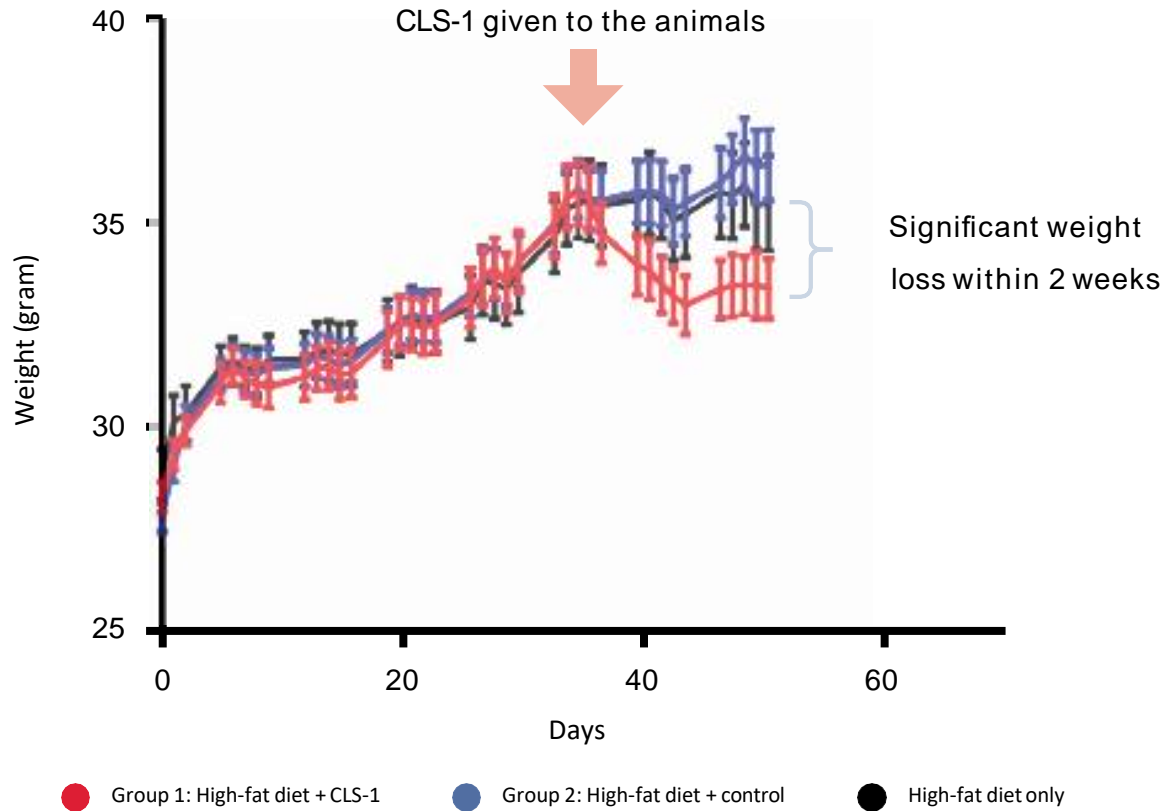
Competing Drugs

- CLS-1 is a drug candidate for obesity treatment that achieves its effect by modulating the chemical signaling of gut microbiota. There are no obesity treatment drugs on the market using similar mechanism³.

1. World Health Organization. Obesity and overweight fact sheet. <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>; 2. "Obesity Treatment Market To Reach USD 19.90 Billion By 2026 * (2019). Reports And Data. <https://www.globenewswire.com/news-release/2019/06/06/1865530/0/en/Obesity-Treatment-Market-To-Reach-USD-19-90-Billion-By-2026-Reports-And-Data.html>; 3. To the extent of our knowledge at the time of writing

CLS-1: Efficacy in a Mouse Model

CLS-1 treatment significantly reduces body weight in mice



The above data are based on Aptorum's internal tests and has not yet been verified by clinical trials or third party testing.

NLS-2: Executive Summary

NLS-2¹

- 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 H2 2020



Timeline²

→ Lead Projects → Other Candidates → Projected timeline

Projects	Modality	Target Customer	Formulation	Commercialisation
NativusWell [®] DOI (NLS-2)	Supplement	Women undergoing menopause	Targeted to launch in HK, UK, Europe in 2020 (registration ongoing)	

1. Lancet. 2003 Feb 8;361(9356):512-9; 2. Data available in this presentation

All conclusory statements on this slide are based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing.

The background of the page is a repeating pattern of blue, semi-transparent molecular models. These models consist of spheres of varying sizes connected by thin, light blue rods, representing atoms and chemical bonds. The models are scattered across the page, creating a scientific and technical atmosphere.

APPENDIX

Income Statement Summary (U.S. GAAP)¹

	Six months ended June 30, 2020	Six months ended June 30, 2019	Year ended December 31, 2019	Year ended December 31, 2018
	US\$	US\$	US\$	US\$
	(Unaudited)	(Unaudited)		
Revenue	327,273	239,792	535,166	383,450
Research and development expenses	(4,315,033)	(2,714,217)	(6,939,051)	(3,101,432)
General and administrative fees	(2,076,634)	(3,232,916)	(7,373,425)	(4,919,626)
Legal and professional fees	(1,540,304)	(2,008,774)	(3,405,705)	(1,811,770)
Net loss attributable to Aptorum Group Limited	(6,204,565)	(9,088,471)	(18,686,762)	(14,831,723)
Net loss per share – basic and diluted	(0.21)	(0.31)	(0.64)	(0.53)
Interest expense, net ²	(144,226)	(3,678,566)	(3,699,672)	(4,458,191)
Depreciation and amortization	(702,633)	(585,701)	(1,299,618)	(682,902)
Share based compensation expenses	(584,094)	(593,806)	(1,612,832)	-

Notes:

1. The following slide contains selected information for the Company's income statement. Please see the Company's filings made with the U.S. Securities and Exchange Commission for the Company's complete financial statements.

2. During the six months period ended June 30, 2019, and years ended December 31, 2019 and 2018, the net interest expenses included USD 3.1M, USD 3.1 M and USD 2.4 M, respectively, amortization of beneficial conversion feature which are non-cash items. No such amortization of beneficial conversion feature was incurred during the six months ended June 30, 2020.

Selected Balance Sheet Items (U.S. GAAP)¹

	June 30, 2020	December 31, 2019	December 31, 2018
	US\$	US\$	US\$
	(Unaudited)		
Cash, restricted cash and marketable securities	4,426,543	6,356,284	27,121,576
Total current assets	6,128,019	8,032,881	28,722,941
Property, plant and equipment, net	6,140,602	7,093,035	4,260,602
Total assets	23,309,075	23,954,218	45,074,640
Convertible debts	-	-	(10,107,306)
Warrant liabilities	-	-	(753,118)
Total current liabilities	(3,080,408)	(2,674,675)	(12,184,865)
Total liabilities	(5,786,690)	(9,102,466)	(12,328,738)
Total equity attributable to the shareholders of Aptorum Group Limited	19,837,917	16,361,208	33,114,435
Working Capital ^{2,3}	3,137,611	5,358,206	16,538,076

1. The following slide contains selected information for the Company's balance sheets. Please see the Company's filings made with the U.S. Securities and Exchange Commission for the Company's complete financial statements.

2. Current assets less current liabilities.

3. As at 30 June 2020, Aptorum Group also has undrawn credit facility of c. USD13m available as additional working capital.



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