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UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

FORM 6-K

REPORT OF FOREIGN PRIVATE ISSUER  
PURSUANT TO RULE 13a-16 OR 15d-16  
UNDER THE SECURITIES EXCHANGE ACT OF 1934

For the month of January 2022

Commission File Number: 001-38764

**Aptorum Group Limited**

17 Hanover Square  
London W1S 1BN, United Kingdom  
(Address of principal executive office)

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F:

Form 20-F  Form 40-F

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1):

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7):

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We are filing this report to disclose a powerpoint presentation the Company will use during corporate presentations; such powerpoint presentation is incorporated herein by reference.

On January 10, 2022, we issued three press releases. A copy of each of the press releases is attached hereto as Exhibit 99.2, Exhibit 99.3 and Exhibit 99.4.

Neither this report nor the exhibits constitute an offer to sell, or the solicitation of an offer to buy our securities, nor shall there be any sale of our securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to the registration or qualification under the securities laws of any such state or jurisdiction.

The information in this Form 6-K, including the exhibits shall not be deemed to be "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and shall not be incorporated by reference into any filing under the Securities Act of 1933, as amended, except as shall be expressly set forth by specific reference in such filing.

This Form 6-K is hereby incorporated by reference into the registration statements of the Company on Form S-8 (Registration Number 333-232591) and Form F-3 (Registration Number 333-235819) and into each prospectus outstanding under the foregoing registration statements, to the extent not superseded by documents or reports subsequently filed or furnished by the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended.

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: January 10, 2022

**Aptorum Group Limited**

By: /s/ Sabrina Khan  
Sabrina Khan  
Chief Financial Officer

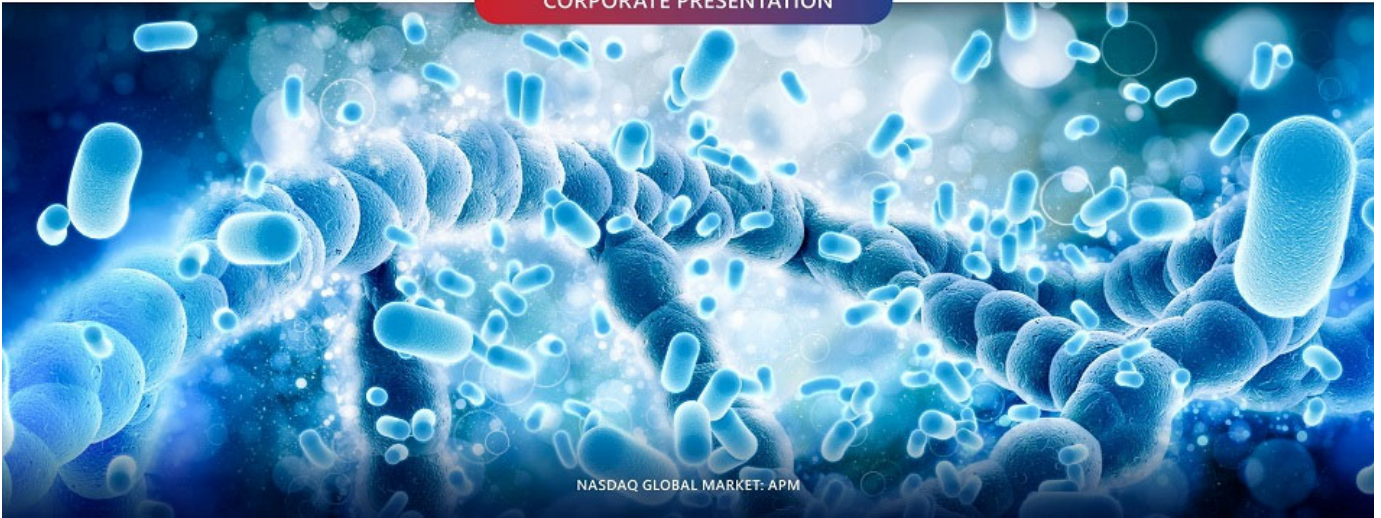
EXHIBIT INDEX

Exhibit No.	Description
99.1	<a href="#">PowerPoint Presentation</a>
99.2	<a href="#">Press Release</a>
99.3	<a href="#">Press Release</a>
99.4	<a href="#">Press Release</a>



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 and results may differ materially from those disclosed herein. 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.

### 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.

Leadership



**Mr. Ian HUEN**

Founder, Chief Executive Officer and Executive Director

- 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)



**MR. Darren LUI**

President 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.



**MISS Sabrina KHAN**

Chief Financial Officer

- Over 10 years serving US & Asian healthcare companies;
- Extensive experience in business development, restructuring, US & Asian IPO, and M&A deals;
- Chartered Accountant at Ernst & Young LLP;
- 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

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



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

Clinical Stage Programs

Project	Candidate / Modality	Indication	Development Stage						
			Target identification & Selection	Lead Discovery	Lead Optimization	IND (Or IND equivalent Enabling)	Clinical Trial Application Submission	Phase I	Phase II / III
<b>Acticure's Series</b>									
ALS-4	Small molecule	Treatment of bacterial infections caused by Staphylococcus aureus including MRSA							
<b>SACT's Series</b>			Computational Discovery	In Vitro Validation	Existing Phase I/II Clinical Safety Data <sup>1</sup>	In Vitro Validation	IND Preparation & Submission	Phase I	Phase IIb / IIIa
SACT-1	Repurposed small molecule	Neuroblastoma and other potential cancer types							
<b>RPIDD</b>			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) <sup>2</sup>	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						
			Computational Discovery	In Vitro Validation	Existing Phase I/II Clinical Safety Data <sup>1</sup>	In Vivo Validation	IND Preparation & Submission	Phase I	Phase II / III
<b>SACT's Series</b>									
SACT - COVID19	Repurposed small molecule	Coronavirus Disease 2019 (COVID-19)							
SACT-2	Repurposed small molecule	To be disclosed							
SACT-3	Repurposed small molecule	To be disclosed							
<b>Acticle's Series</b>			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							
<b>Discovery Stage</b>									
DLS-1+2	Small molecule & Degraders	NSCLC with mutation							
DLS-3	Small molecule	Autoimmune							

<sup>1</sup>. 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.

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



**LEAD PROJECTS:**

**ALS-4**

- Aptorum's lead program ALS-4 is an anti-virulent, non-bactericidal drug candidate for *Staphylococcus aureus* infections including MRSA<sup>1</sup>
- Unlike all major treatments currently on the market, ALS-4 is an orally administered anti-virulent molecule using a non-bactericidal approach<sup>1</sup> 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*<sup>1</sup>
- Viral resistance to Tamiflu and other neuraminidase inhibitors has risen rapidly in recent years<sup>2</sup>
- Has a distinct mechanism of action compared with Tamiflu® and Xofluza®<sup>1,3</sup>

**ALS-2/ALS-3**

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

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

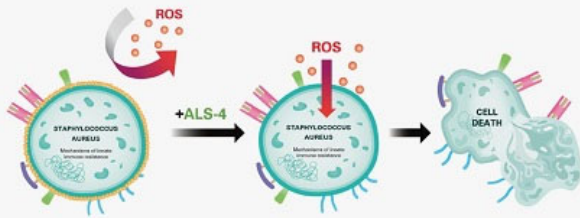
## Vancomycin

- Generic antibiotic that is the most frequently prescribed for MRSA-suspected infections<sup>1,2</sup>
- After >60 years<sup>3</sup> 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<sup>4,5,6,7,8,9</sup>
- The shortcomings of Vancomycin have been compounded since the discovery of vancomycin-resistant *S. aureus* (VRSA) in 2002<sup>10</sup>
- Vancomycin is not orally bioavailable and must be administered intravenously in order to treat systemic infections<sup>11,12</sup>. Oral vancomycin is only effective for treating local intestinal infections<sup>13</sup>. Therefore, for MRSA-suspected infections oral vancomycin is only indicated for the treatment of pseudomembranous colitis<sup>14</sup>

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

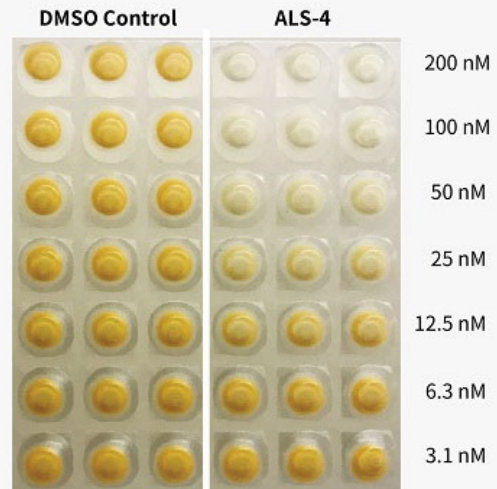
- ALS-4 demonstrated efficacy both on a standalone basis and combination basis (with Vancomycin)<sup>15,17</sup>
- ALS-4 can potentially complement other bactericidal antibiotics as well, therefore ALS-4 is not a direct competitor of antibiotics
- Synergistic effects of other drugs with vancomycin against MRSA has been demonstrated previously with  $\beta$ -lactam antibiotics and vancomycin<sup>16</sup>

1. "Companies Take Aim at MRSA Infections" P T, 2016 Feb; 41(2): 126-128; 2. Clin Infect Dis. 2011 Feb 15;2(3):e18-55; 3. Clin Infect Dis. 2006 Jan 1;42 Suppl 1:55-12; 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 3:5191-5; 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](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/irvanq-vanocoon-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.



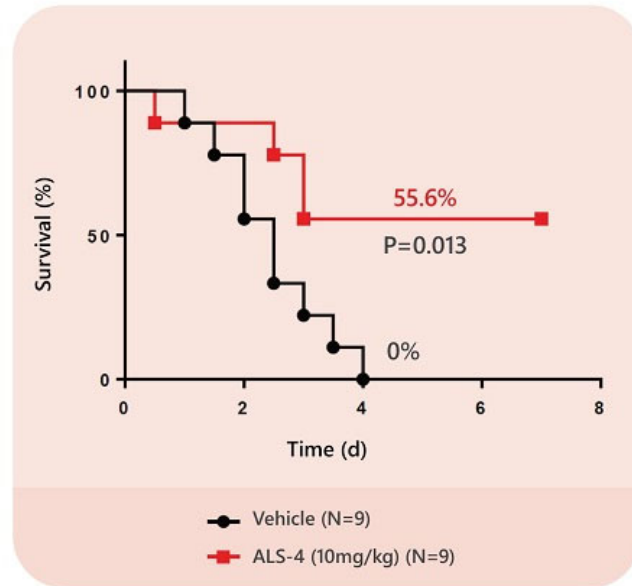
The above diagram summarizes our findings about how ALS-4 inhibits Staphyloxanthin synthesis:

- 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.



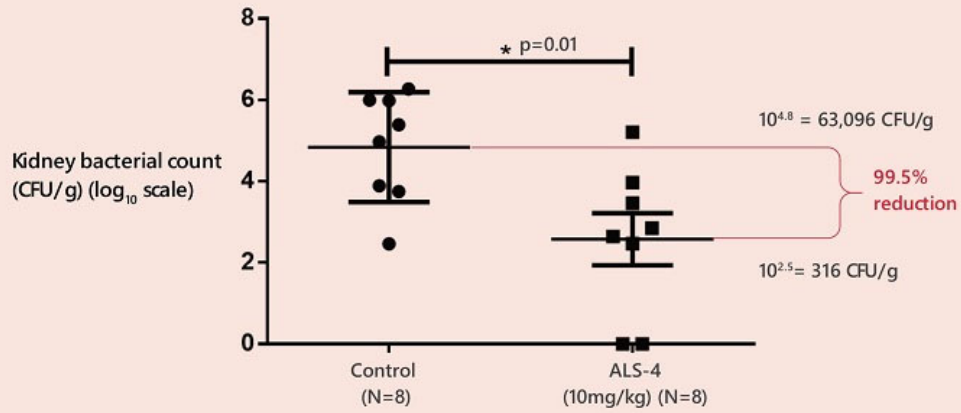
The combination of ALS-4's anti-virulence properties together with host immune system, efficacy is still superior. The *in vivo* data includes rats infected with a lethal dose of MRSA USA300 in a bacteremia model.

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

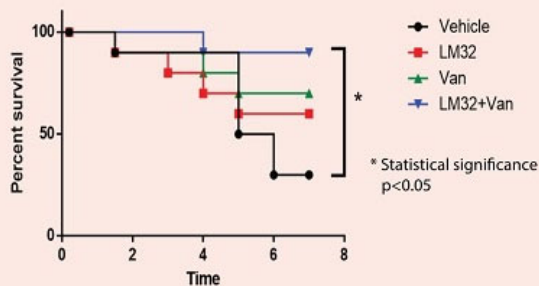
- Rats were challenged with a non-lethal dose ( $10^7$  CFU) of MRSA through the tail vein
- In order to simulate a more realistic clinical scenario, treatment was introduced 14-days after infection, where ALS-4 was administered orally twice a day at 10mg/kg per animal





**IMMEDIATE TREATMENT POST LETHAL DOSE**

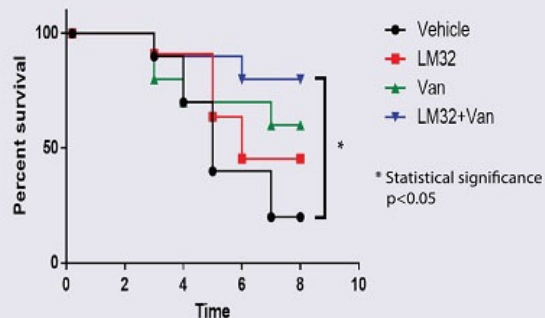
20% bodyweight loss as HEP



N = 10, CFU per mouse is  $6 \times 10^7$ . All of the treatments were administered 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**

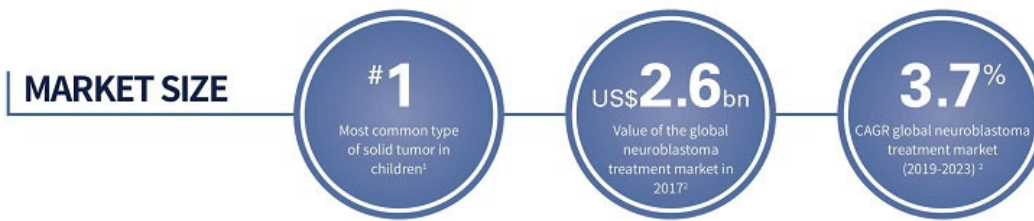


N = 10, CFU per mouse is  $6 \times 10^7$

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'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

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



**PREVALENCE**

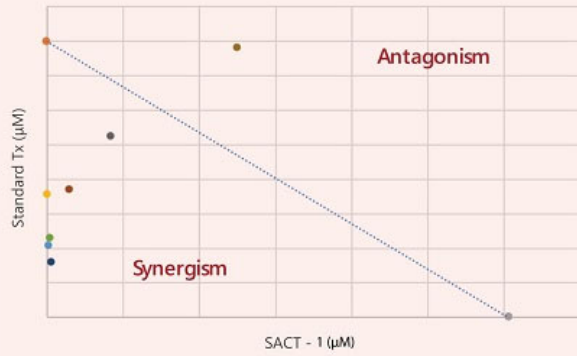
- ~700 cases of high risk neuroblastoma (NB) patients each year in the US<sup>3</sup> and we estimated EU has 1.5x those cases, c. 1050 high risk NB patients per year
- Accounts for ~15% of all cancer-related deaths in the pediatric population<sup>4</sup>

**ORPHAN DRUG DESIGNATION<sup>5</sup>**

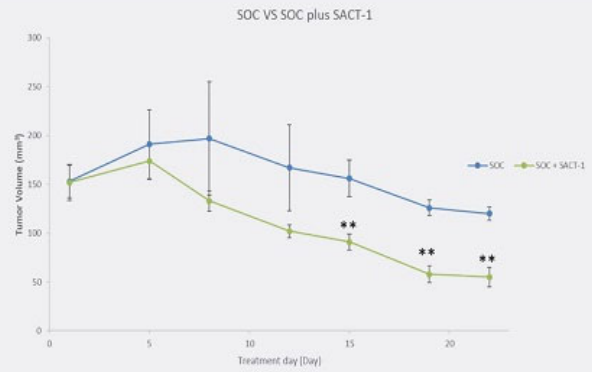
- Neuroblastoma is a rare disease and drugs usually qualify for orphan designation subject to FDA
- Designated orphan drugs receive 7 years of market exclusivity in US and 10 years of marketing exclusivity in EU
- Patents on new indication and reformulation, if granted, will provide up to 20 years of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

1. *Paediatr 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>

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)

- 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 targeted indication is 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<sup>1</sup>.



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**

<sup>1</sup>. Crit Care Med 2012; 40(12): 3277-3282

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)

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<sup>1</sup>**.



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.



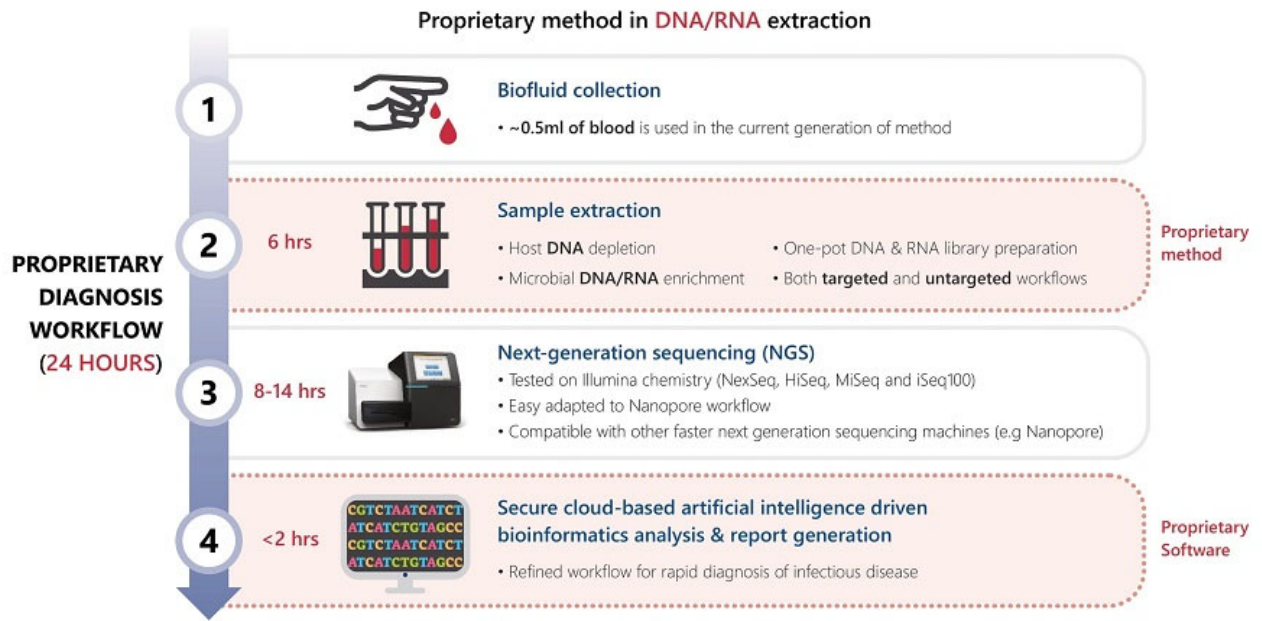
Based on internal results, RPIDD employs an untargeted approach for **detection of all known and mutated pathogens**, as well as genes that cause antibiotic resistance in a single test. It provides valuable information in a timely manner and the appropriate antimicrobial therapy would be initiated as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



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

<sup>1</sup>. 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.





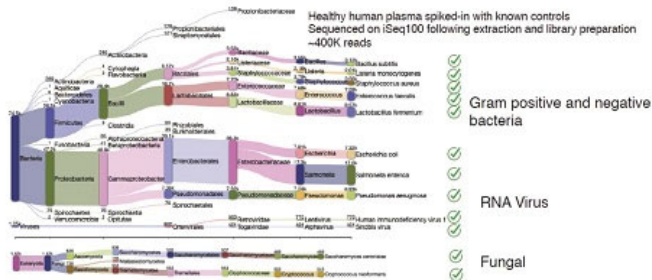
Based on internal results, RPIDD device detected organisms ranging from bacteria, RNA viruses and fungi in ONE TEST

**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



- 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® (NLS-2)

- Global menopause supplement market is projected to exceed US\$50 billion by 2025<sup>1</sup>
- 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<sup>2</sup>:
  - 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





<sup>1</sup> Grand View Research, Isoflavones Market Size Worth \$50.06 Billion By 2025, <https://www.grandviewresearch.com/press-release/global-isoflavones-market>; 2. Sc. 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.

NEW AMBITION IN 2022

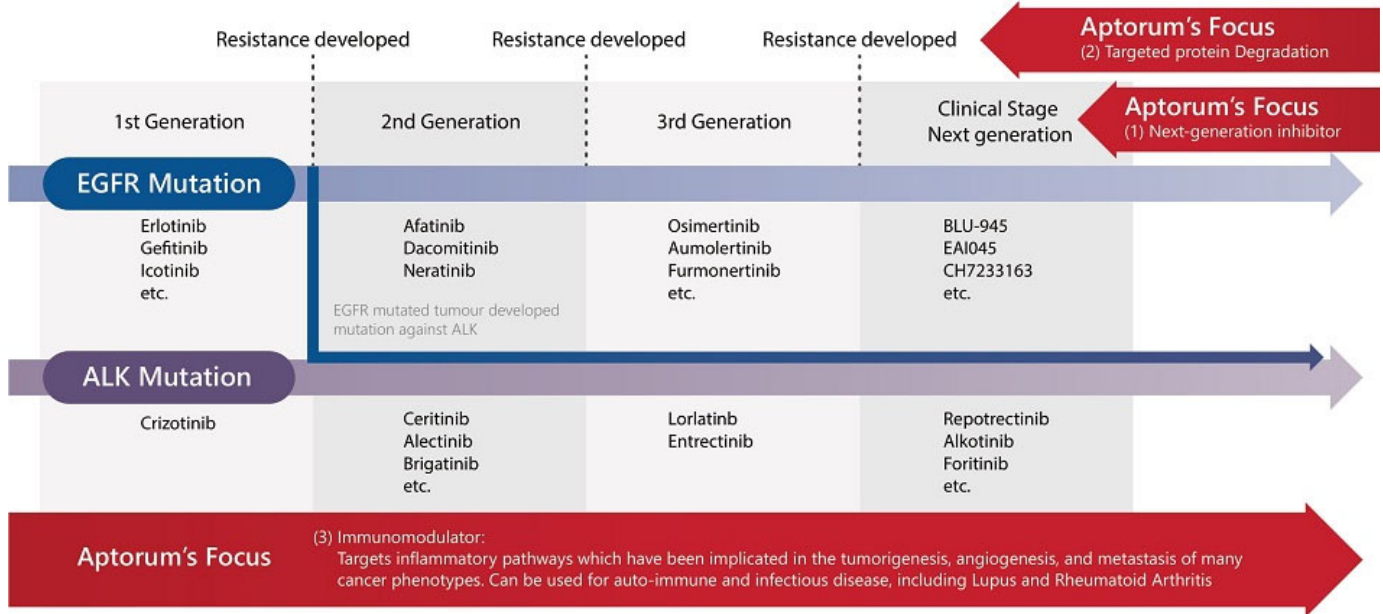
APTORUM'S  
ONCOLOGY AND  
AUTOIMMUNE  
FOCUS IN 2022

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

- 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<sup>1</sup>.
- Targeted therapy (targeting EGFR, ALK and RTKs) is used in biomarker-positive, advanced NSCLC and showed significance in improving progression free survival of patients<sup>2</sup>.
- However, the use of targeted therapy faced limitations:
  - **Resistance** develops within months or years<sup>3</sup> (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 lung cancer)<sup>4</sup>  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



Source of Drug: <https://adinsight.springer.com/search>



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**Aptorum Group Announces the Launch of its Oncology and Autoimmune Discovery and Development Platform Targeting Unmet Mutations and Novel Biomarkers**

**NEW YORK & LONDON & PARIS** - Aptorum Group Limited (Nasdaq: APM, Euronext Paris: APM) (“Aptorum Group” or “Aptorum”), a clinical-stage biopharmaceutical company, announces the launch of its oncology and autoimmune discovery and development platform with an initial focus on indications including, but not limited to, non-small cell lung cancer (“NSCLC”) and autoimmune diseases such as lupus, rheumatoid arthritis, inflammatory bowel diseases, etc.

Under the platform, Aptorum has and will continue to conduct its screening process for novel first-in-class small molecule and PROTAC (Degradable) based drug candidates. On this basis, Aptorum is currently conducting optimisation for selected candidates as part of its small molecule library for major targets including, but not limited to EGFR, ALK, KRAS, p53 mutations. Aptorum has identified major unmet medical needs in third and fourth generation mutations, where applicable, for NSCLC for example and will be leveraging its existing drug discovery platform to deliver novel therapeutics for such targeted patient group.

Mr. Darren Lui, President and Executive Director, commented, “The exciting launch of our oncology and autoimmune platform, culminating with the discovery and development of small molecule and PROTAC based candidates, if achieved, will help address the significant unmet medical needs for patients suffering from NSCLC (and potentially other cancer types) and autoimmune diseases. For example, the current 5-year, average survival rate for NSCLC is 25%<sup>1</sup>, despite existing therapies available. Subject to further optimisation and development, we target to deliver these candidates to their respective clinical trial stage at the earliest for such unmet medical needs.”

**About Aptorum Group Limited**

Aptorum Group Limited (Nasdaq: APM, Euronext Paris: APM) 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 (including orphan oncology indications) and infectious diseases. The pipeline of Aptorum is also enriched through (i) the establishment of drug discovery platforms that enable the discovery of new therapeutics assets through, e.g. systematic screening of existing approved drug molecules, and microbiome-based research platform for treatments of metabolic diseases; and (ii) the co-development of a novel molecular-based rapid pathogen identification and detection diagnostics technology with Accelerate Technologies Pte Ltd, commercialization arm of the Singapore’s Agency for Science, Technology and Research.

For more information about Aptorum Group, please visit [www.aptorumgroup.com](http://www.aptorumgroup.com).

<sup>1</sup> <https://www.cancer.net/cancer-types/lung-cancer-non-small-cell/statistics>

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This announcement is not a prospectus within the meaning of the Regulation (EU) n°2017/1129 of 14 June 2017 as amended by Regulations Delegated (EU) n°2019/980 of 14 March 2019 and n°2019/979 of 14 March 2019.

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**Aptorum Group Announces Completion of Phase I Clinical trials for ALS-4 and SACT-1, Small Molecule Drugs targeted for infections caused by Staphylococcus Aureus and Neuroblastoma**

**NEW YORK & LONDON & PARIS** - Aptorum Group Limited (Nasdaq: APM, Euronext Paris: APM) (“Aptorum Group” or “Aptorum”), a clinical-stage biopharmaceutical company, announces completion of the Phase I clinical trial for ALS-4 (a first in-class anti-virulence based small molecule drug targeting infections caused by Staphylococcus aureus, including, but not limited to Methicillin Resistant Staphylococcus Aureus (“MRSA”)) and the Phase I clinical trial for assessing relative bioavailability and food effect of SACT-1 (a repurposed small molecule drug targeting Neuroblastoma and potentially other cancer types).

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. Dosing and clinical evaluations of the Single Ascending Dose studies (“SAD”) and Multiple Ascending Dose studies (“MAD”) have now been completed for a total of 72 healthy subjects and Aptorum is pleased to announce that no subjects were dropped from the studies. There were no Serious Adverse Events (“SAE”) observed and no relevant clinical changes in respect of vital signs; ECG, clinical laboratory test results and physical examinations were observed compared to the relevant baseline in both SAD (25-200mg) and MAD (50-100mg). The safety data of the last SAD cohort (300mg) and MAD cohort (200mg twice a day for 14 days) are pending. With the encouraging safety data in our Phase I trial, we are on track to submit an IND application to the US FDA this year seeking to initiate a Phase 2 clinical study to assess the efficacy of ALS-4 in patients.

SACT-1’s first in-human clinical trial is a Phase I, Open-label Randomized, Single Cross Over Bioavailability and Food Effect Study of SACT-1 in healthy adult volunteers. Aptorum is pleased to announce the successful completion of the trial, during which no SAE were observed. With the encouraging data in our trial so far, we are on track to submit an IND application to the US FDA this year seeking to initiate our planned Phase 1b/2a trial for SACT-1.

Dr. Clark Cheng, Chief Medical Officer and Executive Director of Aptorum Group, commented: “Further to our previous announcements, we are pleased to announce the completion of the above clinical trials for ALS-4 and SACT-1. This represents another key milestone for the company and one of the targeted strategic goals we had for 2021. This milestone supports the focus of Aptorum Group to embark on the exciting Phase II clinical trials for ALS-4 and planned Phase 1b/2a clinical trials for SACT-1, subject to IND clearance. The World Health Organization deems MRSA a high priority due to its significant mortality risks<sup>1</sup>. Neuroblastoma is a highly unmet solid tumor arising in the nervous system outside of the brain predominantly in pediatric patients. We believe that both ALS-4 and SACT-1 have the potential to effectively target these diseases, respectively and address the unmet needs in this area.”

**About ALS-4**

As part of Aptorum Group’s Acticle infectious disease platform, ALS-4 is a novel first-in-class orally administered small molecule drug based on an anti-virulence approach targeting staphylococcus aureus including MRSA. ALS-4 targets the antimicrobial resistant properties of the bacteria and is believed to render the bacteria highly susceptible to the host’s immune clearance. ALS-4 is targeted for potential administration on a standalone or on a combination basis with other existing antibiotics such as vancomycin.

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<sup>1</sup> <https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed>

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## **About SACT-1**

SACT-1 is an orally administered repurposed small molecule drug to target neuroblastoma. SACT-1's mechanism has been investigated in our preclinical studies to enhance tumor cell death and suppress MYCN expression (a common clinical diagnosis in high-risk or relapsed neuroblastoma patients where an amplification of MYCN is usually observed). SACT-1 is designed to be used especially in combination with standard-of-care chemotherapy.

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**Aptorum Group Announces Updates on the Clinical Validation of its RPIDD Infectious Disease Liquid Biopsy Technology**

**NEW YORK & LONDON & PARIS** - Aptorum Group Limited (Nasdaq: APM, Euronext Paris: APM) (“Aptorum Group” or “Aptorum”), a clinical stage biopharmaceutical company focused on novel technologies including treatments and diagnosis of infectious diseases, announced that its subsidiary company, Aptorum Innovations Holding Limited (“Aptorum Innovations”), has commenced clinical validation of its molecular based rapid pathogen diagnostics liquid biopsy technology (“RPIDD”) for the diagnosis of pathogens including viruses, bacteria, fungi and parasites.

Aptorum Innovations is pleased to announce that under ongoing planned clinical validations in Singapore for RPIDD, 12 patients have been enrolled with febrile neutropenia and sepsis conditions and that over 53 samples have been collected and analyzed. So far, various bacteria and viruses have been detected in these patient samples, including *Escherichia coli*, *Klebsiella pneumoniae* and Herpesviridae. The data have been cross-validated by standard of care diagnostics results such as blood culture technology. RPIDD achieved analytical sensitivity and specificity of spiked samples of at most 100% and 90% respectively at both low depth (60,000 reads) and high depth (1 million reads) sequencing. RPIDD will continue to undergo validations during 2022, in parallel with its pre-commercialization process in 2022.

Mr Ian Huen, Chief Executive Officer and Executive Director of Aptorum Group, commented: “We are very pleased to announce this exciting update on our RPIDD technology. The high sensitivity and specificity demonstrated so far further support our objective to deliver a rapid, accurate and cost-effective liquid biopsy-based technology for infectious disease diagnostics. We hope that RPIDD will revolutionize traditional first line clinical diagnostics approaches that are time consuming or that fail to detect or identify disease causing pathogens. We believe that a rapid molecular based diagnostics approach for infectious diseases will significantly reduce mortality and morbidity. In 2022, we are commencing pre-commercialization processes of our RPIDD technology, including but not limited to identifying clinical partners to support its roll out.”

**About Aptorum’s Rapid Pathogen Identification and Detection Diagnostics Technology (RPIDD)**

RPIDD is an innovative liquid biopsy-driven rapid pathogen molecular diagnostics technology. Proprietary technologies are being developed to enrich pathogenic DNA / RNA for analysis through harnessing the power of Next-Generation Sequencing platforms and proprietary artificial intelligence-based software analytics with the goal to rapidly identify and detect any foreign pathogens (virus, bacteria, fungus, parasites) without bias through its genome composition and to identify other unknown pathogens and novel mutated pathogens. RPIDD has been and continues to be validated in human samples and so far, such testing has been able to detect pathogens – ranging from bacteria, fungi and viruses in an unbiased manner. RPIDD is currently under validation in-human.

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