APTORUM

Facilitating Life Science Innovations to Serve Unmet Medical Needs

CORPORATE PRESENTATION

NASDAQ GLOBAL MARKET: APM

Disclaimer

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Company Information

- Established in 2010, Aptorum is a clinical stage biopharmaceutical company dedicated to the discovery, development and commercialization of therapeutic assets to treat diseases with unmet medical needs, particularly in oncology, auto-immune and infectious diseases.
- **Business Strategy**: from Discovery to Phase II Proof-of-Concept (PoC).
- **Markets and Regulatory**: targeted for clinical and market approval by US FDA, China NMPA, Europe EMA and regulatory authorities in other major countries.
- **IPO**: listed on NASDAQ Global Market (ticker symbol: APM) since December 18, 2018 and cross-listed on Euronext Paris (ticker symbol: APM) since July 24, 2020.
- Company's principal executive office is based in London, United Kingdom
- Development of key products in partnership with North America based CROs (US and Canada), including GLP studies, GMP manufacturing and clinical trials coordination.
- Completion of Phase I clinical trials for 2 therapeutic drugs ALS-4 (MRSA) and SACT-1 (Neuroblastoma), Clinical validation phase for RPIDD (liquid biopsy infectious disease molecular diagnostics) and Commercialization stage for NLS-2 (Nativuswell), a Women's menopause supplement product.

Directors, Management and Significant Employees

Leadership

MR. Darren LUI
CEO and Executive Director

- Over 15 years in global capital market;
- Director of Structured Capital Markets at Barclays Capital.;
- Chartered Accountant (ICAS), Chartered Financial Analyst & 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.

MR. Martin SIU
Head of Finance

- Over 18 years in the field of audit;
- Supported over 8 listed companies and licensed corporations in Asia;
- Led a professional team to provide strategic consultancy services to sizable corporate clients;
- BBA (Hons) in Accounting at City University of Hong Kong

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

Non-Executive Director

MR. Ian HUEN

- Founder of Aptorum Group
- Over 18 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)

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

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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 Clinical and Discovery Programs

Clinical Stage Programs

Project	Candidate / Modality	Indication	Development Stage						
Acticule's Series			Target identification & Selection	Lead Discovery	Lead Optimization	IND (Or IND equivalent Enabling)	Clinical Trial Application Submission	Phase I	Phase II / III
ALS-4	Small molecule	Treatment of bacterial infections caused by Staphylococcus aureus including MRSA	→	→	→	→	→	→	
SACT's Series			Computational Discovery	*In Vitro* Validation	Existing PhI/II Clinical Safety Data[1]	*In Vivo* Validation	IND Preparation & Submission	Phase I	Phase Ib / IIa
SACT-1	Repurposed small molecule	Neuroblastoma and other potential cancer types	→	→	→	→	→	→	**(Orphan drug designation approved by FDA)**
RPIDD			Development and Experimentation		Product Optimization		Clinical validation & Pre-Commercialization preparation		Commercialization
RPIDD	Liquid biopsy rapid pathogen diagnostics	Pathogen molecular diagnostics	→	→	→	→	→		

Project	Modality	Target Customer	Formulation	Commercialization and Distribution
NativusWell® DOI (NLS-2)[2]	Dietary Supplement	Women undergoing menopause	→	→

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. Commercialization in the UK, Hong Kong and EU in 2022. Targeted for US in 2023 subject to registration.

Discovery Stage Programs

Project	Candidate / Modality	Indication	Development Stage
SACT's Series			Computational Discovery → *In Vitro* Validation → Existing PhI/II Clinical Safety Data[1] → *In Vivo* Validation → IND Preparation & Submission → Phase I → Phase Ib / IIa
SACT - COV19	Repurposed small molecule	Coronavirus Disease 2019 (COVID-19)	
SACT-2	Repurposed small molecule	To be disclosed	
SACT-3	Repurposed small molecule	To be disclosed	
Acticule's Series			Target identification & Selection → Lead Discovery → Lead Optimization → IND (Or IND equivalent Enabling) → Clinical Trial Application Submission → Phase I → Phase II / III
ALS-1	Small molecule	Treatment of viral infections caused by influenza virus A	
ALS-2/3	Small molecule	Treatment of gram+ve bacterial infections	
Discovery Stage			
DLS-1+2	Small molecule & Degraders	NSCLC with mutation	
DLS-3	Small molecule	Autoimmune	

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.

Executive Summary: Acticule Projects

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

MARKET SIZE

LEAD PROJECTS:

ALS-4

- Aptorum's lead program ALS-4 is an anti-virulent, non-bactericidal drug candidate for *Staphylococcus aureus* infections including MRSA[1]
- Unlike all major treatments currently on the market, ALS-4 is an orally administered anti-virulent molecule using a non-bactericidal approach[1] to potentially reduce significant risks of developing *S. aureus* resistance
- Phase I clinical study in North America completed in 2021.

ALS-1

- A unique antiviral therapeutic against Influenza A with a more upstream target that is shown to be more effective than Tamiflu® *in vitro*[1]
- Viral resistance to Tamiflu and other neuraminidase inhibitors has risen rapidly in recent years[2]
- Has a distinct mechanism of action compared with Tamiflu® and Xofluza®[1,3]

ALS-2/ALS-3

- Additional novel anti-virulent, non-bactericidal approach therapeutics targeting Gram-positive bacteria[1]
- In discovery/lead optimization stage and generating good traction towards doing IND-enabling studies[1]

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

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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 have been compounded since the discovery of vancomycin-resistant S. aureus (VRSA) in 2002[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[13]. Therefore, for MRSA-suspected infections oral vancomycin is only indicated for the treatment of pseudomembranous colitis[14]

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

- ALS-4 demonstrated efficacy both on a standalone basis and combination basis (with Vancomycin)[15,17]
- 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[16]

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; 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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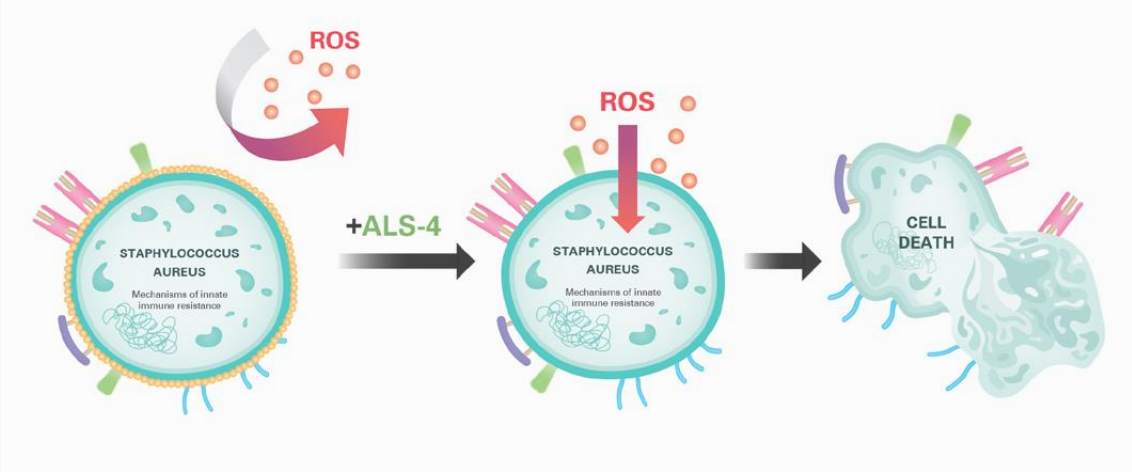
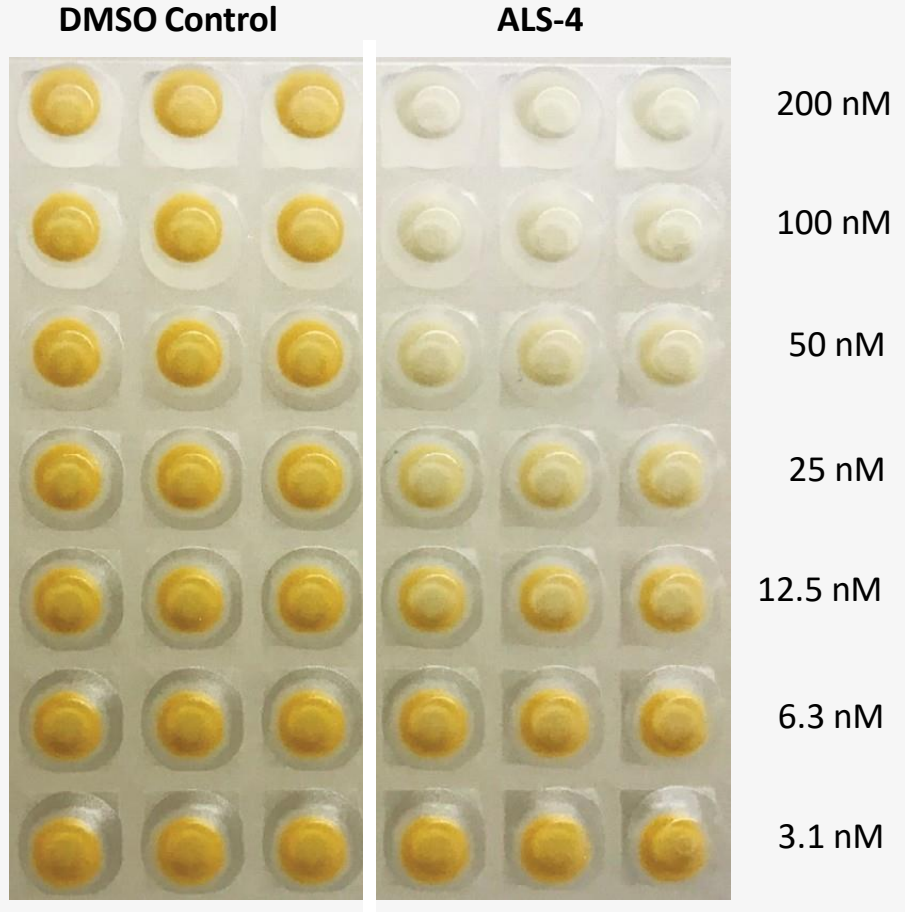
Mechanism of Action: ALS-4 on Staphyloxathin Synthesis



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

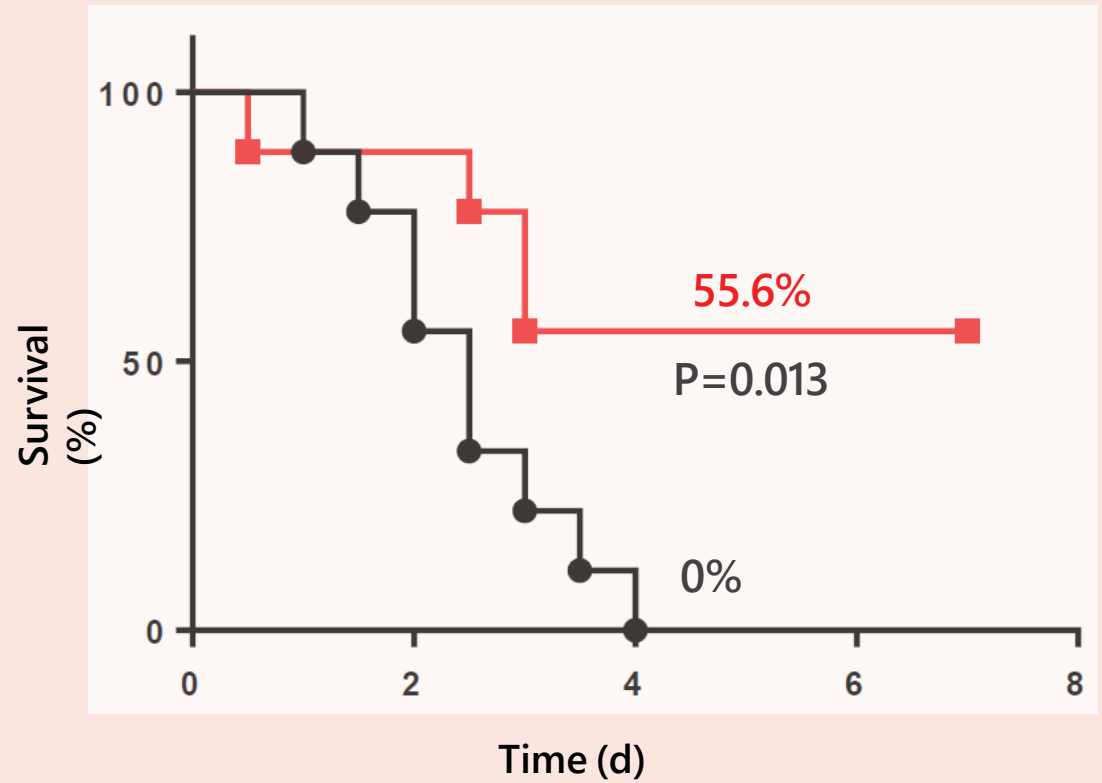
- ALS-4 inhibits a key enzyme in the biosynthesis of Staphyloxanthin with an IC_{50} = 20nM.
- In the absence of Staphyloxanthin, the bacteria become susceptible to damage by ROS, triggering the usual series of mechanisms by neutrophils that ultimately leads to bacterial cell death.



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

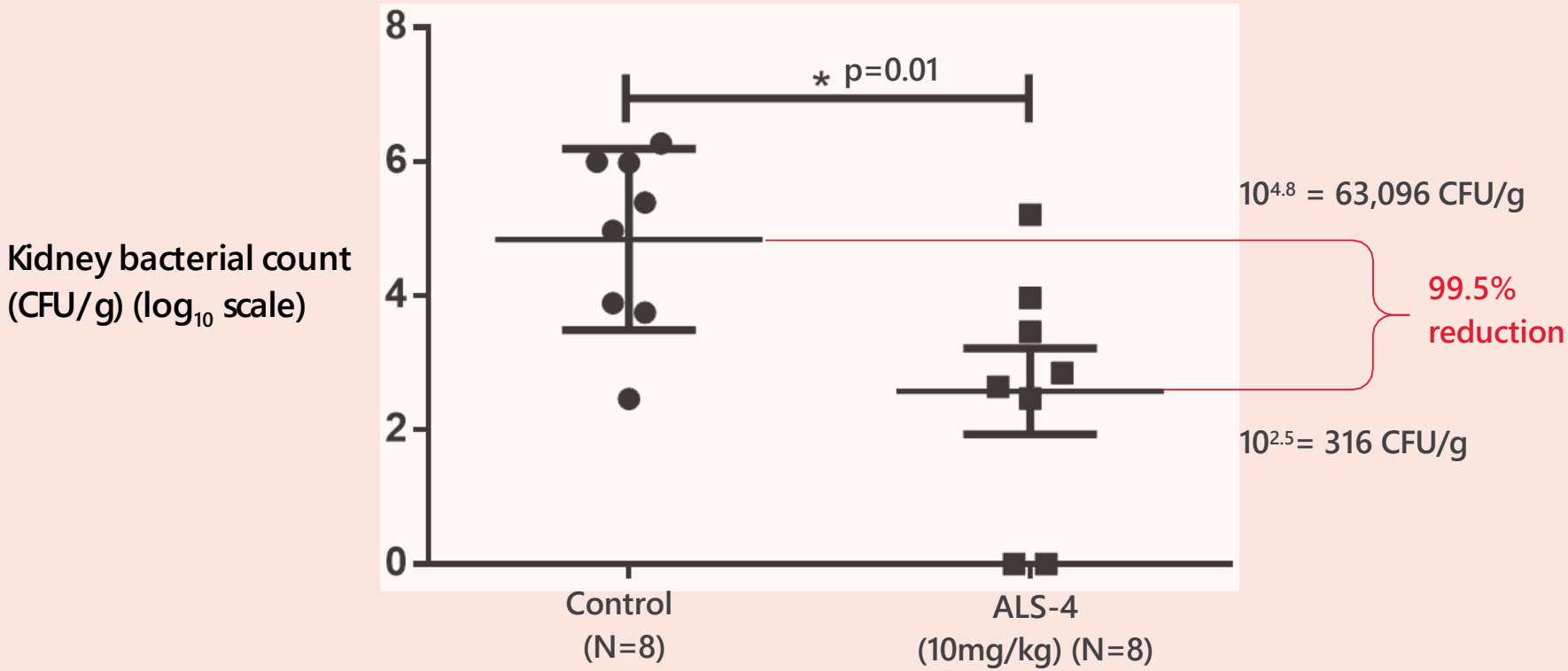
- A lethal dose (10^9 CFU) of MRSA was introduced through the tail vein
- ALS-4 was administered orally 30 minutes after infection for twice a day thereafter



ALS-4: Oral Formulation Treatment in a Non-Lethal Bacteremia Model

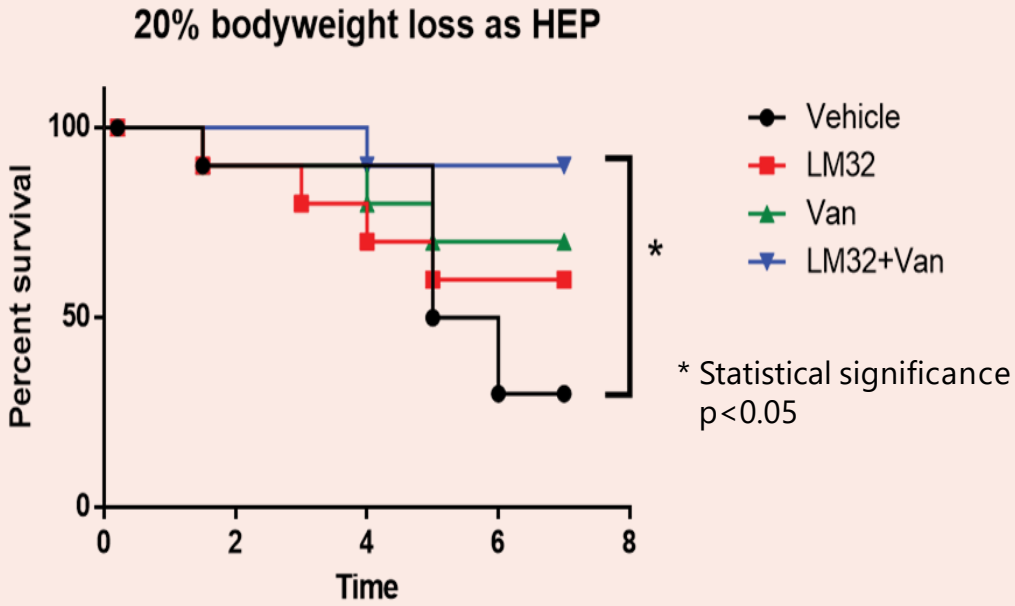
ALS-4 is shown to greatly reduce organ bacterial count in a bacteremia animal model.

- 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



ALS-4: Survival Study of ALS-4 in Combination of Vancomycin in a Mouse Model Infected with MRSA USA 300

IMMEDIATE TREATMENT POST LETHAL DOSE

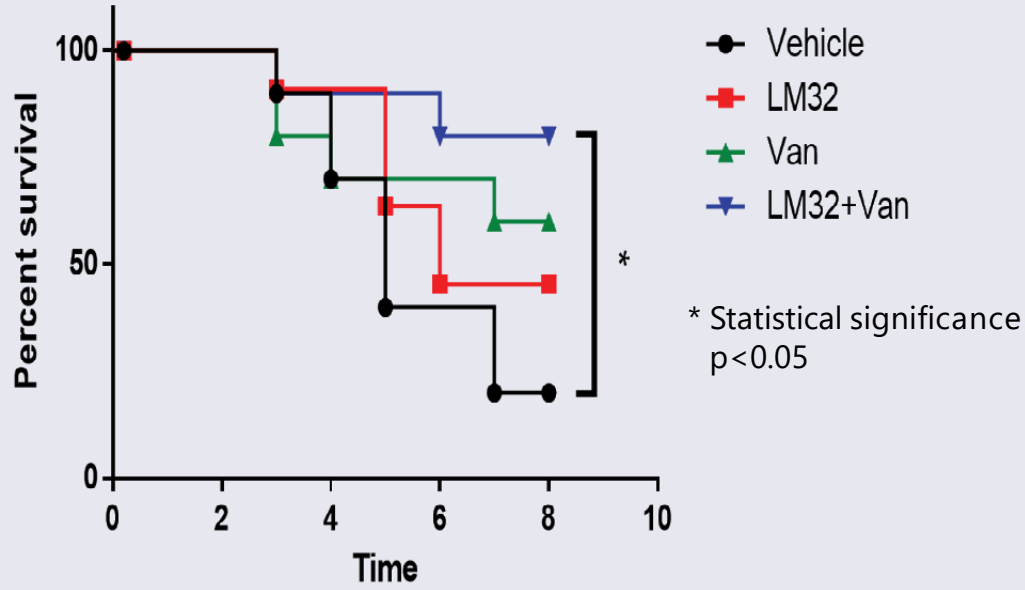


* Statistical significance $p<0.05$

N = 10, CFU per mouse is 6 x 10^7. All of the treatments were administrated through i.p. 15 hours after infection;

(a) Vehicle
(b) ALS-4: 4.5mg/kg
(c) Vancomycin: 4.5mg/kg
(d) Combo: 4.5mg/kg LM32+4.5mg/kg Vancomycin

DELAYED TREATMENT



* Statistical significance $p<0.05$

N = 10, CFU per mouse is $6x10^7$

ALS-4 at 6.75mg/kg/dose and treatment started 2 hrs post infection twice daily Vancomycin, 4.5 mg/kg/dose and treatment started 18 hrs after infection twice daily

ALS-4: Summary of Clinical Study

- **ALS-4's first-in-human Phase I trial is a randomized, double-blinded, placebo-controlled, single and multiple ascending dose study designed to evaluate safety, tolerability, and pharmacokinetics of orally administered ALS-4 in healthy male and female adult volunteers**
- **Clinical parts for both Single Ascending Dose (SAD) and Multiple Ascending Dose (MAD) have been completed. SAD from 25mg to 300mg, MAD from 50mg to 200mg twice daily, dosing for 14 days.**

  i. No human subjects were dropped out of the studies and there were no Serious Adverse Events (SAE) observed

  ii. No relevant clinical changes in respect of vital signs; ECG, clinical laboratory test results and physical examinations were observed compared to the relevant baseline

Lead Project #2 - SACT-1 (Neuroblastoma): Market Overview

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

MARKET SIZE

PREVALENCE

- ~700 cases of high risk neuroblastoma (NB) patients each year in the US[3] 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 population[4]

ORPHAN DRUG DESIGNATION[5]

- Neuroblastoma is a rare disease and drugs usually qualify for orphan designation subject to FDA
- Designated orphan drugs receive 7 years of market exclusivity in US and 10 years of marketing exclusivity in EU
- Patents on new indication and 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

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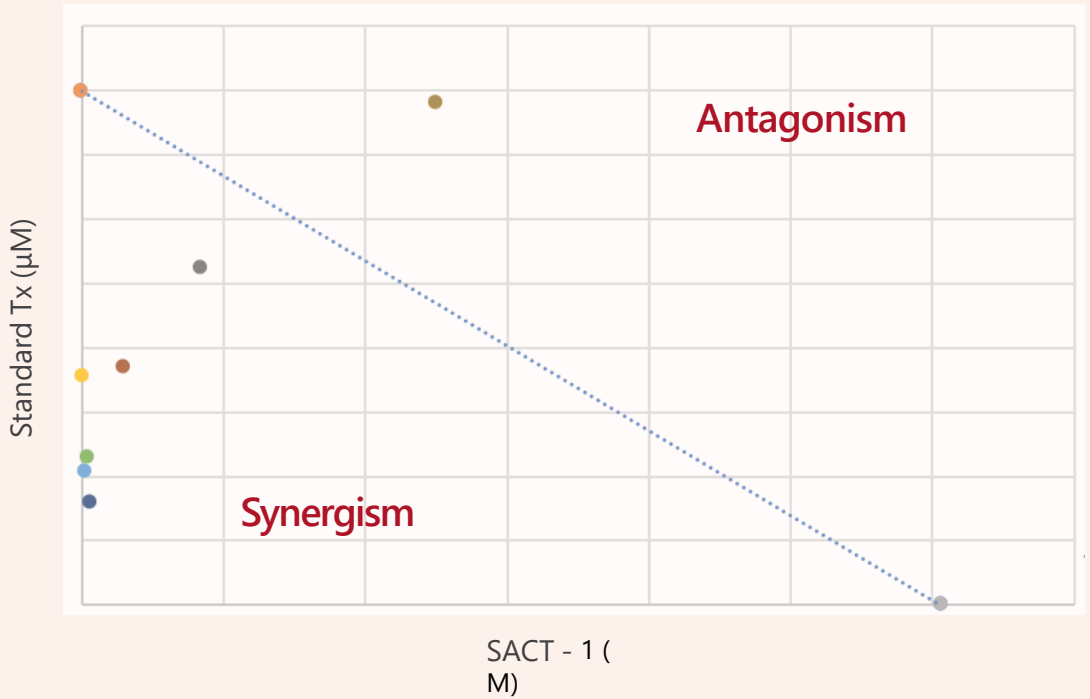
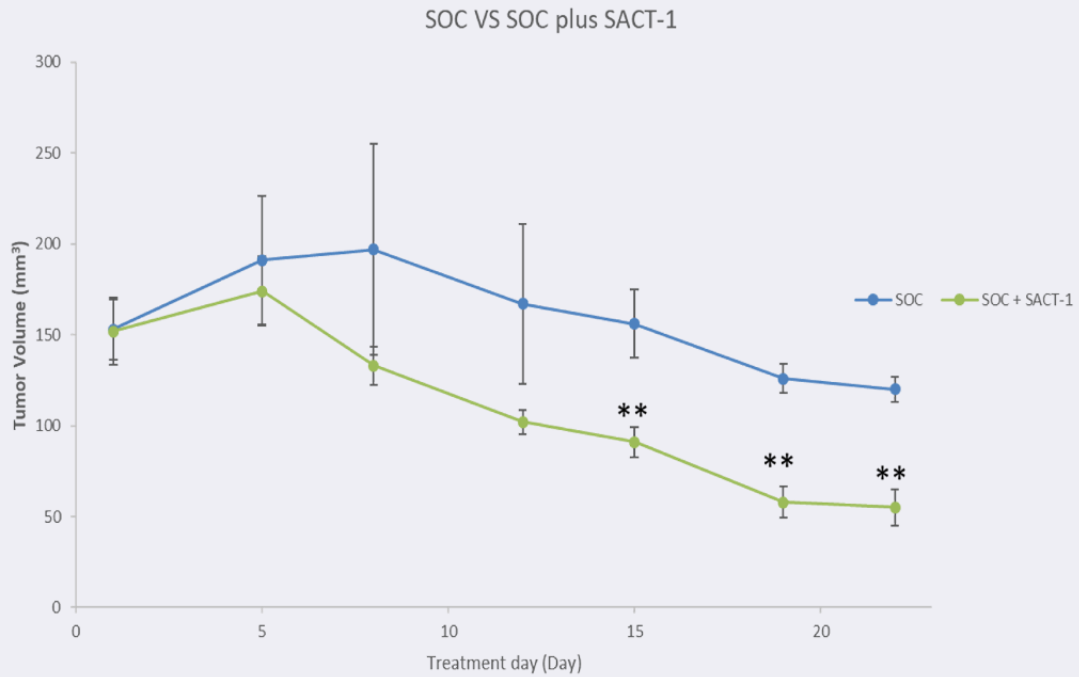
SACT-1: *In vivo* Study and Synergistic Effect with Chemotherapy

Synergistic effect observed for SACT-1 in combination with standard treatment in 2 different neuroblastoma cell lines, as seen in the isobologram



SACT-1 when combined with standard of care chemotherapy showed a statistically significant reduction in tumor 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)

SACT-1: Summary of Clinical Study

- **A repurposed small molecule drug discovered from our SMART-ACT® platform, which has the potential to help develop drugs with well-established safety profiles in a time- and cost-effective manner**

- **SACT-1 has gained FDA Orphan Drug Designation for the treatment of neuroblastoma, an orphan oncology disease predominantly in children.**

- **In our studies, SACT-1 has been shown to:**
  - Enhance DNA damage and tumor cell death *in vitro*
  - Promote neuroblastoma tumor reduction with standard of care chemotherapy *in vivo*
  - Exhibit similar anti-tumor efficacy *in vitro* across major cancer types, such as colorectal cancer and triple negative breast cancer

- **Further to the FDA approval of our IND application in 2021, Phase I study on bioavailability/ food effect has been completed. We are on track for submission for Phase Ib/IIa clinical trial in 2022.**

INFECTIOUS DISEASES OF UNKNOWN CAUSES REMAIN HIGH

Although hospitals have extensive laboratory testing for infectious diseases, it is estimated that aetiology in over 30% of infectious disease cases remained unknown[1].

Current most common clinical diagnostics for infectious disease: **Blood Culture**

- ✖ Cheap (average $50 per test) but inaccurate
- ✖ Labour intensive
- ✖ Analytically insensitive
- ✖ Trial and error approach and takes up to 5 days to culture at which point the patient may already have worsened in condition

Without accurate data, clinicians typically are unable to prescribe appropriate medication or can only apply broad spectrum antibiotics or antivirals that may have limited efficacy on the patient.

Other technology used in current clinical diagnosis for infectious disease :

Other diagnostic technologies including PCR is affordable (average $130 per test) but is biased to "known" specific pathogens only and unable to detect broad spectrum of both known and unknown pathogens. – It is not ready for **new emerging infectious diseases (e.g. COVID-19)**

CONCLUSION

A new technology for a rapid, cost-effective, sensitive and unbiased detection for ALL type of pathogens is needed

1. Crit Care Med 2012 40(12): 3277-3282

OUR SOLUTION: RPIDD (Rapid Pathogen Identification and Detection Device Technology)

Executive Summary

OVERVIEW

- **RPIDD**: Next-generation molecular-based diagnostics for "unbiased" detection of any foreign pathogens (virus, bacteria, fungus, parasites) in infected patients using DNA/RNA
- <24 hours turnaround time + cost effective
- Blood sample and adaptable to others (including swab)
- Collaboration with technology from Nobel prize winner Sydney Brenner / A*Star Sg
- Patented proprietary technology to prepare and enrich the pathogenic DNA/RNA and deplete the background human host DNA simultaneously + AI analysis

TARGET

- Next generation technology to transform diagnostic procedures for infectious diseases
- To become a first line of diagnostics in line or ahead of traditional methods

OUR TECHNOLOGY
(based on internal results)

- ✓ Lower costs: < USD$400 wholesale costs vs >USD$2000 NGS sequencing services
- ✓ Unbiased and broad range of pathogen detection
- ✓ <24 hour turnaround time
- ✓ Unbiased detection of a wide range of foreign pathogens

VS

EXISTING METHODS

- × **Blood culture**: slow (5 days) and inaccurate (c. 80% accuracy)
- × **PCR-based diagnosis**: biased only to specific pathogens (selective)
- × **NGS sequencing**: expensive (may cost as much as US$2,000 per test)

CAPABILITIES

Based on internal tests, our technology can detect:

- A full range of DNA/RNA viruses, bacteria, fungi, parasites, including coronavirus such as COVID19
- Pathogen genes that cause antibiotic/antimicrobial resistance (e.g. MRSA)
- Previously unknown and novel mutated pathogens (e.g. new virus)

Based on internal tests, our technology can:

- REDUCE diagnosis time to 24 hours or less (vs avg. 3 – 5 days using blood culture)
- REDUCE cost of existing NGS-based diagnosis by more than 50%
- TARGET TO ACHIEVE analytical specificity >99.99% per pathogen + sensitivity >95%
- "Personalized Medicine" approach to infections allowing clinicians to prescribe suitable and targeted treatments at an early stage of patient's admittance

	Blood Culture	PCR and Film Array	Existing NGS Technologies	Our Technology
Rapid	No (5 days)	Yes (1 day)	Yes (2 days)	Yes (1 day)
Detect unknown pathogens	No	No (biased & specific to pathogen)	Yes	Yes
Detect antibiotic resistance	Yes (limited)	Yes (limited)	Yes	Yes
Average Costs	USD$100-150 per culture / pathogen BUT no broad range detection; specific only		>USD$2,000 cost	Current <USD$400 cost (target USD$100)

RPIDD Aims to Shift mRDT Methods to First-line Diagnosis

But Why Is Molecular Rapid Diagnostic Testing (mRDT) Currently Not First-line?

Current commercially available mRDT are **limited in scope** for pathogens and antimicrobial resistance marker due to a **lack of primers/probes**[1].

Emerging pathogens and known pathogens with new mutations **may not be detected**.

If a medical laboratory develops its own test using mRDT, the **quality of the results will be significantly influenced by the manufacturing source** of the reagents used. This limits the flexibility and adds extra costs to the labs.

Therefore, a technology for a rapid, cost-effective, sensitive and unbiased detection for ALL types of pathogens is urgently needed: RPIDD

RPIDD is an **NGS based** (Next generation sequencing) molecular diagnostic technology.

Based on internal results, RPIDD employs an untargeted approach for **detection of all known and mutated pathogens**, as well as genes that cause antibiotic resistance in a single test. It provides valuable information in a timely manner and the appropriate antimicrobial therapy would be initiated as rapidly as possible.

RPIDD is a **scalable service integrated in hospitals** to support local and regional hospital services for blood-based rapid pathogen diagnostics.

1. Karumaa, S.; Karpanoja, P.; Sarkkinen, H. PCR Identification Of Bacteria In Blood Culture Does Not Fit The Daily Workflow Of A Routine Microbiology Laboratory. Journal of Clinical Microbiology 2011, 50 (3), 1031-1033.

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RPIDD Device Workflow Overview

PROPRIETARY DIAGNOSIS WORKFLOW (24 HOURS)

Proprietary method in DNA/RNA extraction

1

Biofluid collection

- **~0.5ml of blood** is used in the current generation of method

2 6 hrs

Sample extraction

- Host **DNA** depletion
- Microbial **DNA/RNA** enrichment
- One-pot DNA & RNA library preparation
- Both **targeted** and **untargeted** workflows

Proprietary method

3 8-14 hrs

Next-generation sequencing (NGS)

- Tested on Illumina chemistry (NexSeq, HiSeq, MiSeq and iSeq100)
- Easy adapted to Nanopore workflow
- Compatible with other faster next generation sequencing machines (e.g Nanopore)

4 <2 hrs

Secure cloud-based artificial intelligence driven bioinformatics analysis & report generation

- Refined workflow for rapid diagnosis of infectious disease

Proprietary Software

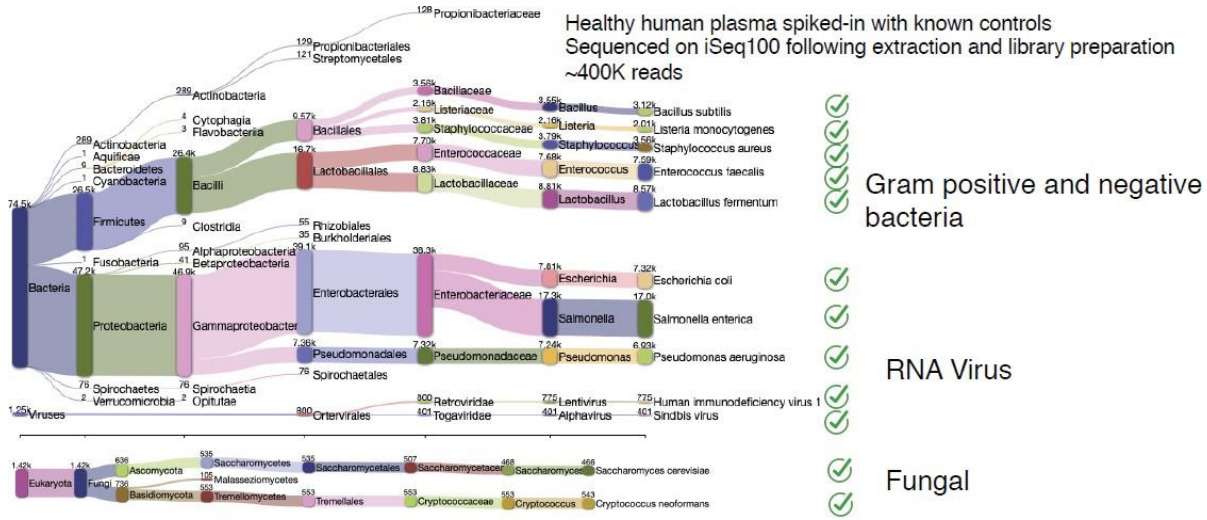
Analytical Performance: Sensitivity and Specificity

Based on internal results, RPIDD device detected organisms ranging from bacteria, RNA viruses and fungi in ONE TEST

Sensitivity	1.25 copies of DNA/RNA per µl plasma
Specificity	Controls: ZymoBIOMICS Microbial Community Standard, Lentivirus and Seracare AccuSpan recombinant virus

- **8** species of bacteria,
- **2** species of RNA virus, and
- **2** fungal samples were spiked into human plasma

All 12 species identified in ONE TEST



RPIDD : Summary of Clinical Validation

- **Sensitivity and specificity targeted to improve with further validation**
  - **Sensitivity**: Achieved 99.99%
  - **Specificity**: Achieved 90%, targeted to exceed 95% (subjected to ongoing clinical validation)

- **Clinical Validation in progress in Singapore**
  - 12 patients have been enrolled to the scheme
  - 53 reactions have been analysed as of 31 December 2021

- **Further clinical validation planned for 2022 including United States and Singapore.**

- **Further protocol updates to expand the use of RPIDD in different samples are progressing (e.g. Cerebrospinal fluid, nasal swab, saliva).**

NativusWell®: Executive Summary

NativusWell® (NLS-2)

- **Global menopause supplement market is projected to exceed US$50 billion by 2025[1]**
- **NativusWell® is a novel nutraceutical supplement targeting women who are between 45 and 65 years old and experiencing menopausal, perimenopausal and postmenopausal syndromes**
- **Commercialization in the UK, Hong Kong and EU in 2022. Targeted for US market in 2023 subject to registration.**
- **Consists of Chinese yam extract containing DOI, a novel non-hormonal, bioactive compound found to[2]:**
  - Significantly increase estradiol biosynthesis and aromatase expression in an *in vitro* granulosa cell model and in an *in vivo* preclinical model
  - Increase the apparent bone mineral density, bone volume fraction and trabecular thickness in an *in vivo* preclinical model
  - Act in a tissue-specific manner. DOI causes upregulation of aromatase, an enzyme involved in the production of estrogen, in the ovary but not in other tissues
  - Appear to be safe as indicated in both *in vitro* cellular and *in vivo* preclinical models

1. Grand View Research. Isoflavones Market Size Worth $50.06 Billion By 2025. https://www.grandviewresearch.com/press-release/global-isoflavones-market; 2. Sci. Rep. 5, 10179; doi: 10.1038/srep10179 (2015).
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.

APTORUM

APTORUM'S ONCOLOGY AND AUTOIMMUNE FOCUS IN 2022

- SACT-1
- DLS-1 + 2
- DLS-3

NEW AMBITION IN **2022**

- Work on further improving Cancer Treatment
- Lung cancer is by far the **leading cause of cancer death** among both men and women, making up almost 18% of all cancer deaths in 2020, with over 2 million new cases diagnosed globally[1].
- Targeted therapy (targeting EGFR, ALK and RTKs) is used in biomarker-positive, advanced NSCLC and showed significancy in improving progression free survival of patients[2].
- However, the use of targeted therapy faced limitations:
  - **Resistance** develops within months or years[3] (varied by the type of cancer and the targeted therapy used) → Next-Generation gene mutation inhibitors
  - Some cancer is **not responsive** to targeted treatments (e.g. RAS-mutated lunch cancer)[4] → Proteolysis-Targeting Chimera (PROTAC)

1. Data Source: GLOBOCAN 2020 2. Trends Mol Med. 2019 Mar; 25(3): 185–197. doi: 10.1016/j.molmed.2018.12.009 3. Chin J Cancer. 2015; 34: 43. doi: 10.1186/s40880-015-0047-1 3. Prog Tumor Res. 2014;41:62-77. doi: 10.1159/000355902. Epub 2014 Feb 17.

Drug resistance is a difficult obstacle to overcome

Resistance developed | Resistance developed | Resistance developed

Aptorum's Focus
(2) Targeted protein Degradation

Aptorum's Focus
(1) Next-generation inhibitor

	1st Generation	2nd Generation	3rd Generation	Clinical Stage Next generation
EGFR Mutation	Erlotinib Gefitinib Icotinib etc.	Afatinib Dacomitinib Neratinib EGFR mutated tumour developed mutation against ALK	Osimertinib Aumolertinib Furmonertinib etc.	BLU-945 EAI045 CH7233163 etc.
ALK Mutation	Crizotinib	Ceritinib Alectinib Brigatinib etc.	Lorlatinb Entrectinib	Repotrectinib Alkotinib Foritinib etc.

Aptorum's Focus

(3) Immunomodulator:
Targets inflammatory pathways which have been implicated in the tumorigenesis, angiogenesis, and metastasis of many cancer phenotypes. Can be used for auto-immune and infectious disease, including Lupus and Rheumatoid Arthritis

Source of Drug: https://adisinsight.springer.com/search

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