
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 February 2020

Commission File Number: 001-38764

APTORUM GROUP LIMITED

17th Floor, Guangdong Investment Tower
148 Connaught Road Central
Hong Kong
(Address of principal executive offices)

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):

On February 10, 2020, Aptorum Group Limited (the “Company”) issued two press releases regarding certain of its lead projects and drug candidates under development. Copies of the press releases are attached hereto as Exhibit 99.1 and Exhibit 99.2. We are also filing this report to disclose the revised power point presentation the Company will use during corporate presentations; such power point presentation is incorporated herein by reference.

Neither this report, the press releases, nor the power point presentation attached as exhibits hereto 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Number 333-235819) and into each prospectus outstanding under the foregoing registration statements, to the extent not superseded by documents or reports subsequently filed or furnished by the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as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.

EXHIBIT INDEX

Exhibit No.	Description
99.1	Press Release
99.2	Press Release
99.3	Power Point Presentation

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.

Aptorum Group Limited

Date: February 10, 2020

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

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99.1	Press Release
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Aptorum Group Announces Significant Progress of Repurposed Drug Candidate, SACT-1 for Neuroblastoma Targeting IND Submission in H2 2020

NEW YORK -- (BUSINESS WIRE) – Aptorum Group Limited (Nasdaq: APM) (“Aptorum Group”), a biopharmaceutical company focused on the development of novel therapeutics to address global unmet medical needs, announces positive data and development in relation to its repurposed drug candidate, SACT-1, for the treatment of neuroblastoma, a *rare* type of *childhood cancer* that develops in infants and young *children*. Subject to completion of current validation studies, Aptorum Group plans to leverage the 505(b)(2) pathway and submit an IND submission with the FDA for SACT-1 in H2 2020.¹

SACT-1 is the first repurposed drug candidate to be developed under the Smart-ACT™ drug discovery platform, which employs a systematic approach to identify, repurpose and develop existing approved drugs against a currently identified universe of 7000+ (and increasing) orphan diseases.²

Through this platform, Aptorum Group intends to accelerate and fast track repurposed drug candidates, which usually have well established human safety and toxicity profiles and data, through the development and clinical phases in order to address the rapidly growing market of orphan diseases. Aptorum Group aims to screen a number of orphan disease areas including, but not limited to, oncology, autoimmune, metabolic and genetic diseases.

Through the Smart-ACT™ platform, Aptorum has successfully identified potential efficacy for and develops SACT-1 for the treatment of neuroblastoma, being an entirely new therapeutic area from its approved indication. In our recent studies, SACT-1 has been shown to be effective against numerous neuroblastoma cell lines, of which 2 are MYCN-amplified cells, which represent the high-risk neuroblastoma patient group. In addition, by using a combination index as a quantitative measure of the extent of drug interaction, Aptorum Group has seen a high and robust synergism between SACT-1 and traditional chemotherapy *in vitro*, indicating a potential efficacy enhancement/dose reduction of the chemotherapy. In addition, in our recent study, the maximum tolerable dose of SACT-1 in a rodent model was determined to be higher than 400mg/kg. Compared with the MTD of standard chemotherapy such as paclitaxel (20-30mg/kg)³ and cisplatin (6mg/kg)⁴, the safety profile of SACT-1 appears to be very impressive.

The reformulation of SACT-1 is a pediatric formulation to better address the needs of neuroblastoma patients who are exclusively children younger than 5. Based on our internal observations of pre-existing information from approved products,⁵ SACT-1 also exhibits a well-established safety profile: at 150mg/day, the death rate was 0% in prior clinical studies with no dosage related adverse events.

¹ If the FDA deems the 505(b)(2) pathway as an acceptable route for approval of SACT-1, the Company will be able to leverage existing clinical and nonclinical data in conjunction with sponsor-initiated studies to accelerate development and approval of SACT-1.

² See <https://rarediseases.info.nih.gov/diseases/pages/31/faqs-about-rare-diseases>

³ Clin Cancer Res. 5(11):3632-8.

⁴ BMC Cancer 17: 684 (2017).

⁵ Subject to FDA's approval and on a case-by-case basis, a 505(b)(2) application can rely in part on existing information from approved products (such as the FDA's previous findings on safety and efficacy) or products in literature (such as data available). However, typically speaking, the applicant is nonetheless required to carry out a Phase 1 bridging study to compare the Reference Listed Drug and reference the established safety and efficacy information.

About neuroblastoma

Neuroblastoma is a rare form of cancer, and classified as an orphan disease, that forms in certain types of nerve tissue and most frequently in the adrenal glands as well as spine, chest, abdomen or neck, predominantly in children, especially for those aged 5 years and below. For the high-risk group, which is close to 20%⁶ of total new patient population per year, the 5-year survival rate of this condition is around 40-50% as observed by the American Cancer Society⁷. The current high drug treatment cost for high risk patients can average USD200,000 per regimen (all 6 cycles)⁸. In addition, most pediatric patients often do not tolerate or survive the relevant chemotherapy stage which we believe, subject to further clinical studies, may be positively addressed by the SACT-1 candidate due to the potential synergistic effects when applied with standard chemotherapy as described above.

For further general presentation, please visit:

<http://ir.aptorumgroup.com/static-files/bcf77574-7bd6-4b9d-8110-d53837238f16>

For further technical presentation, please visit:

<http://ir.aptorumgroup.com/static-files/66346f79-7a03-474a-89be-0eaafaa00d9d>

About Aptorum Group Limited

Aptorum Group Limited (Nasdaq: APM) is a pharmaceutical company dedicated to developing and commercializing novel therapeutics to tackle unmet medical needs. Aptorum Group is pursuing therapeutic projects in orphan diseases, infectious diseases, metabolic diseases and other disease areas.

For more information about Aptorum Group, please visit www.aptorumgroup.com.

About Smart Pharma Group

Smart Pharma Group is wholly owned by Aptorum Group Limited. Smart Pharma Group focuses on systematically identifying and repurposing existing approved drugs for the treatment of a large array of orphan diseases. Smart Pharma Group conducts both computational based screening and clinical validations in advancing the development of its repurposed candidates.

Disclaimer and Forward-Looking Statements

This press release 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 and trials, 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 press release 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 press release as a result of new information, future events or otherwise.

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⁶ Annu Rev Med. 2015; 66: 49–63.

⁷ <https://www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/survival-rates.html>

⁸ https://www.cadth.ca/sites/default/files/pcodr/Reviews2019/10154DinutuximabNeuroblastoma_fnEGR_NOREDACT-ABBREV_Post_26Mar2019_final.pdf



Aptorum Group Announces Further Positive Data For Its ALS-4 Small Molecule Anti-virulence (Non-bactericidal) Drug Candidate For The Treatment of Infections Caused By Staphylococcus Aureus and On Track Targeted For IND Submission in H2 2020

NEW YORK -- (BUSINESS WIRE) – Aptorum Group Limited (NASDAQ: APM) (“Aptorum Group”), a biopharmaceutical company focused on the development of novel therapeutics to address global unmet medical needs, announces further positive data from its current investigational new drug (IND)-enabling studies for ALS-4, a small drug molecule candidate indicated for the treatment of infections caused by *Staphylococcus aureus* (or “*S. aureus*”), including methicillin-resistant *Staphylococcus aureus* (MRSA, one of the “super-bugs”), based on a novel anti-virulence non-bactericidal approach. Subject to completion of the current studies, Aptorum Group targets to submit IND for ALS-4 in second half of 2020 and commence a phase 1 trial in North America.

ALS-4 is a small molecule which inhibits dehydroqualene desaturase of *S. aureus* (incl. MRSA), an enzyme that is critically involved in the biosynthesis of staphyloxanthin, a commonly visible “golden pigment” covering the bacteria. Staphyloxanthin is believed to be primarily responsible for the bacteria’s defense mechanism against the attack from reactive oxygen species (ROS) deployed by phagocytic cells and neutrophils.¹

Through inhibiting the production of staphyloxanthin, we believe that ALS-4 renders *S. aureus* highly susceptible to the host’s immune defense (see below for in vivo data and experimental outline). This novel mechanism is significantly different from the bactericidal approach found in currently marketed antibiotics used to treat *S. aureus*, which are experiencing increasing drug resistance issues². Specifically, MRSA infections in humans typically exhibit high rates of morbidity and mortality and can cause metastatic or complicated infections such as infective endocarditis or sepsis, with relapse and hospital readmission after *S. aureus* bacteremia common and costly³.

Based on our testing in a rat bacteremia survival model, a lethal (10^9 CFU) dose of MRSA (USA300-LAC) was introduced through the tail vein. ALS-4 was administered orally at 10mg/kg per animal 30 minutes after the infection for twice a day thereafter (N=9). A control untreated group was given a sterile vehicle solution (N=9). Survival was monitored for 7 days. 0 out of 9 animals (0%) in the control untreated group survived past day 4, in contrast, 5 out of 9 animals (56%) treated with ALS-4 survived past day 7, which is determined to be statistically significant compared with the control group ($p=0.013$).

¹mBio 2017 8(5): e01224-17

² Microbiol Spectr. 2019 Mar;7(2)

³ Clin Infect Dis. 2019 Nov 27;69(12):2112-2118

In addition we conducted a study in a non-lethal rat bacteremia infection model. The animals were challenged with a non-lethal (10^7 CFU) dose of MRSA (USA300-LAC) through the tail vein. In order to simulate a more realistic clinical scenario, treatment was introduced 14-days after the model induction, where ALS-4 was administered orally twice a day at 10mg/kg per animal (N=8). A control untreated group was given a sterile vehicle solution (N=8). After 7 days of ALS-4 treatment, the kidneys were collected and the bacterial titers were measured. Remarkably, ALS-4 reduced the organ bacterial load by 99.5%, from $63,096 \pm 18$ CFU/g in the control group to 316 ± 49 CFU/g in the ALS-4 treated group, which is determined to be statistically significant ($p=0.01$).

Last but not least, ALS-4 has successfully inhibited staphyloxanthin production in 11 strains of *S. aureus*. These include 5 strains of Methicillin-sensitive *S. aureus* (MSSA): SH1000, HG003, USA300-JE2, Newman, and ATCC29213 with an IC_{50} of 70.5 ± 6 nM, 54.4 ± 4 nM, 37.7 ± 4 nM, 23.7 ± 1 nM, and 30.02 ± 5 nM respectively; 5 strains of Methicillin-resistant *S. aureus* (MRSA): USA300, USA300-3, USA300-LAC, ST239III, and COL, with an IC_{50} of 30.8 ± 5 nM, 42.8 ± 6 nM, 43.6 ± 5 nM, 16.3 ± 8 nM, and 0.9 ± 1 nM respectively; and 1 strain of vancomycin-intermediate *S. aureus* (VISA), Mu3 with an IC_{50} of 2.6 ± 1 nM.

Based on our testing, we believe ALS-4 increases the susceptibility of *S. aureus* including MRSA to oxidative damage by inhibiting production of staphyloxanthin. In a hydrogen peroxide killing assay, after the addition of 1.5% H_2O_2 , ALS-4 demonstrated an additional reduction of bacterial CFU by 93.5%, from $61,600 \pm 6437$ CFU/ml in the untreated group to $4,000 \pm 230$ CFU/ml in the ALS-4 treated group, which is determined to be statistically significant ($p=0.003$).

With respect to the study carried out to investigate the capability of ALS-4 to induce antibiotic resistance in *S. aureus* after prolonged exposure, USA300-LAC was cultured in 3 different conditions for 10 days. For the treatment group 1 μ M of ALS-4 was added; for the positive control group 0.12 μ g/mL of clindamycin and 16 μ g/mL of erythromycin was added from day 1 to day 4, after which clindamycin was withdrawn. For the negative control group, dimethyl sulfoxide (DMSO) was added. On day 11, the bacteria were harvested and then cultured for 16 hr for the determination of the MIC of clindamycin. The prolonged exposure to ALS-4 or DMSO does not affect the MIC value of clindamycin (0.12 μ g/mL); while the prolonged exposure to clindamycin + erythromycin triggers antibiotics resistance rapidly with the MIC increased from 0.12 μ g/mL to greater than 5 μ g/mL.

Based on our study, we believe ALS-4 is unlikely to be prone to drug resistance since it is non-bactericidal. Growth inhibition studies were performed on different strains of *S. aureus* and other bacteria, including 3 strains of MSSA (ATCC29212, SH1000 and HG003), 1 strain of MRSA (USA300), 1 strain of VISA (ATCC700698 Mu3), as well as 6 different bacteria (*E. coli*, *A. baumannii*, *S. cerevisiae*, *B. subtilis*, *E. faecalis*, and *K. pneumoniae*). In all of the tested strains of bacteria, no growth inhibition effect was observed at the highest tested concentration of ALS-4 (250 μ M). Therefore ALS-4 does not appear to have any direct bacteriostatic or bactericidal activity against many species of bacteria, thus greatly reducing the selection pressure for drug resistance to emerge.

We also assessed the potential impact on the efficacy of vancomycin, the mainstay of treatment for infections caused by MRSA, when used in conjunction with ALS-4. 8 different strains of *S. aureus* (USA300 FPR3757, USA300-3, USA300-LAC, USA300-JE2, Mu3, HG003, ATCC29213 and clinical isolate ST239III) were used in this study. Our data showed that no effect on the MIC of vancomycin was observed when the concentration of ALS-4 was below 25 mM. Therefore, we believe that ALS-4 does not interfere with the action of vancomycin.

In addition, compared with the current mainstay of treatment for *S. aureus* infections such as vancomycin or daptomycin which is typically administered in an IV injectable form (with the exception of an oral form vancomycin specifically for treatment of *Clostridium difficile* diarrhea and staphylococcal enterocolitis only), an oral active agent enables wider market penetration targeting both outpatient as well as potential prophylactic markets.

GLP Toxicity Data

ALS-4 is currently undergoing IND-enabling studies and has so far shown positive safety profiles. As elucidated in our previous press release dated September 9, 2019, ALS-4 did not show any mutagenicity in the in vitro Ames tests. Our currently generated in vitro micronucleus test results also showed that ALS-4 is not genotoxic, indicating the non-mutagenic nature of the drug. Furthermore, the results of the in vitro hERG assay study predicts a low risk of ALS-4 causing cardiac QT prolongation.

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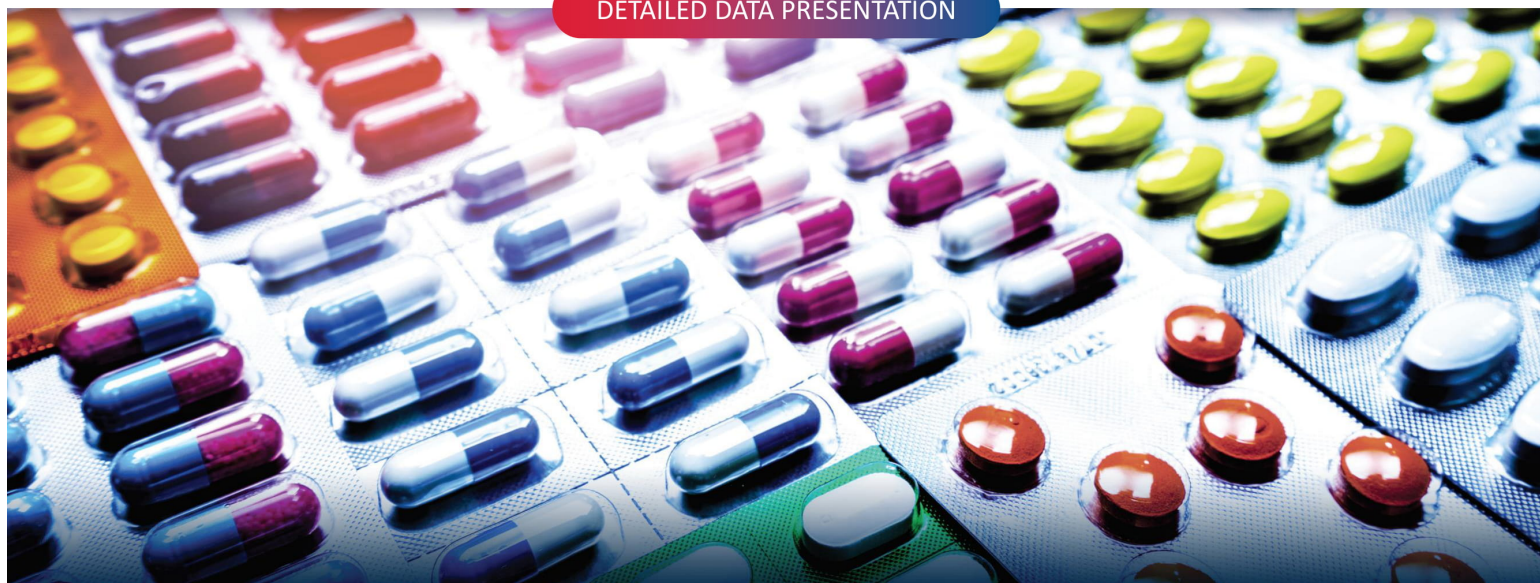
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Facilitating Life Science Innovations to Serve Unmet Medical Needs

DETAILED DATA PRESENTATION



Disclaimer

Certain information included in this presentation and other statements or materials published by Aptorum Group Limited (the "Company") are not historical facts but are forward looking statements.

These forward-looking statements refer in particular to the Company's management's business strategies, its expansion and growth of operations, future events, trends or objectives and expectations, which are naturally subject to risks and contingencies that may lead to actual results materially differing from those explicitly or implicitly included in these statements. Forward-looking statements speak only as of the date of this presentation and, subject to any legal requirement, the Company does not undertake to update or revise the forward-looking statements that may be presented in this document to reflect new information, future events or for any other reason and any opinion expressed in this presentation is subject to change without notice. Such forward looking statements are for illustrative purposes only. Forward-looking information and statements are not guarantees of future performances and are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of the Company. These risks and uncertainties include among other things, the uncertainties inherent in research and development of new products, including future clinical trial results and analysis of clinical data (including post-marketing data), decisions by regulatory authorities, such as the Food and Drug Administration or the European Medicines Agency, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates.

This presentation does not constitute an offer to sell or solicitation of an offer to buy securities of the Company. This presentation accordingly does not contain the information that would be required in a prospectus or offering memorandum intended to be distributed to persons in an offering of securities of the Company.

SMART-ACT™ : pipeline overview

Current progress of pipeline programs: → Lead Projects → Other Candidates → Projected timeline¹

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

Pillar 1: SMART-ACT™ (SACT series) - Orphan disease drug repurposing platform							
Over 7,000 orphan diseases to be screened in the next 5 years							
Program	Indication	Computational Discovery	In vitro validation	Existing Ph/I/II clinical safety data ¹	IND 505(b)(2) filing ²		
					In vivo validation	Bridging studies	Ph I / II with limited population ³
SACT-1	Neuroblastoma	→			Q4 2019	→	ready for clinical trial by 2H 2020
SACT-2	To be disclosed	→	→	→			
SACT-3	To be disclosed	→	→	→			

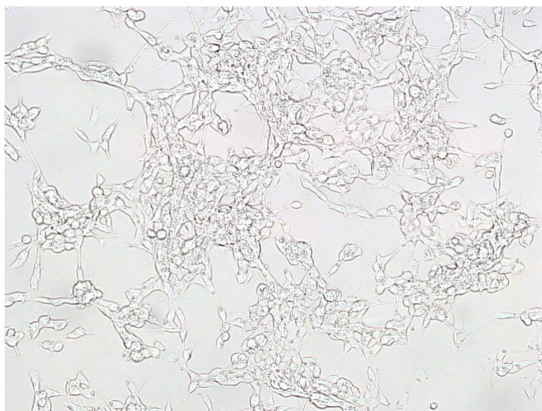
1. All projected timelines refer to the estimated commencement time of the indicated stages 2. Refers to the drug's existing Phase I/II safety data previously conducted by a third party. Does not refer to clinical trials conducted by Aptorum 3. Subject to FDA's approval on a case-by-case basis, a 505(b)(2)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

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

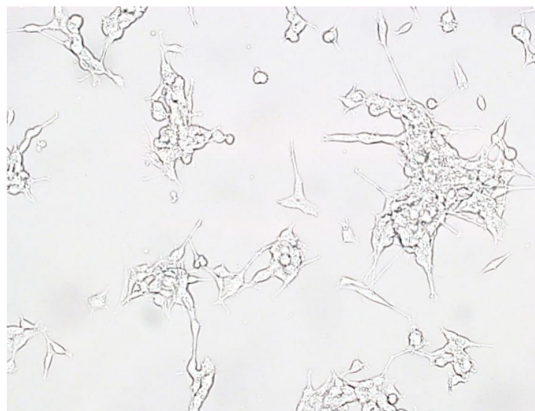
In vitro drug activity against neuroblastoma cell lines

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

Control treatment on neuroblastoma cells



SP055 treatment on neuroblastoma cells



Drug candidates under SACT-1

SP055

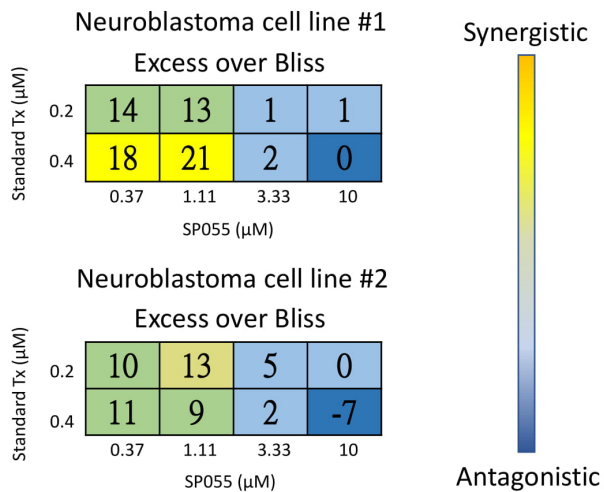
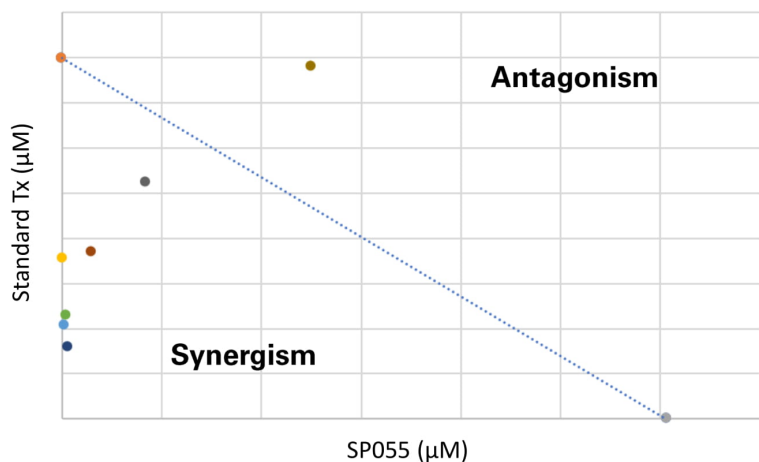
IC₅₀ [μM]

2.97

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

Synergistic effect of SP055 in combination with standard treatment

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



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

SP055: safety & tolerability

FDA approved safety profile

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

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

SP055: pharmacokinetics

FDA approved pharmacokinetics profile

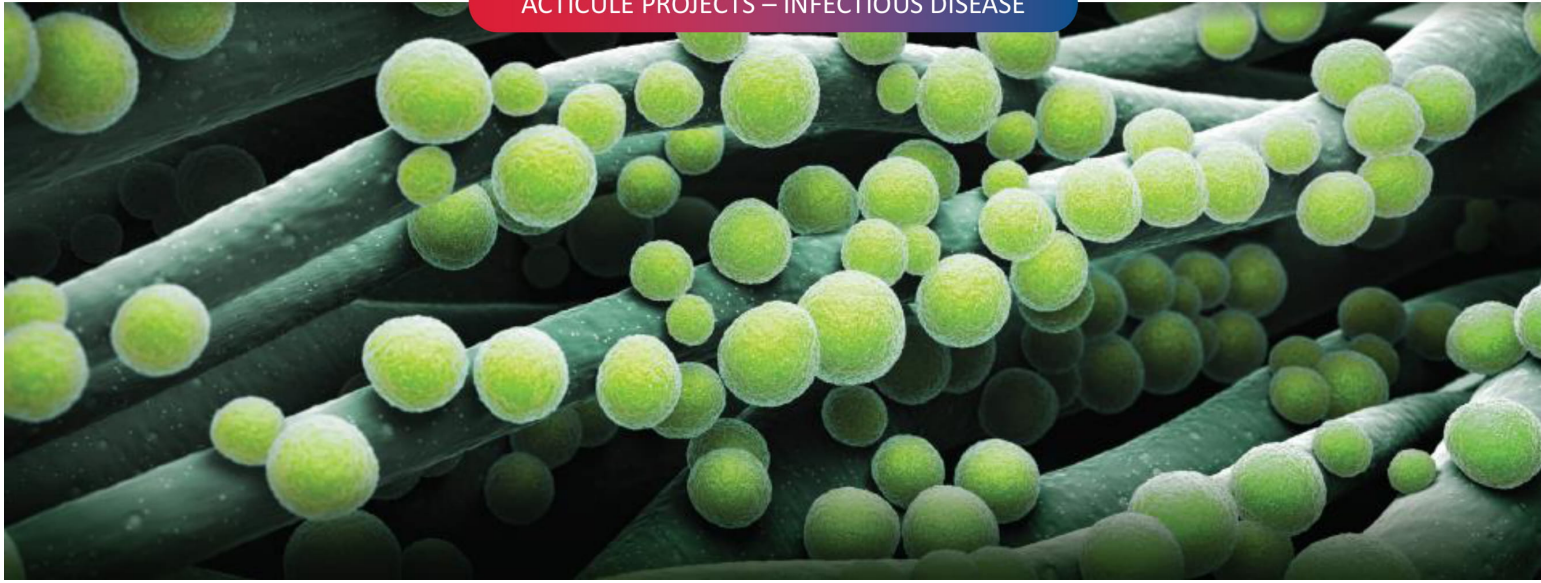
- Data package can be potentially accepted by the FDA in our 505(b)(2) new drug application
- Relatively long half-life ($t_{1/2} = 43-55h$). Frequent dosing may not be required

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



Facilitating Life Science Innovations to Serve Unmet Medical Needs

ACTICULE PROJECTS – INFECTIOUS DISEASE



Executive summary: Acticle 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 market², ALS-4 relies on an anti-virulent non-bactericidal approach¹, potentially reducing significant risks of developing *S. aureus* resistance
- IND-enabling studies commenced in Q2 2019, Targeting IND submission by Q1/2 2020
- Upon IND approval, a hybrid Phase I clinical study to commence in 2020 in North America to obtain preliminary efficacy readout
- 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

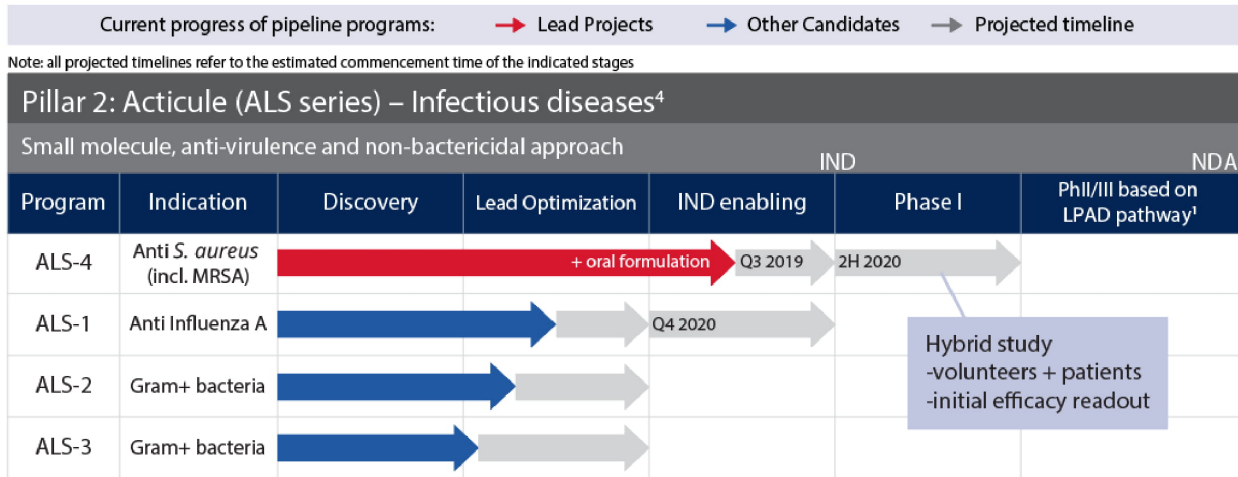
- A unique antiviral therapeutic against Influenza A that has a more upstream target than Tamiflu which is shown to be more effective in vitro¹
- Viral resistance to Tamiflu and other neuraminidase inhibitors has risen rapidly in recent years³
- ALS-1 has a distinct mechanism of action compared with Tamiflu and Xofluza^{1,4}

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. P T. 2016 Feb; 41(2): 126-128; 3. Influenza Antiviral Medications: Summary for Clinicians. CDC. <https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>; 4. Nat Biotechnol. 2010 Jun;28(6):600-5

ALS pipeline overview



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

ALS-4: mechanism of action

ALS-4

inhibits a key enzyme in the biosynthesis of staphyloxanthin¹

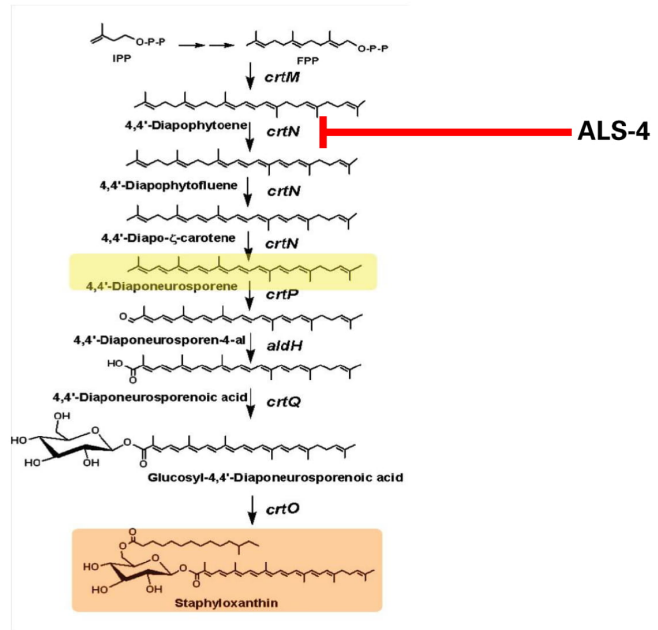


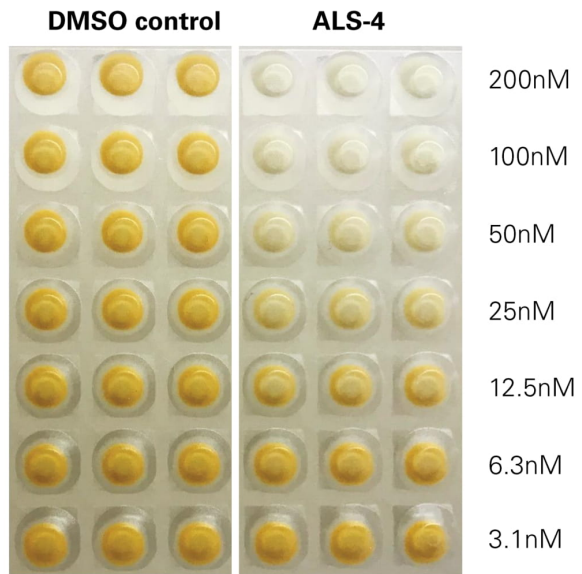
Figure adapted from MBio. 2017 Sep 5;8(5). pii: e01224-17.

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

ALS-4: mechanism of action

ALS-4

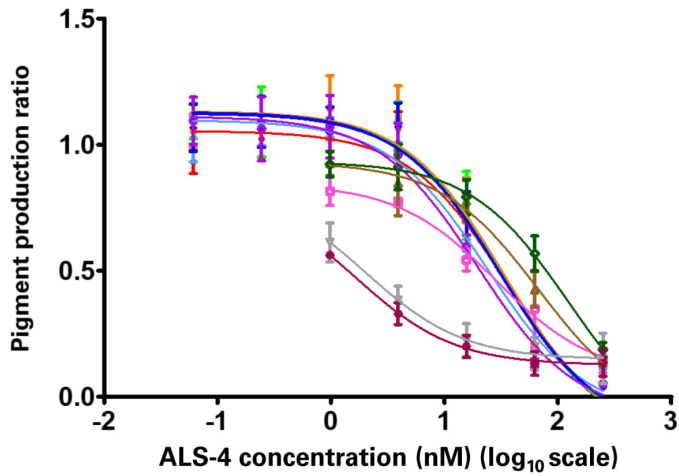
inhibits *S. aureus*
pigment production
with an $IC_{50} = 20nM$



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 is shown to be effective across 11 strains of *S. aureus*

ALS-4 is believed to inhibit the production of staphyloxanthin in 11 strains of *S. aureus* *in vitro*



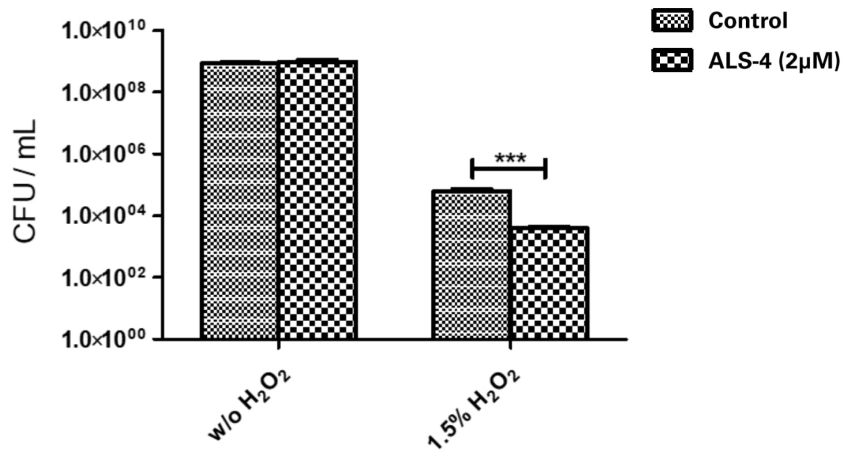
Strain	Type	IC ₅₀ (nM)
SH1000	MSSA	70.5 ± 6
HG003	MSSA	54.4 ± 4
USA300-JE2	MSSA	37.7 ± 4
USA300 (FPR-3757)	CA-MRSA	30.8 ± 5
USA300-3	HA-MRSA	42.8 ± 6
Newman	MSSA	23.7 ± 1
USA300-LAC	MRSA	43.6 ± 5
ATCC29213	MSSA	30.0 ± 5
Clinical isolate ST239III	HA-MRSA	16.3 ± 8
Mu3	VISA	2.6 ± 1
COL	HA-MRSA	0.9 ± 1

- JE2 ■ USA300 (FPR-3757) ▲ USA300-3 ▼ Newman ◆ USA300-LAC
- Clinical isolate ST239III ■ ATCC29213 ▲ HG003 ▼ Mu3 ◆ SH1000 ● COL

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 is shown to increase sensitivity of *S. aureus* to oxidative damage

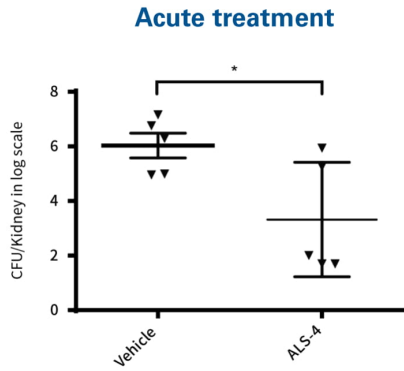
ALS-4 is believed to reduce bacteria number by an additional 10-fold in the presence of hydrogen peroxide



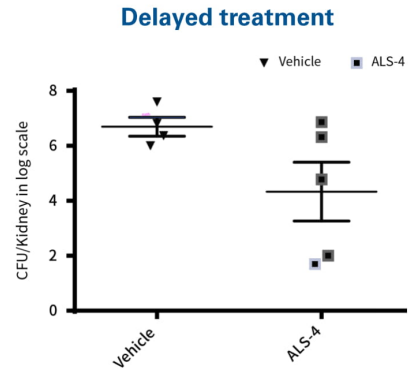
The results shown in this slide are based on Aptorum's internal (in vitro/in vivo) tests/experiments that have not been verified in clinical trials and/or third party testing

ALS-4: *in vivo* efficacy

ALS-4 inhibits *S. aureus* pigment production with an $IC_{50} = 20nM$



ALS-4 concentration: 1 mM
Inoculum: 5×10^6 per mouse
Treatment: twice for first 7 days
First inject: 30 min after infection

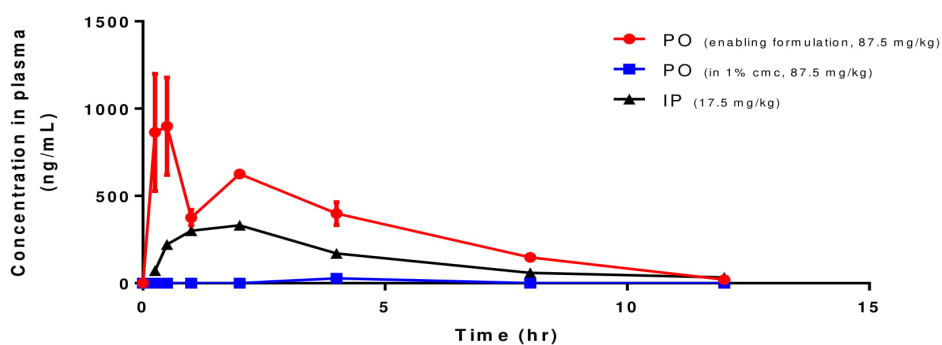


ALS-4 concentration: 1 mM
Inoculum: 2×10^7 per mouse
Treatment: twice for first 7 days
First inject: 11 days after infection

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

Enabling oral formulation (red) vastly improved ALS-4 bioavailability in mice

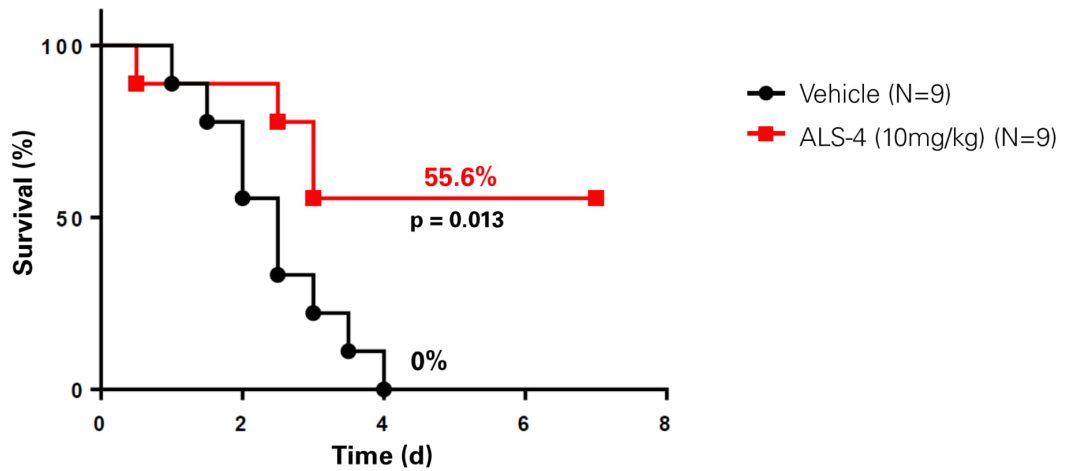


- The enabling oral formulation is being scaled up and stability is being assessed
- GMP manufacturing of the drug product is expected to commence in Q1 2020

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 an MRSA survival study

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

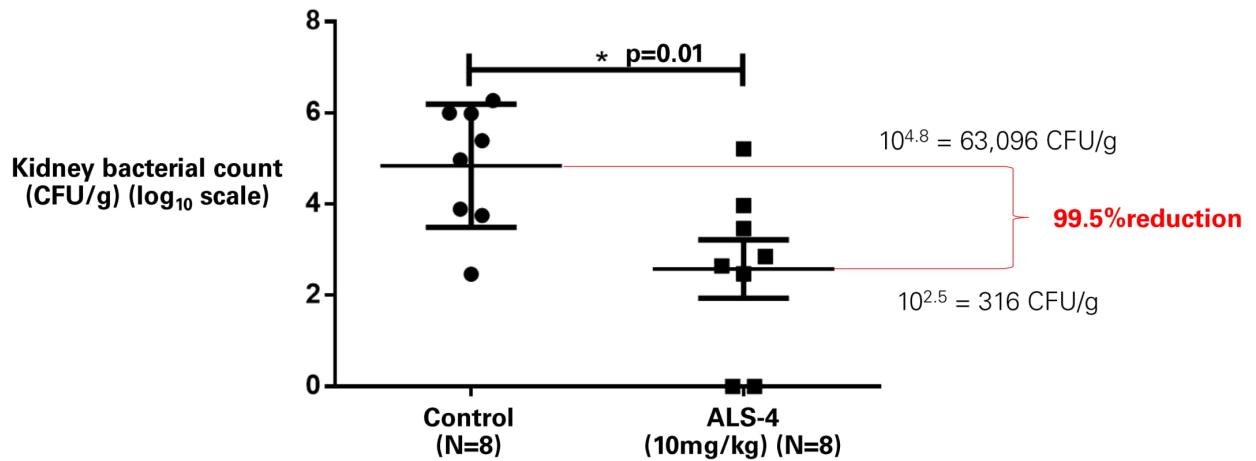


- A lethal dose (10^9 CFU) of MRSA was introduced through the tail vein
- ALS-4 was administered **orally** 30 minutes after infection for twice a day thereafter

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



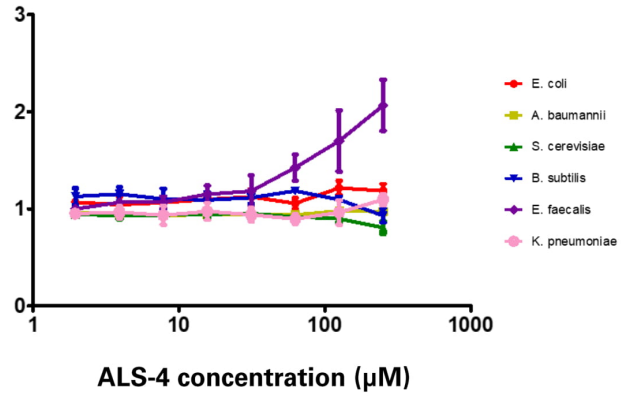
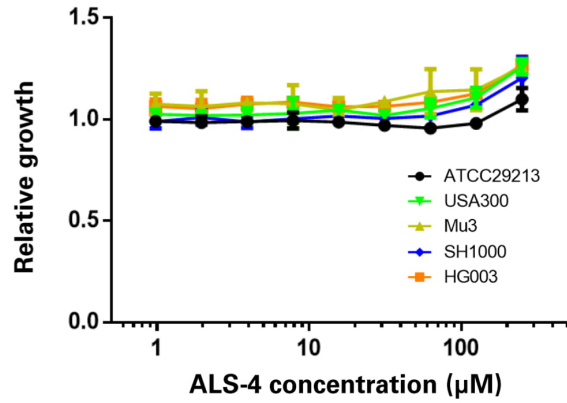
- Rats were challenged with a non-lethal dose (10^7 CFU) of MRSA through the tail vein
- In order to simulate a more realistic clinical scenario, treatment was introduced 14-days after infection, where ALS-4 was administered orally twice a day at 10mg/kg per animal

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 is shown not to directly inhibit bacterial growth *in vitro*

Lack of direct selection pressure makes it unlikely for drug resistance to emerge

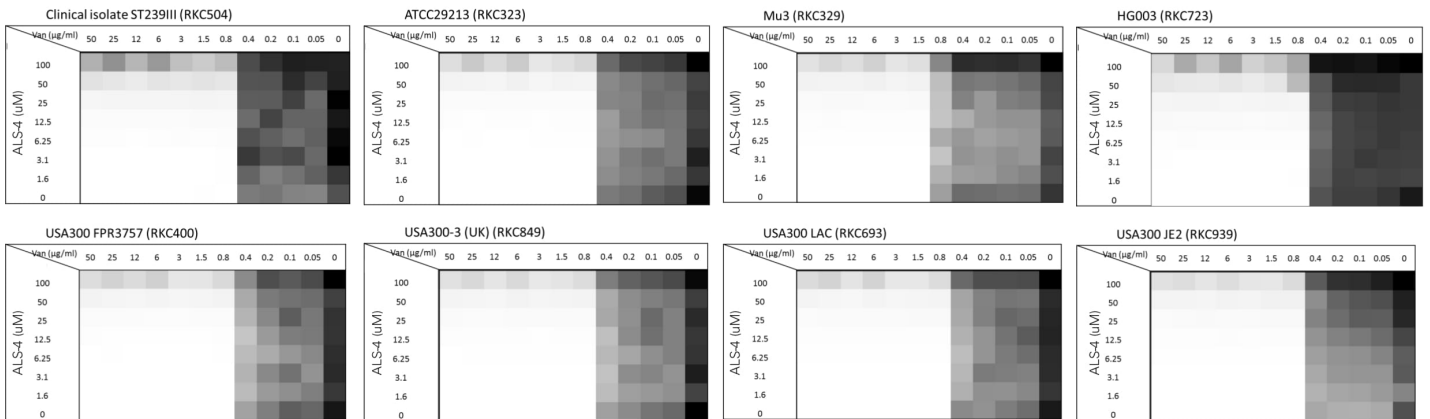
Does not inhibit in growth in 5 strains of *S. aureus* (left) and 6 different species of bacteria (right)



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

ALS-4 does not interfere with the action of vancomycin

ALS-4 does not affect the minimum inhibitory concentration (MIC) of vancomycin in 8 strains of *S. aureus*



- No effect on the MIC of vancomycin was observed *in vitro* when the concentration of ALS-4 was below 25µM

Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing. Applies to all content on this slide.

ALS-4 resistance raising in MRSA

Protocol

1. Inoculum preparation: USA300-3 (LAC) was cultured overnight in BHI broth at 37°C, 250 rpm.
2. Subculture preparation: 60 µl overnight culture was added to 6 ml BHI broth with different drugs.

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

3. Clindamycin (CLI): 0.12 µg/ml; Erythromycin (Ery): 16 µg/ml; ALS-4: 1 µM. The use of Ery was to ensure no contamination of environmental bacteria as USA 300 (LAC) is resistance Ery.
4. Culturing: during culturing, medium was changed everyday by centrifugation of the bacteria and replacing the supernatant with new medium plus DMSO or antibiotics or compounds as specified.
5. Bacteria collection: on day 11, 1 ml bacteria was centrifuged and resuspended in PBS with 10% DMSO for further testing.
6. MIC testing: in BHI medium in 96-well plate and cultured for 16h
7. Pigment production: in 96 deep-well plate and cultured for 36 h

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

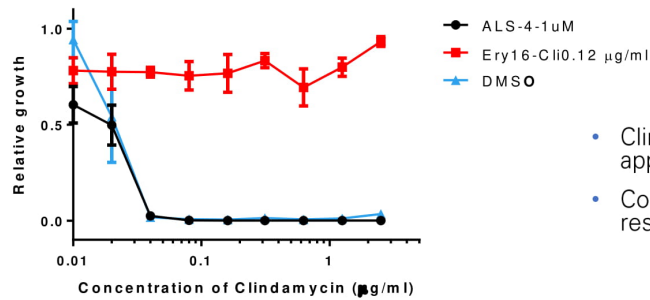
Resistance of *S. aureus* USA 300(lac) to clindamycin after various treatment conditions

Pre-treatment

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

(Clindamycin withdrawn between day 5-10)

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



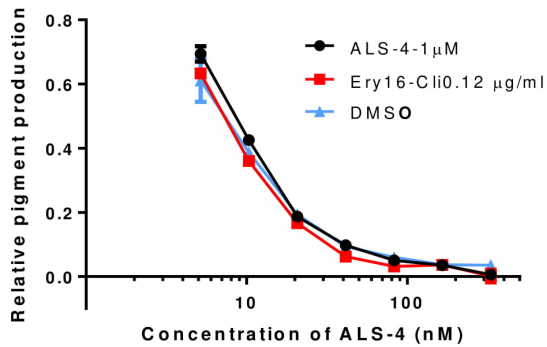
- Clindamycin resistance (MIC from 0.12 µg/ml to >5 µg/ml) appeared rapidly after a 10-day intermittent treatment
- Controls without the addition of antibiotics showed no resistance to clindamycin

Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing. Applies to all content on this slide.

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

ALS-4 efficacy test

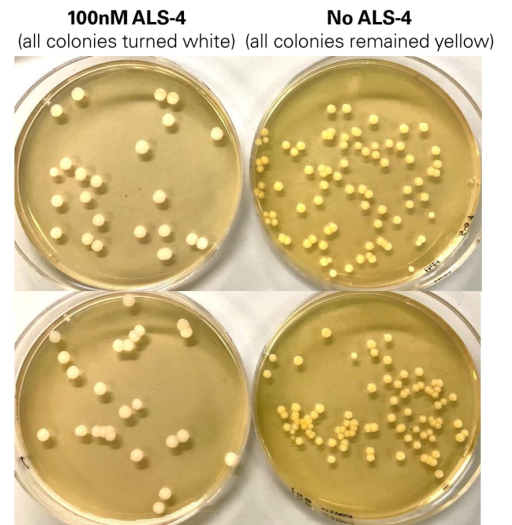
(Bacterial inoculum: 4×10^7 /ml)



BHI agar plates

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

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



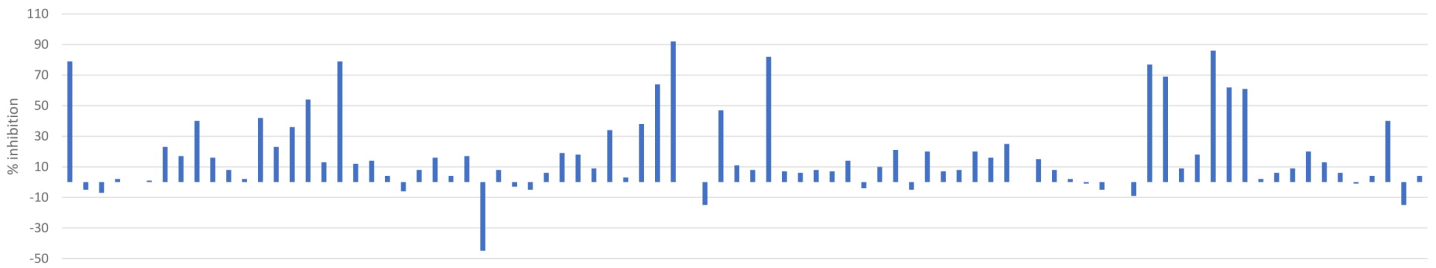
No bacterial resistance to ALS-4 detected after continuous incubation of the bacteria in the presence of 1 μM ALS-4 for 11 days

Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing. Applies to all content on this slide.

ALS-4: pharmacology & toxicology

In vitro safety screening

Average % inhibition across 86 key human enzymes

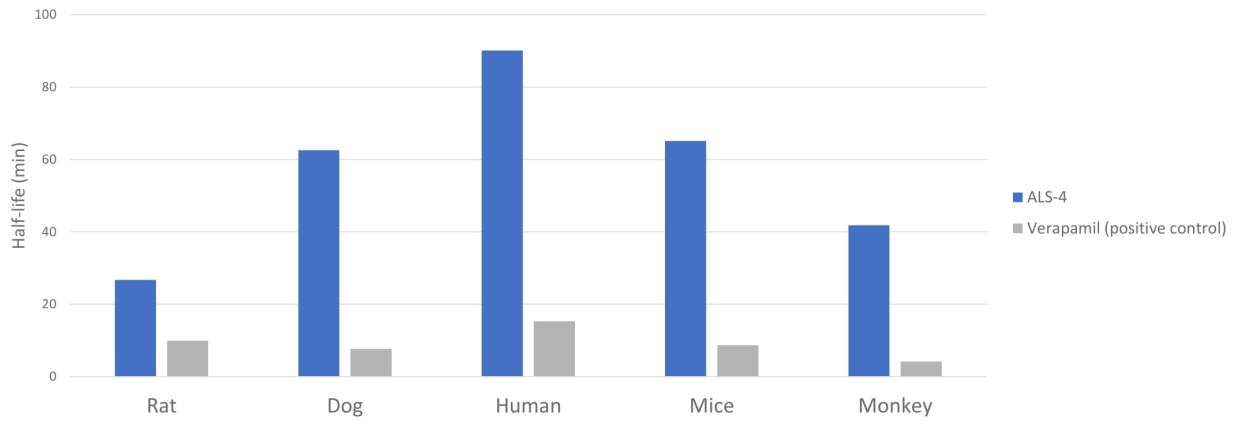


- Average inhibition of 17.5% across 86 key human enzymes
- Enzyme inhibition assay shows that ALS-4 has a clean profile with little off-target inhibition
- Key enzymes including hERG, P450, MAO and UDP are all unaffected

Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing. Applies to all content on this slide.

ALS-4: pharmacology & toxicology

In vitro metabolism study using liver microsomes from 5 different species



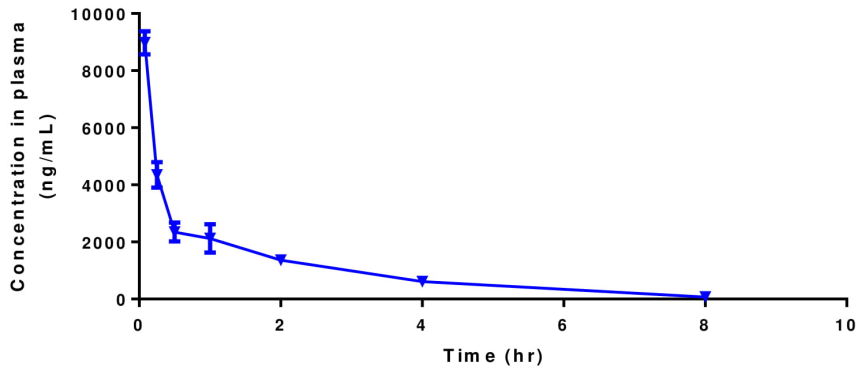
- Liver microsome studies show low intrinsic clearance in 5 different species, including human. Results suggests indicating slow metabolism

Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing. Applies to all content on this slide.

ALS-4: pharmacology & toxicology

Pharmacokinetics

- Biological half-life of ALS-4 is around 2 hours in mice (N=3). Rat pharmacokinetics study ongoing



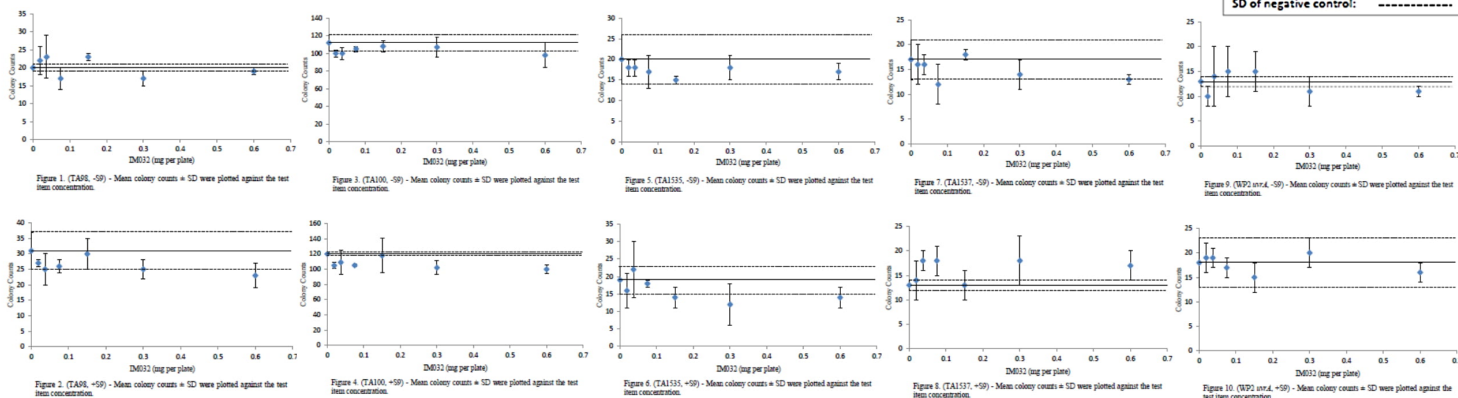
C_{max} (ng/mL)	12624.55
$AUC_{0-Tlast}$ (ng*hr/mL)	9732
$AUC_{0-\infty}$ (ng*hr/mL)	9927
K_{el} (hr ⁻¹)	0.37
$t_{1/2}$ (hr)	1.87
Extrap AUC (%)	1.97
Vz_{obs} (L/kg)	4.75
Cl_{obs} (L/hr/kg)	1.76
MRT_{obs} (hr)	2.11
Vss_{obs} (L/kg)	3.71

Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing. Applies to all content on this slide.

ALS-4: pharmacology & toxicology

Results for Plate Incorporation Assay

GLP AMES test for mutagenicity



- AMES mutagenicity study using *Salmonella typhimurium* strain TA98, TA100, TA1535, TA1537 and *Escherichia coli* strain WP2 *uvrA*; with and without the presence of rat liver S9 for metabolic activation
- Negative result in all tested strains

Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing. Applies to all content on this slide.

ALS-4: chemistry, manufacturing and controls

ALS-4 properties

Molecular weight (g/mol)	449.36
LogD ¹ pH7.4	4.43
pka(s) ¹	14.5
Caco-2 permeability	2.27 x 10 ⁻⁴ cm/s (non-pgp substrate)
Permeability (Human jejunum, pH 6.5)	7.39 x 10 ⁻⁴ cm/s
In vitro CL (human, monkey, dog, rat, mouse liver microsomes)	94.97, 335.4, 170.92, 145.8, 180 (μL/min/mg)
Plasma protein binding ¹	98.53%
DDI risk (CYP450 reversible inhibition, TDI and induction)	Low

¹Calculated properties using ACD/Labs (Release 2017.2.1)

Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing. Applies to all content on this slide.

ALS-4: chemistry, manufacturing and controls

ALS-4 is an attractive candidate for formulation

- Only 1 physical form identified from polymorph screening
- Physically and chemically stable
- Not hygroscopic

API (active pharmaceutical ingredient) manufacturing

- Successfully scaled up to 200-300g batch
- GLP toxicology batch of API has been synthesized
- GMP manufacturing is expected to commence in Q4 2019

ALS-4 has low solubility in water

- Developed an enabling formulation to improve bioavailability

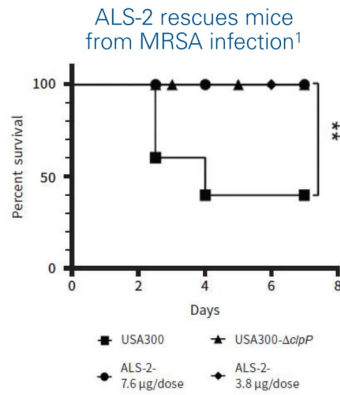
Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing. Applies to all content on this slide.

ALS-2 & ALS-3

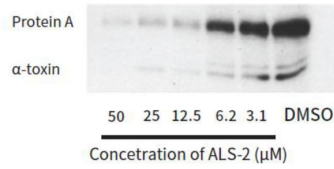
Additional anti-virulence, non-bactericidal therapeutics for the treatment of infections caused by Gram Positive bacteria

ALS-2

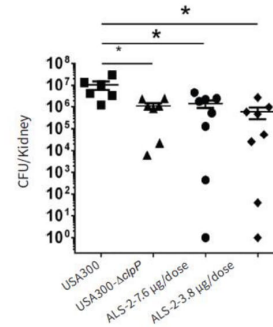
Anti-virulence compound that suppresses multiple unrelated virulence factors in *S. aureus*¹



ALS-2 reduces virulence gene production¹



ALS-2 reduces bacterial load in mice¹



ALS-3

Antibiotic-potentiating compound by using a non-bactericidal approach

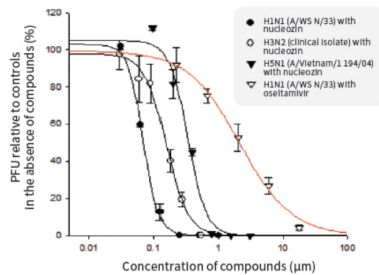
1. Proc Natl Acad Sci U S A. 2018 Jul 31;115(31):8003-8008

ALS-1: targeting a novel druggable target for Influenza A

ALS-1 inhibits influenza A nucleoprotein (NP)

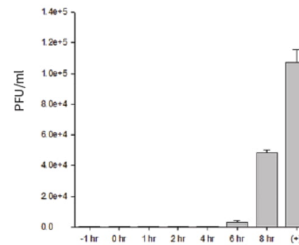
- NP is the most abundantly expressed protein during the course of an infection¹. Its primary function is to encapsidate the virus genome for RNA transcription, replication and packaging. It is also a key adapter molecule between virus and host processes¹
- ALS-1, by targeting NPs, acts upstream of Neuraminidase 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".

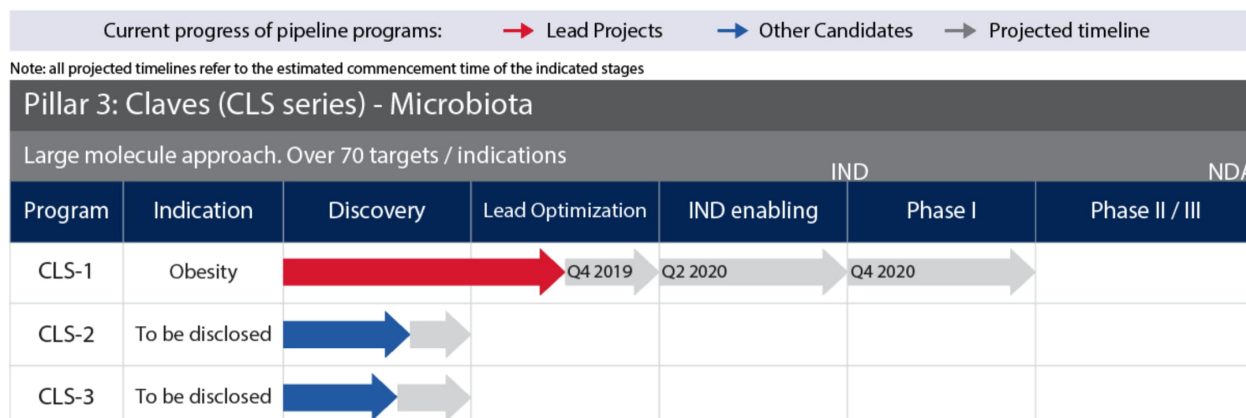


Facilitating Life Science Innovations to Serve Unmet Medical Needs

CLAVES PROJECTS



Claves pipeline overview



CLS-1: binding to therapeutic target

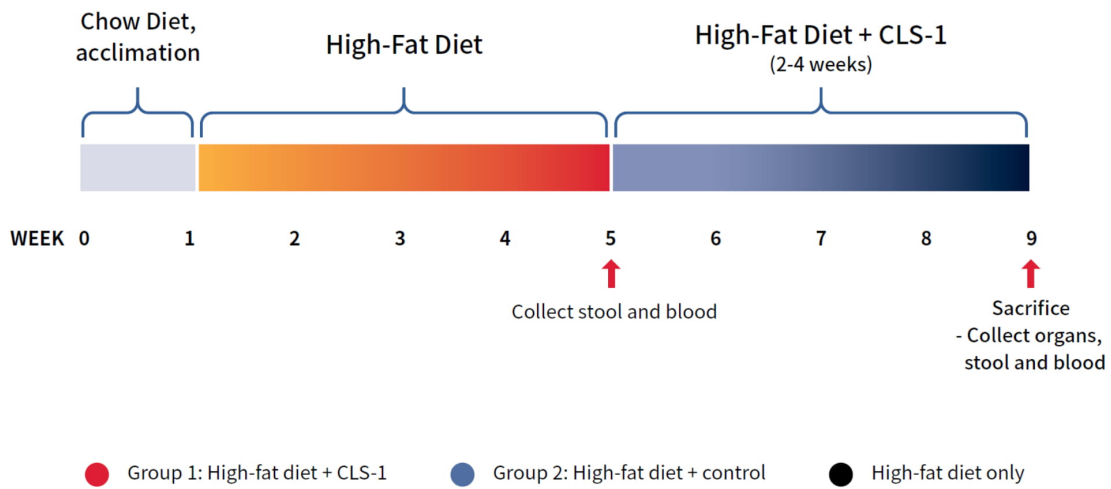
- Identified key microbiota metabolite linked to obesity (therapeutic target)
- Screened different candidates using the Claves platform to target obesity-linked metabolite, by testing the binding capacity of different CLS-1 candidates (with different compositions) to the target metabolites
- A7 was selected for further development

Claves Candidate	Candidate binding of obesity-linked metabolite (mg/g)
A1	2.42
A2	12.32
A3	8.2
A4	7.82
A5	71.9
A6	10.37
A7	33.47

Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing. Applies to all content on this slide.

CLS-1: efficacy in a mouse model

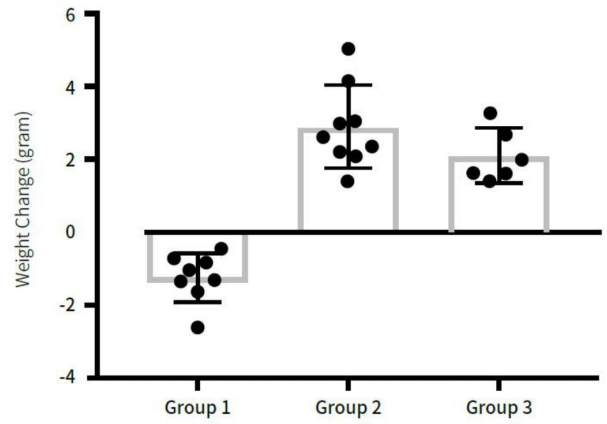
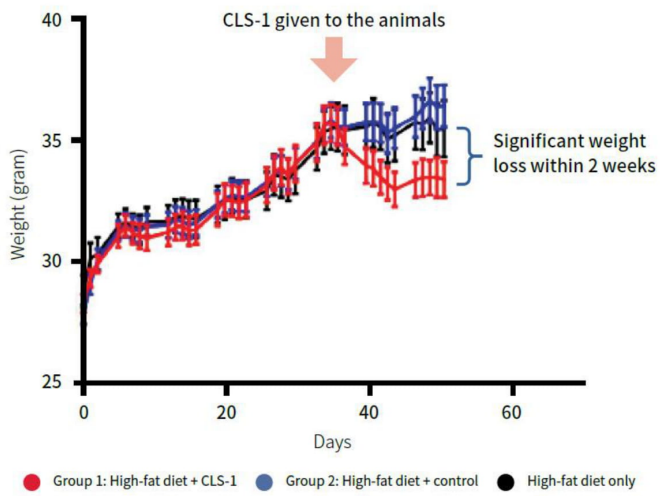
Experimental outline to test efficacy of CLS-1 treatment
(orally available, non-absorbable) in mice on a high-fat diet



Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing. Applies to all content on this slide.

CLS-1: efficacy in a mouse model

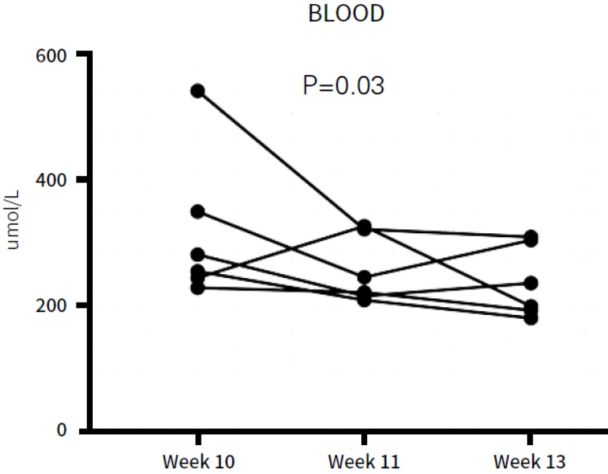
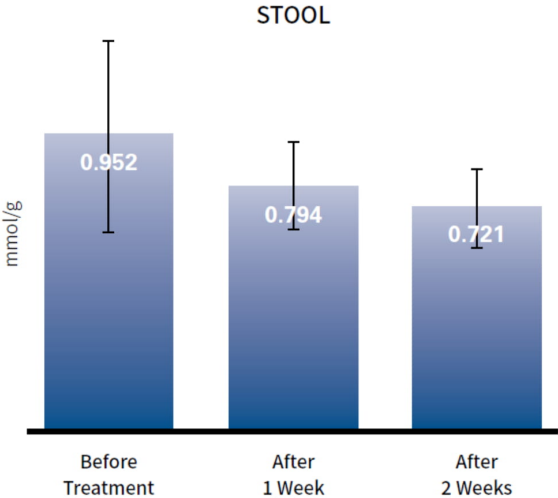
CLS-1 treatment significantly reduces body weight in mice



Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing. Applies to all content on this slide.

CLS-1: pharmacodynamics

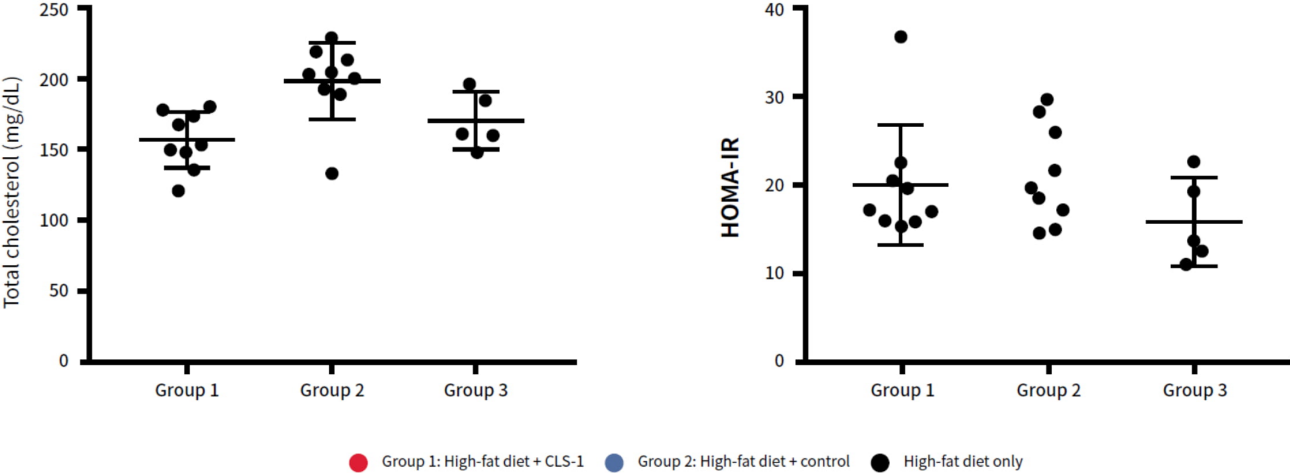
Amount of therapeutic target present in stool and in blood before and after administration of CLS-1



Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing. Applies to all content on this slide.

CLS-1: pharmacodynamics

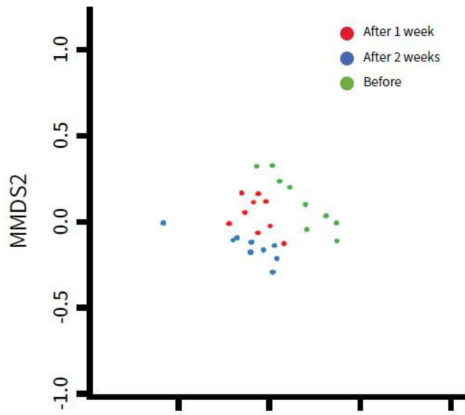
Cholesterol and Insulin Resistance



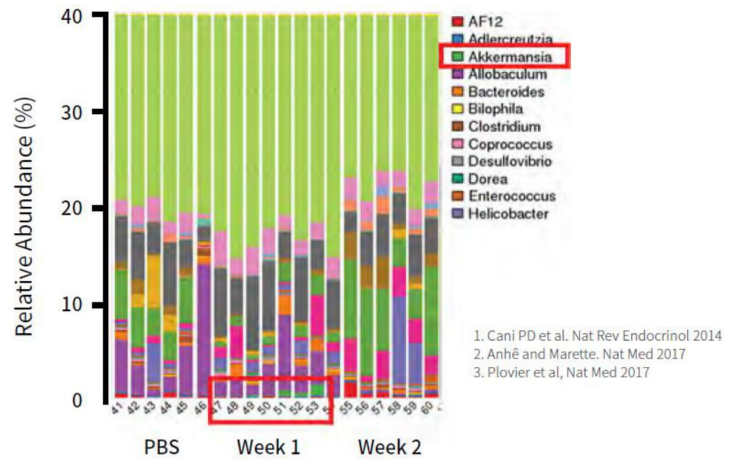
Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing. Applies to all content on this slide.

CLS-1: mechanism of action

CLS-1 induced progressive changes in the microbiota



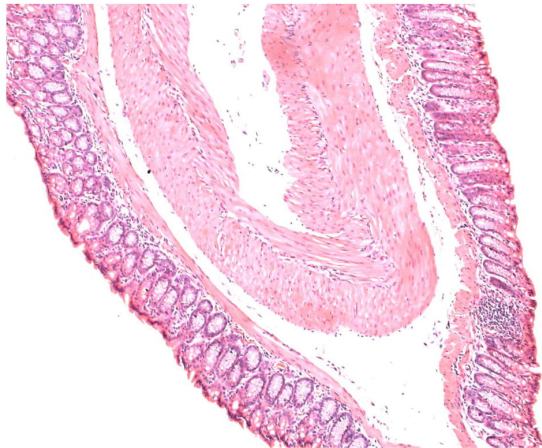
CLS-1 may act by promoting Akkermansia proliferation, a species of beneficial gut bacteria linked to obesity^{1,2,3}



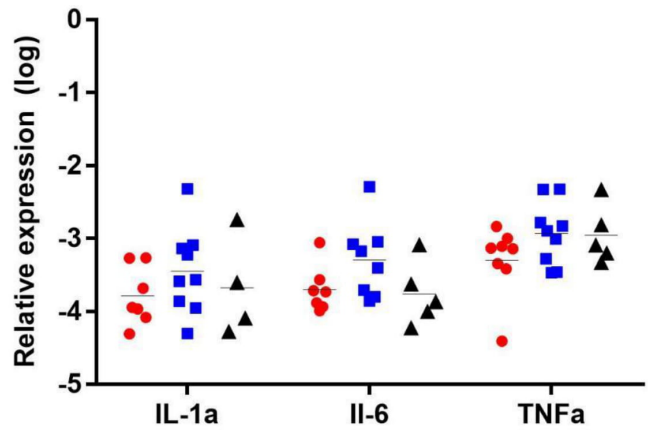
Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing. Applies to all content on this slide.

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

Mucosa and Inflammatory Markers



● Group 1: High-fat diet + CLS-1 ● Group 2: High-fat diet + control ● High-fat diet only



CLS-1 does not upregulate inflammatory markers

Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing. Applies to all content on this slide.

CLS-1: Towards Clinical Trials

Pharmacology & Pharmacokinetics

- *In vivo* non-absorbability and mass balance testing is under planning

Toxicology

- Non-GLP Ames test indicates CLS-1 is not mutagenic

Chemistry, Manufacturing & Control

- CLS-1 is likely a non-absorbable macromolecule
- API manufacturing process has been scaled up to 100g, GLP batch manufacturing is under planning
- Process scale-up at a CRO is currently in progress

Clinical Trial Strategy & Protocol

- Plan to conduct a hybrid Phase 1 trial with both healthy volunteers and patients to provide preliminary efficacy readout, subject to a discussion with the FDA in the IND meeting to be conducted
- Targeting unmet need in obesity

Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing. Applies to all content on this slide.



Facilitating Life Science Innovations to Serve Unmet Medical Needs

DIETARY SUPPLEMENT FOR MENOPAUSAL SYMPTOMS (NLS-2)

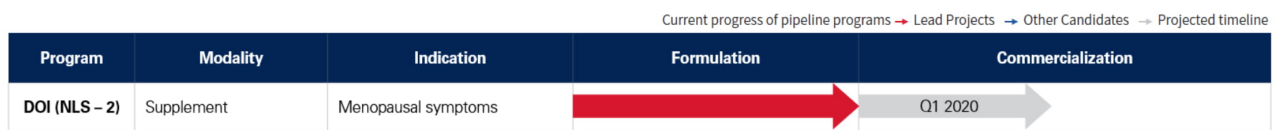


NLS-2: Executive Summary

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 Q1 2020

Timeline



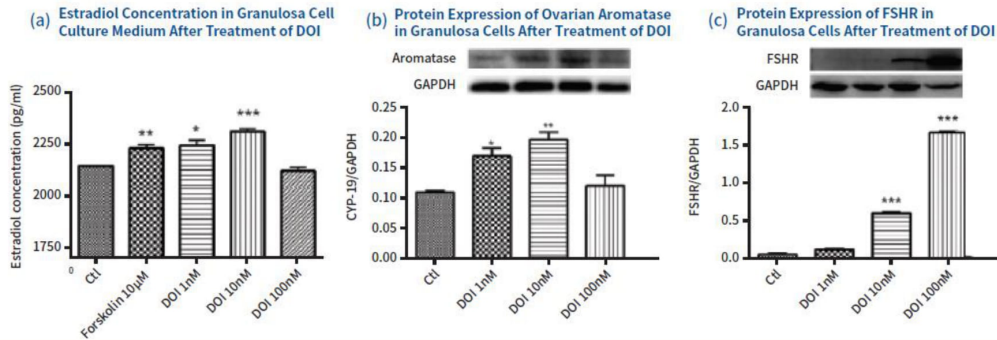
1. Lancet. 2003 Feb 8;361(9356):512-9; 2. Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing; 3. Data available in this presentation

DOI- a Chinese yam extract to address menopausal syndrome

DOI, a novel bioactive peptide with estrogen-stimulating activity¹

- Discovered an estrogen-stimulating activity from an extract obtained from the Chinese yam, *Dioscorea opposita* Thunb
- Identified and isolated a novel bioactive component, DOI, which conferred the estrogen-stimulating activity¹
- DOI significantly increased estradiol biosynthesis and aromatase expression in granulosa cells
- The upregulation of aromatase, an enzyme involved in the production of estrogen, by DOI was found in ovary but not in other cells/tissues

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

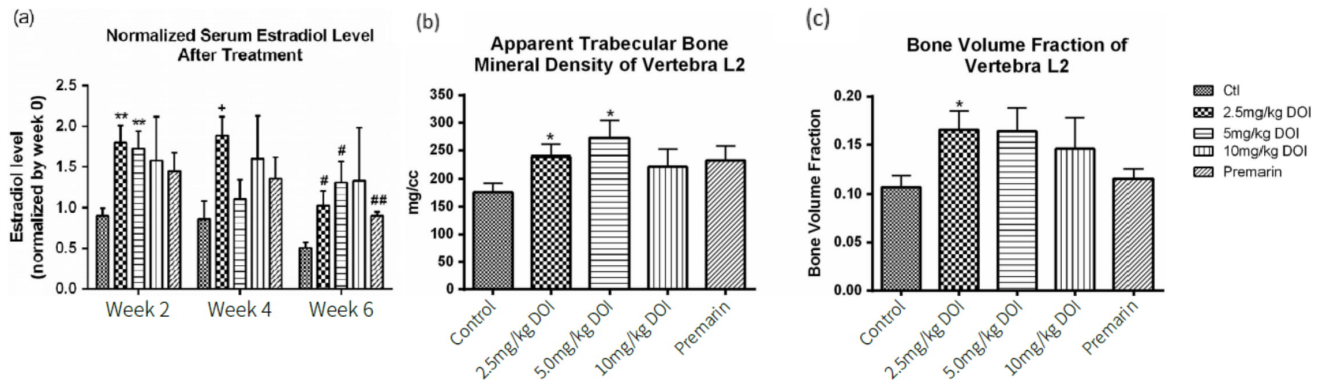


(a) Stimulatory activity of DOI on estrogen biosynthesis in granulosa cells. Protein expression of (b) aromatase and (c) follicle-stimulating hormone receptor (FSHR) in ovarian granulosa cells. Results are expressed as means \pm SEM (n = 3). *P < 0.05, **P < 0.01, ***P < 0.001 compared with the control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

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

DOI- a Chinese yam extract to address menopausal syndrome

In *in vivo* rat models, DOI is shown to stimulate estradiol level and induce estrogen-related gene expressions¹



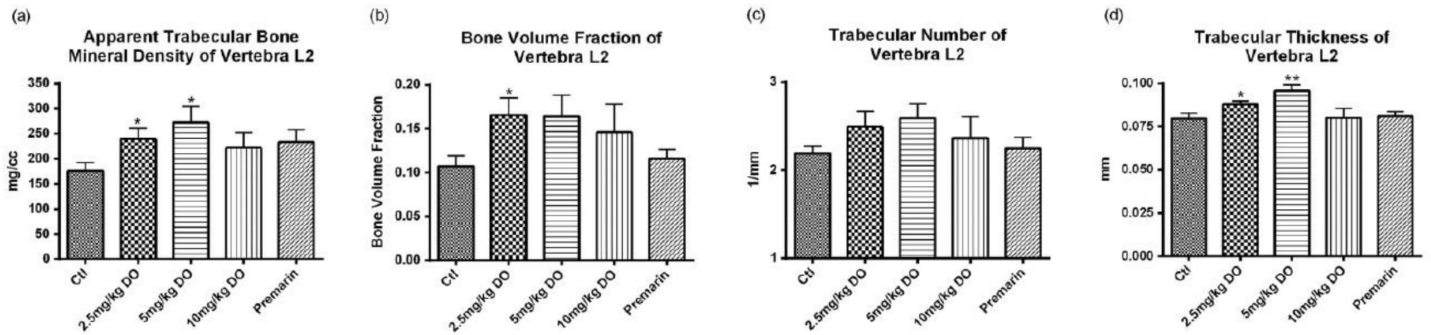
(a) Serum estradiol, (b) apparent trabecular bone mineral density, (c) bone volume fraction of Sprague Dawley rats after treatment with DOI for 2, 4, and 6 weeks. Results are expressed as means \pm SEM (n = 6; except Premarin group, where n = 3). *p < 0.05, **p < 0.01 compared with the control group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

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

DOI- a Chinese yam extract to address menopausal syndrome

DOI and bone density¹

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



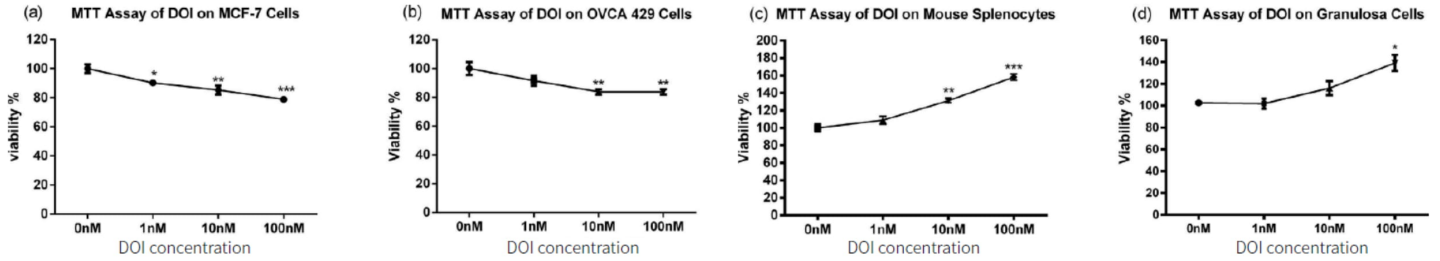
(a) Serum estradiol, (b) apparent trabecular bone mineral density, (c) bone volume fraction of Sprague Dawley rats after treatment with DOI for 2, 4, and 6 weeks. Results are expressed as means \pm SEM (n = 6; except Premarin group, where n = 3). *p < 0.05, **p < 0.01 compared with the control group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

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

DOI- a Chinese yam extract to address menopausal syndrome

DOI does not cause toxicity in vitro based on cell viability in the MTT assay¹

- DOI demonstrated the decrease in viability of MCF-7 breast cancer cells and OVCA-429 ovarian cancer cells, indicating that DOI is not expected to display any of the side effects of hormone replacement therapy, such as the increase in risk of breast and ovarian cancer



Viability of (a) MCF-7 breast cancer cells, (b) OVCA-429 ovarian cancer cells, (c) mouse splenocytes, and (d) ovarian granulosa cells after treatment with DOI for 48h. Results are expressed as means±SEM (n=3). **p

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



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