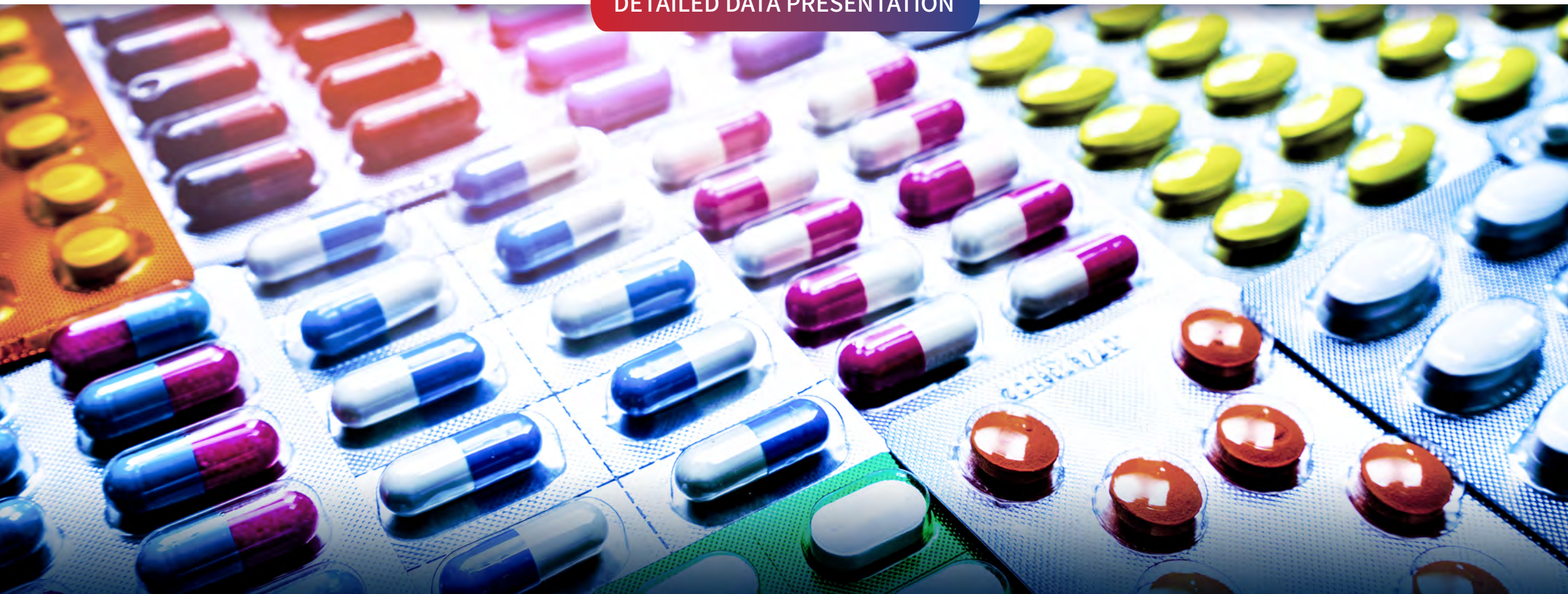
APTORUM

Facilitating Life Science Innovations to Serve Unmet Medical Needs

DETAILED DATA PRESENTATION



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SMART-ACT™: pipeline overview

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

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 PhI/II clinical safety data[1]	*In vivo* validation	Bridging studies	PhII / III with limited population[3]
SACT-1	Neuroblastoma				Q4 2019		ready for clinical trial by Q2/Q3 2020
SACT-2	To be disclosed						
SACT-3	To be disclosed						

IND 505(b)(2) filing[2]

1. Refers to the drug's existing Phase I/II safety data previously conducted by a third party. Does not refer to clinical trials conducted by Aptorum
2. Subject to FDA's approval 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 domain
3. Subject to the FDA's approval

- 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

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

In vitro drug activity against neuroblastoma cell lines IMR-32

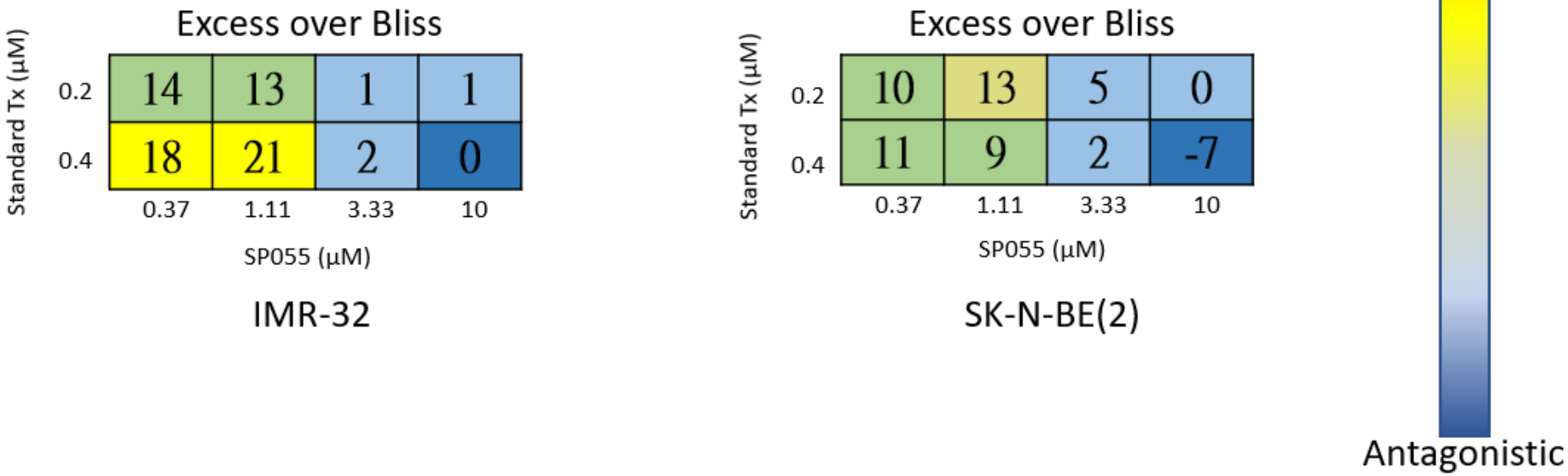
- 48 drug candidates were screened computationally and they were evaluated *in vitro* for activity validation
- 1 candidate, SP055, were found to provide favorable anticancer activities and the results against IMR-32 were tabulated as follow:

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

The above data is based on Aptorum's internal tests and has not yet been verified by clinical trials 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 measured by the Excess over Bliss



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

SP055: safety & tolerability

FDA approved safety profile

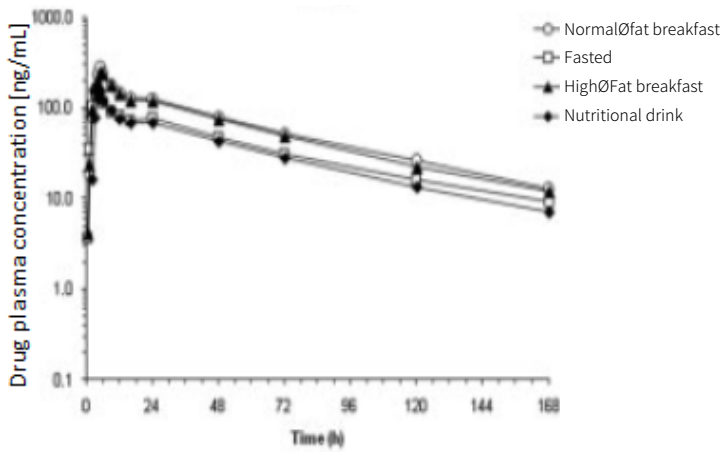
- Did not show a genotoxic potential even at the highest feasible concentration dose (*in vitro* and *in vivo*)
- In a phase IIb study, all SP055 doses were safe and well tolerated over 96 weeks
- Most frequently reported mild adverse drug reactions were nausea and dizziness
- Grade 1-2 rash was reported

	TMC278 25 mg q.d. (*N* = 93)	TMC278 75 mg q.d. (*N* = 95)	TMC278 150 mg q.d. (*N* = 91)	All TMC278 (*N* = 279)	EFV 600 mg q.d. (*N* = 89)
Median treatment duration, weeks (range)	101.4 (1.0–116)	100.1 (0.1–115)	100.4 (2.0–118)	100.4 (0.1–118)	100.4 (0.7–118)
AEs, *n* (%)					
Any grade 2–4 AE at least possibly related to TMC278 or EFV	19 (20.4)	19 (20.0)	19 (20.9)	57 (20.4)**	33 (37.1)
AEs leading to discontinuation	8 (8.6)	11 (11.6)	13 (14.3)	32 (11.5)	8 (9.0)
Any serious AEs	12 (12.9)	13 (13.7)	9 (9.9)	34 (12.2)	13 (14.6)
Deaths	0	2 (2.1)	0	2 (0.7)	0
Most common grade 2–4 AEs at least possibly related to TMC278 or EFV and occurring in ≥ 2% of patients in the combined TMC278 group or EFV group, *n* (%)					
Nausea	3 (3.2)	5 (5.3)	2 (2.2)	10 (3.6)	5 (5.6)
Dizziness	1 (1.1)	1 (1.1)	1 (1.1)	3 (1.1)	3 (3.4)
Abnormal dreams/nightmare	0	2 (2.2)	0	2 (0.7)	3 (3.3)
Dyspepsia	1 (1.1)	1 (1.1)	0	2 (0.7)	2 (2.2)
Asthenia	0	1 (1.1)	1 (1.1)	2 (0.7)	2 (2.2)
Any rash[a]	0	1 (1.1)	0	1 (0.4)***	7 (7.9)
Somnolence	0	1 (1.1)	0	1 (0.4)	2 (2.2)
Vertigo	1 (1.1)	0	0	1 (0.4)	2 (2.2)
[b]Neurological AEs of interest, irrespective of relatedness, *n* (%)					
All grades	31 (33.3)	32 (33.7)	28 (30.8)	91 (32.6)***	53 (59.6)
Grade 1	25 (26.9)	27 (28.4)	21 (23.1)	73 (26.2)**	40 (44.9)
Grade 2	6 (6.5)	5 (5.3)	7 (7.7)	18 (6.5)*	12 (13.5)
Grade 3	0	0	0	0	1 (1.1)
[c]Psychiatric AEs, irrespective of relatedness, *n* (%)					
All grades	16 (17.2)	16 (16.8)	13 (14.3)	45 (16.1)	19 (21.3)
Grade 1	7 (7.5)	7 (7.4)	9 (9.9)	23 (8.2)	9 (10.1)
Grade 2	8 (8.6)	7 (7.4)	2 (2.2)	17 (6.1)	9 (10.1)
Grade 3	1 (1.1)	2 (2.1)	0	3 (1.1)	1 (1.1)
Grade 4	0	0	2 (2.2)	2 (0.7)	0
[a]Rash AEs, irrespective of relatedness, *n* (%)					
All grades	5 (5.4)	9 (9.5)	12 (13.2)	26 (9.3)**	19 (21.3)
Grade 1	3 (3.2)	4 (4.2)	10 (11.0)	17 (6.1)	9 (10.1)
Grade 2	2 (2.2)	4 (4.2)	2 (2.2)	8 (2.9)**	10 (11.2)
Grade 3	0	1 (1.1)	0	1 (0.4)	0
[d]Treatment-emergent grade 3 or 4 laboratory abnormalities observed in ≥2% of patients in the combined TMC278 group or EFV group, *n* (%)					
Any laboratory abnormality	31 (33.7)	21 (22.3)	22 (24.4)	74 (26.8)	21 (24.4)
Decreased neutrophils	9 (9.9)	7 (7.4)	4 (4.4)	20 (7.3)	4 (4.7)
Increased ALT	6 (6.6)	5 (5.3)	5 (5.6)	16 (5.8)	3 (3.5)
Prolonged aPTT	4 (4.3)	3 (3.2)	3 (3.3)	10 (3.6)	4 (4.7)
Increased pancreatic amylase	5 (5.5)	1 (1.1)	4 (4.4)	10 (3.6)	3 (3.5)
Increased LDL-cholesterol	3 (3.3)	3 (3.2)	2 (2.2)	8 (2.9)	4 (4.7)
Increased AST	3 (3.3)	3 (3.2)	3 (3.3)	9 (3.3)	3 (3.5)
Increased lipase	4 (4.4)	0	3 (3.3)	7 (2.5)	0
Decreased haemoglobin	2 (2.2)	2 (2.1)	2 (2.2)	6 (2.2)	0
Increased total cholesterol	1 (1.1)	1 (1.1)	0	2 (0.7)*	4 (4.7)
Hypocalcaemia	2 (2.2)	0	0	2 (0.7)	2 (2.3)
Increased INR	0	0	3 (3.3)	3 (1.1)	2 (2.3)
Mean change from baseline (SD) in lipid parameters at 96 weeks					

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



Pharmacokinetics of SP055 administered with different meal types and under fasting conditions

Pharmacokinetic parameter	Normal-fat breakfast (reference; n = 19)	Fasting conditions (test; n = 19)	High-fat breakfast (test; n = 19)	Protein-rich drink (test; n = 18)
t_{max}, h	5.0 (2.0–9.0)	4.0 (2.0–24.0)	5.0 (3.0–9.0)	5.0 (4.0–9.0)
C_{max}, ng/mL	296 ± 118	170 ± 66	280 ± 103	156 ± 60
AUC_{last}, ng · h/mL	10,340 ± 3,894	6,230 ± 2,339	9,717 ± 3,535	5,437 ± 2,421
AUC_{inf}, ng · h/mL	11,450 ± 4,431	7,202 ± 3,024	10,670 ± 4,331	6,094 ± 3,047
$t_{1/2,term}$, h[a]	48 ± 22	55 ± 28	43 ± 17	47 ± 23
Least-squares means ratio for test to reference (90% confidence interval)				
C_{max}	—	0.54 (0.43–0.69)	0.92 (0.81–1.05)	0.50 (0.40–0.63)
AUC_{last}	—	0.57 (0.46–0.72)	0.92 (0.80–1.07)	0.50 (0.41–0.61)
AUC_{inf}	—	0.59 (0.47–0.74)	0.91 (0.79–1.05)	0.51 (0.42–0.62)

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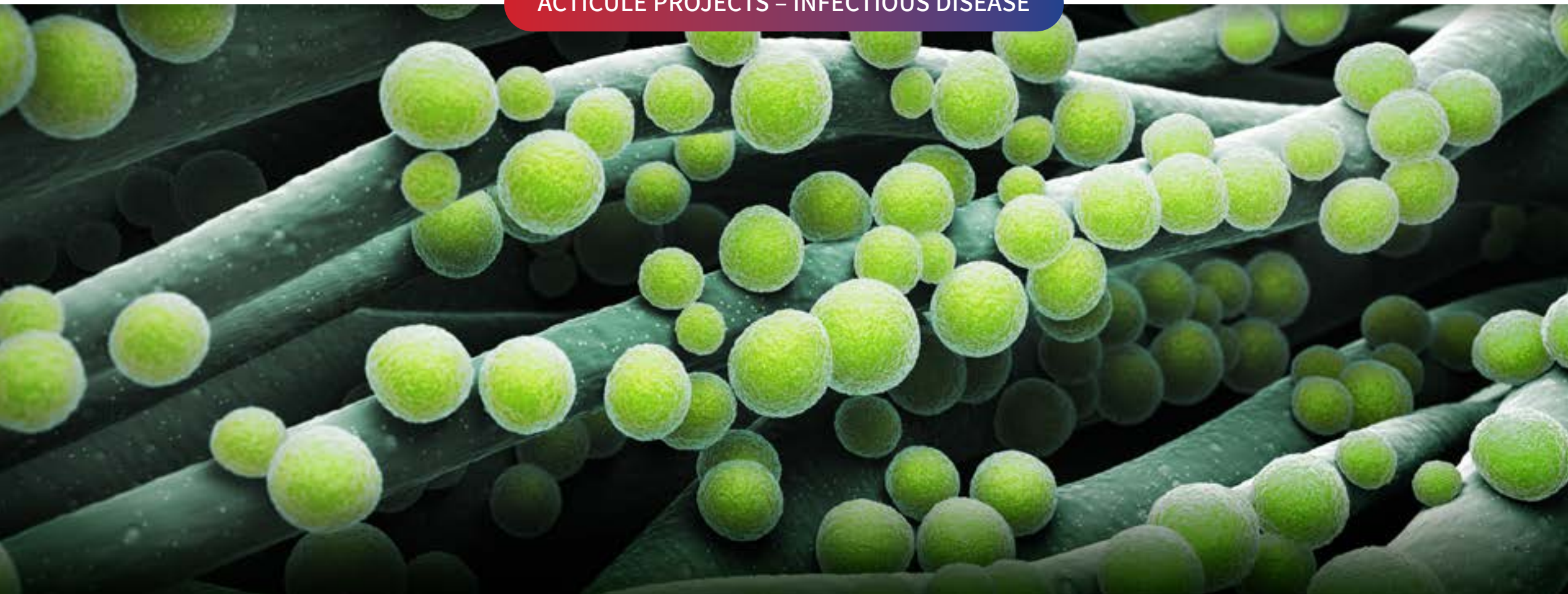
ACTICULE PROJECTS – INFECTIOUS DISEASE



Executive summary: Acticule projects

ALS-4

- Aptorum's lead program ALS-4 is an anti-virulent, non-bactericidal drug candidate for *Staphylococcus aureus* infections including MRSA[1]
- Unlike all major treatments on the market[2], ALS-4 relies on an anti-virulent non-bactericidal approach[1], 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 vitro*[1]
- Viral resistance to Tamiflu and other neuraminidase inhibitors has risen rapidly in recent years[3]
- 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 bacteria[1]
- In discovery/lead optimization stage and generating good traction towards doing IND-enabling studies[1]

1. Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing; 2. 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

For illustrative purposes only. There is no guarantee of any project being completed or having a specific outcome.

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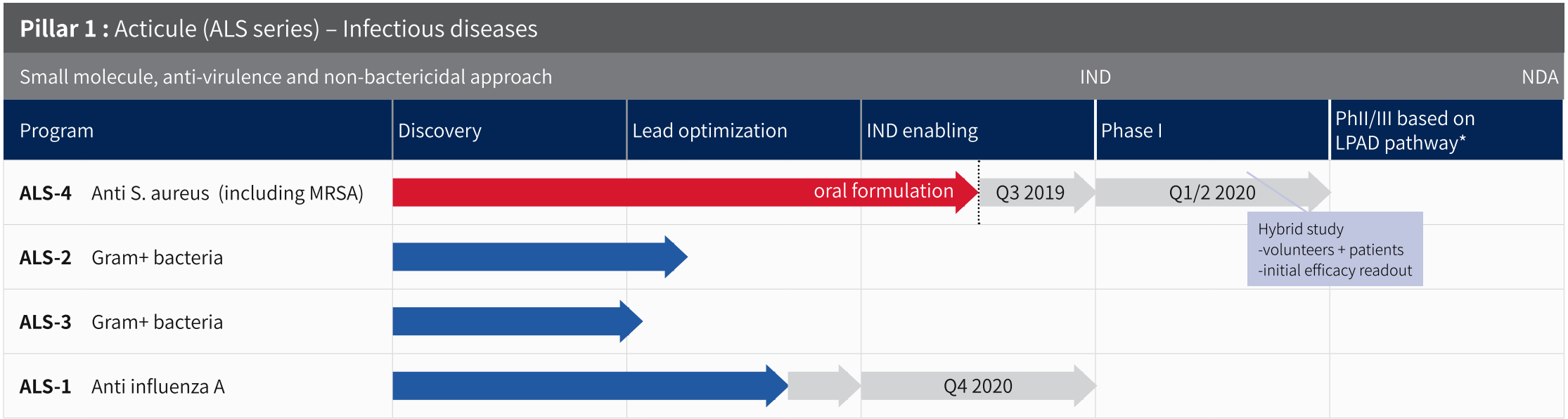
ALS pipeline overview

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

Pillar 1 : Acticule (ALS series) – Infectious diseases

Small molecule, anti-virulence and non-bactericidal approach



*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.

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

For illustrative purposes only. There is no guarantee of any project being completed or having a specific outcome.

ALS-4: mechanism of action

ALS-4
inhibits a key enzyme in the biosynthesis of staphyloxanthin[1]

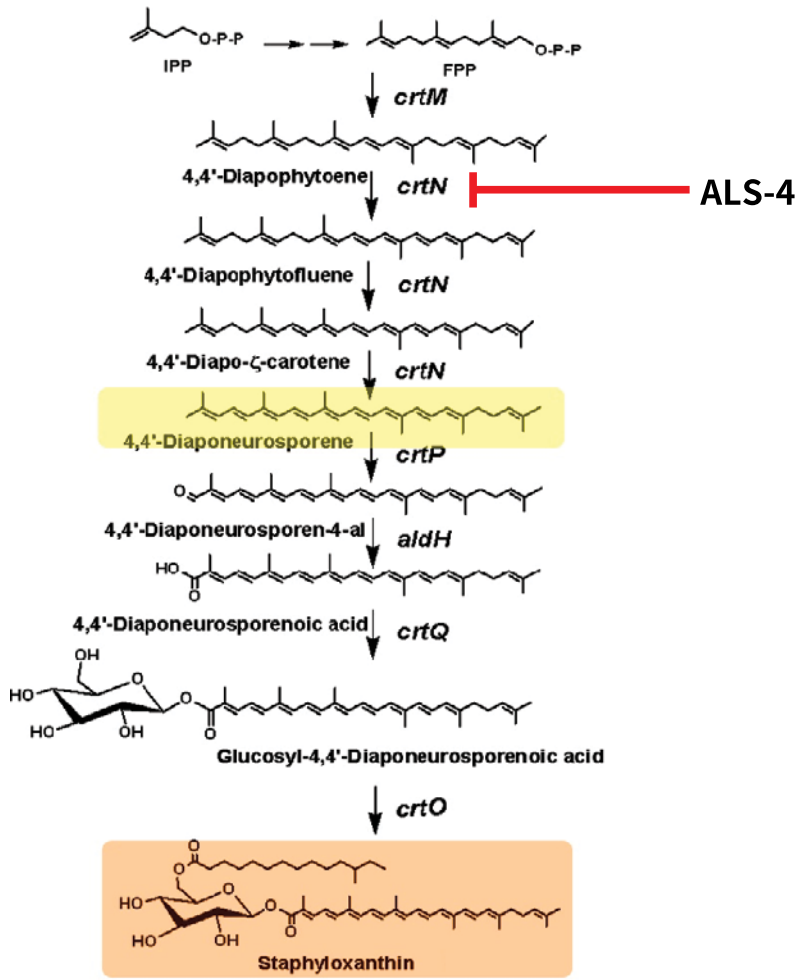
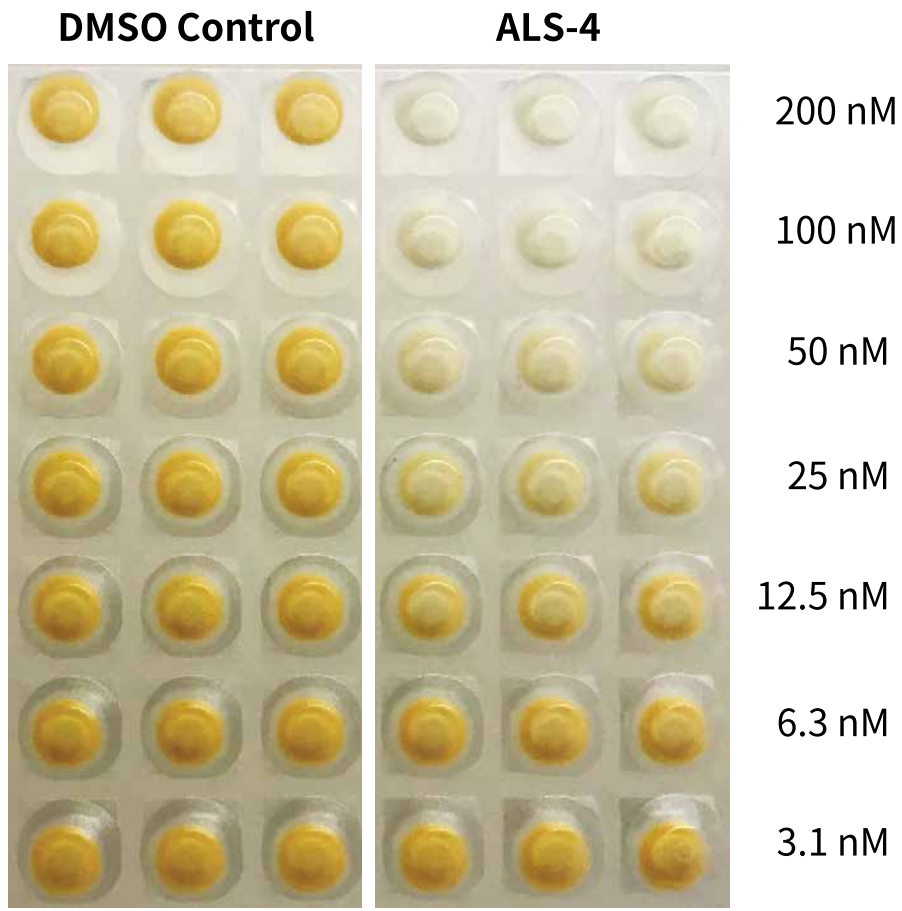


Figure adapted from MBio. 2017 Sep 5;8(5). pii: e01224-17.

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

ALS-4: mechanism of action

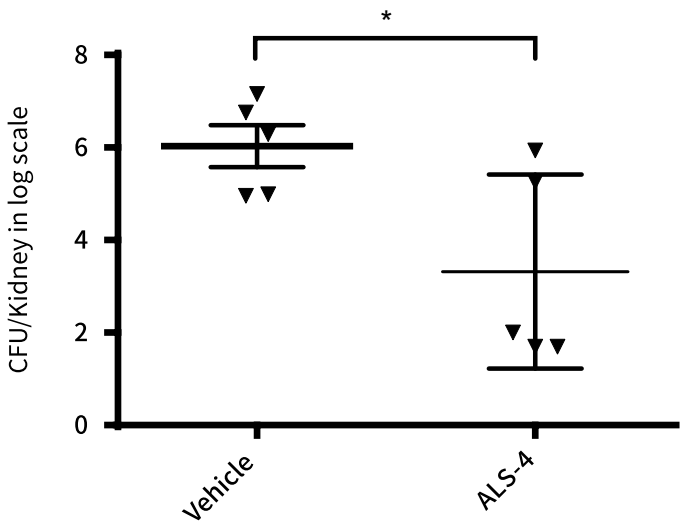
ALS-4
inhibits S. aureus pigment production with an IC_{50} = 20nM



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.

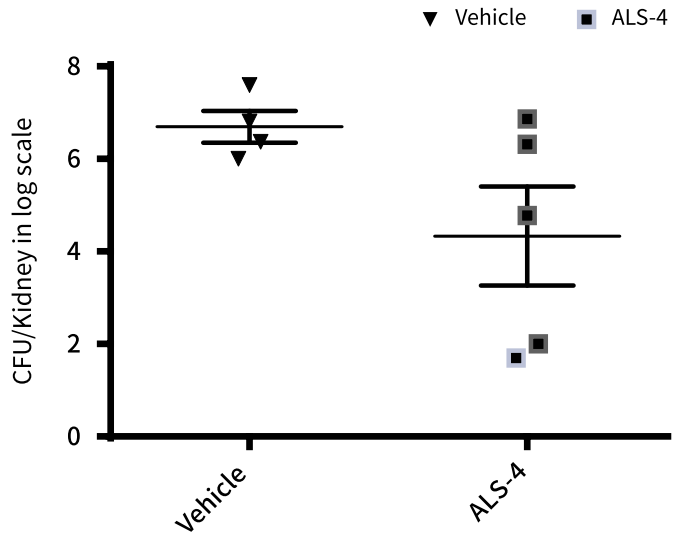
ALS-4 inhibits S. aureus pigment production with an IC_{50} = 20nM

ACUTE TREATMENT



Compound concentration:	1 mM
Inoculum:	5 X 10^6 per mouse
Treatment:	twice for first 7 days
First inject:	30 min after infection

DELAYED TREATMENT



Compound concentration:	1 mM
Inoculum:	2 X 10^7 per mouse
Treatment:	twice for 7 days
First inject:	11 days after infection

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: 60µl overnight culture was added to 6ml BHI broth with different drugs.
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 Ery resistant)

Groups	Day 1-4	Day 5-10
1	DMSO	DMSO
2	ERY + CLI	ERY
3	ALS-4	ALS-4

3. Culturing: medium was changed every day by centrifugation of the bacteria and replacing the supernatant with new medium plus DMSO or antibiotics or compounds as specified

4. Bacteria collection: on day 11, 1ml bacteria was centrifuged and resuspended in PBS with 10% DMSO for further testing

5. MIC testing: in BHI medium in 96-well plate and cultured for 16hr

6. Pigment production: in 96 deep-well plate and cultured for 36hr

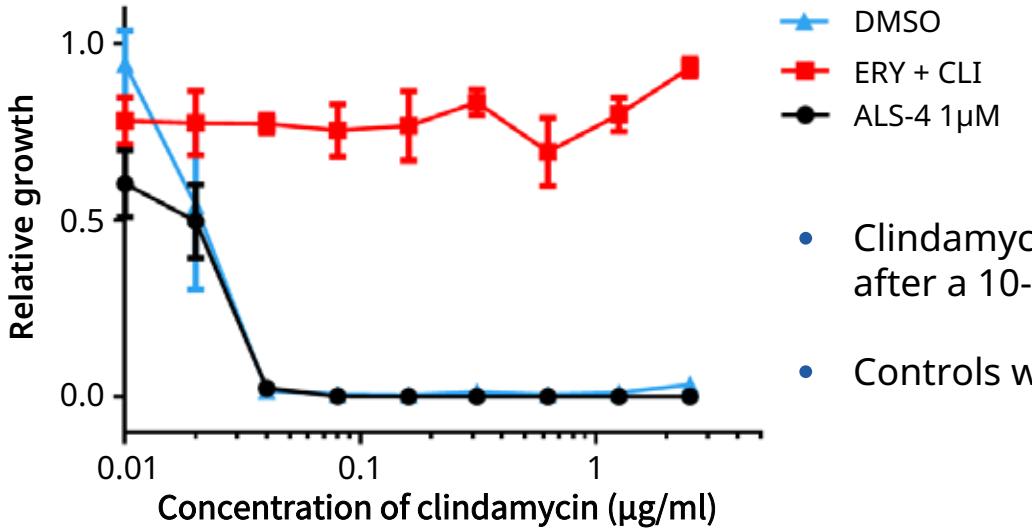
Resistance of *S. aureus* USA 300(lac) to clindamycin after various treatment conditions

Pre-treatment

Groups	Day 1-4	Day 5-10
1	DMSO	DMSO
2	ERY + CLI	ERY
3	ALS-4	ALS-4

(Clindamycin withdrawn between day 5-10)

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

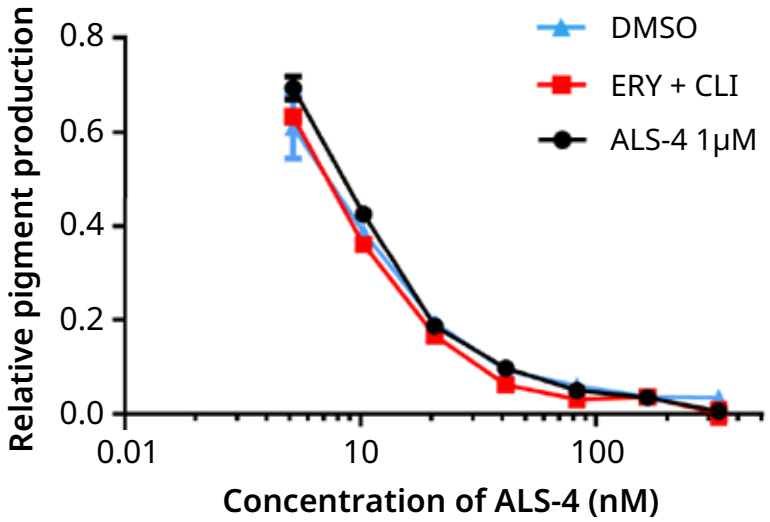


- Clindamycin resistance (MIC from 0.12 µg/ml to >5 µg/ml) appeared rapidly after a 10-day intermittent treatment
- Controls without the addition of antibiotics showed no resistance to clindamycin

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

Pigment production of *S. aureus* with different treatments

ALS-4 efficacy test (Bacterial inoculum: 4 x 10^7/ml)



BHI agar plates

	No ALS-4 (all colonies turned white)	100nM ALS-4 (all colonies remained yellow)
Recovered bacteria after 11-day resistance-raising with 1μM ALS-4		
Recovered bacteria after 11-day resistance-raising with DMSO as control		

No bacteria were resistant to ALS-4 after continuous incubation of the bacteria in the presence of 1μM ALS-4 for 11 days

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

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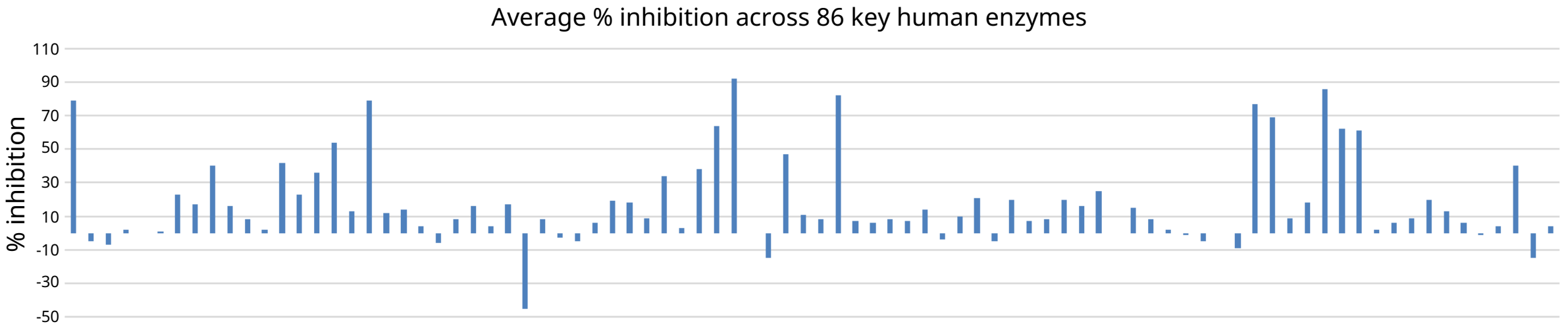
ALS-4: pharmacology & toxicology

In vitro safety screening

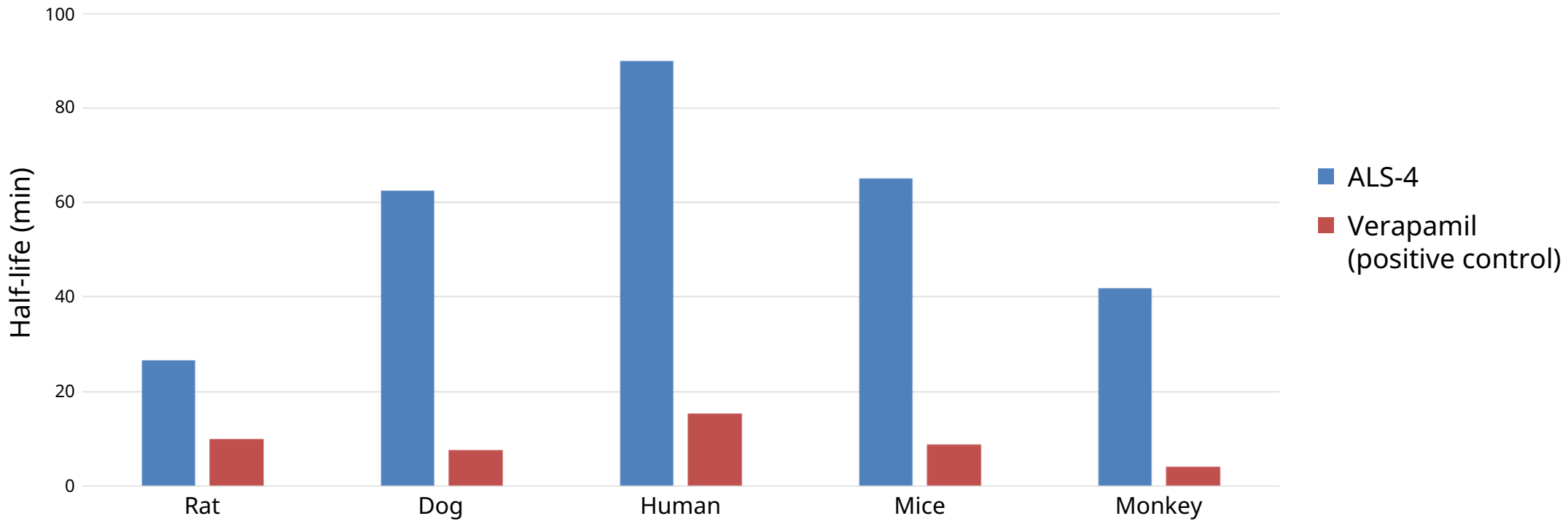


- Average inhibition of 17.5% across 86 key human enzymes
- Enzyme inhibition assay shows that ALS-4 has a clean profile with little off-target inhibition
- Key enzymes including hERG, P450, MAO and UDP are all unaffected

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

ALS-4: pharmacology & toxicology

In vitro metabolism study using liver microsomes from 5 different species



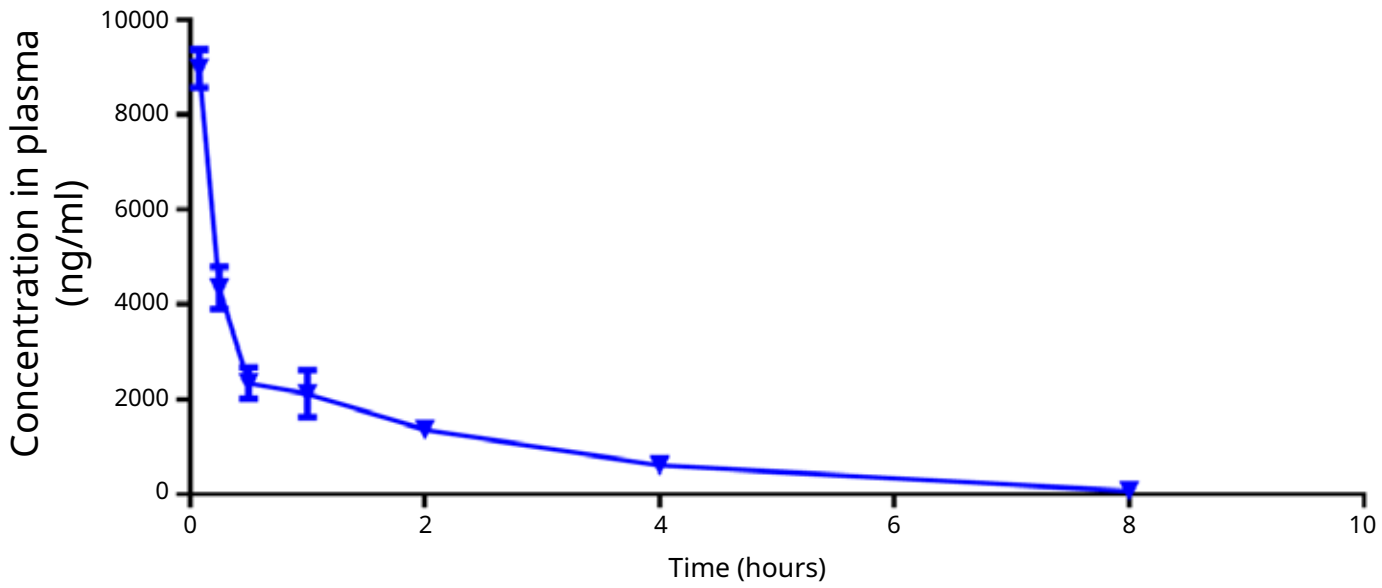
- Liver microsome studies show low intrinsic clearance in 5 different species, including human. Results suggests indicating slow metabolism

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

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
$AUC_{0\text{-}Tlast}$ (ng*hr/mL)	9732
$AUC_{0\text{-}\infty}$ (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

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

ALS-4: pharmacology & toxicology

GLP AMES test for mutagenicity

Mean of negative control
SD of negative control

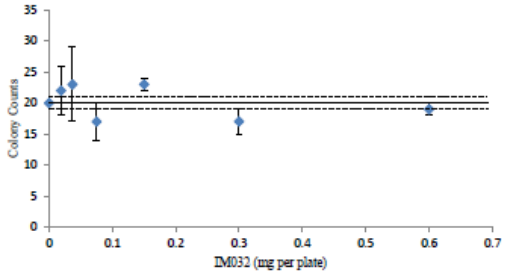


Figure 1. (TA98, -S9) - Mean colony counts ± SD were plotted against the test item concentration.

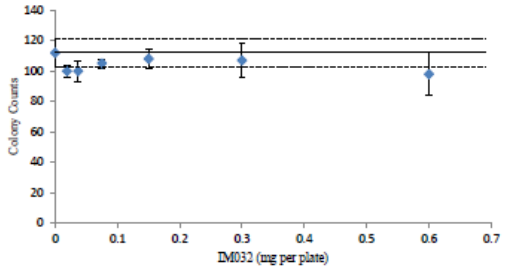


Figure 3. (TA100, -S9) - Mean colony counts ± SD were plotted against the test item concentration.

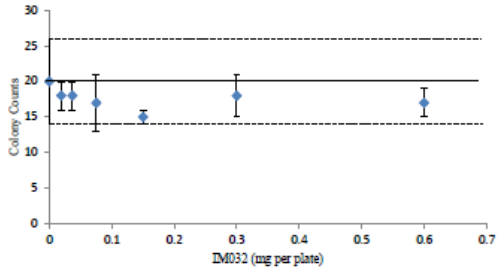


Figure 5. (TA1535, -S9) - Mean colony counts ± SD were plotted against the test item concentration.

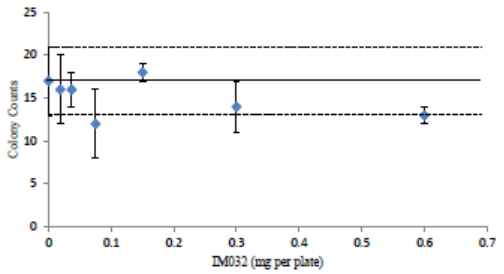


Figure 7. (TA1537, -S9) - Mean colony counts ± SD were plotted against the test item concentration.

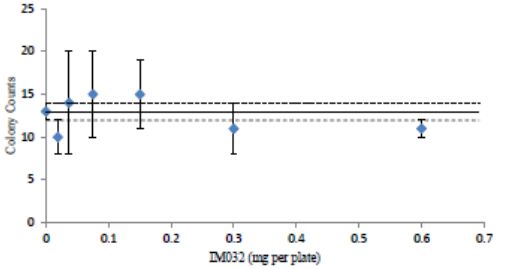


Figure 9. (WP2 *uvrA*, -S9) - Mean colony counts ± SD were plotted against the test item concentration.

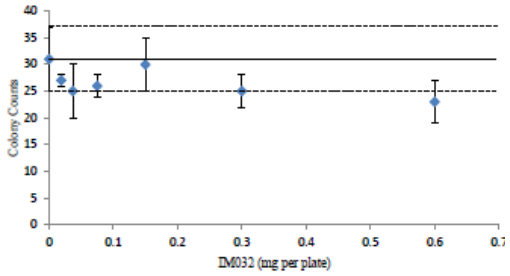


Figure 2. (TA98, +S9) - Mean colony counts ± SD were plotted against the test item concentration.

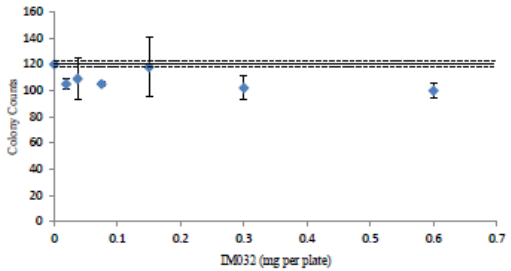


Figure 4. (TA100, +S9) - Mean colony counts ± SD were plotted against the test item concentration.

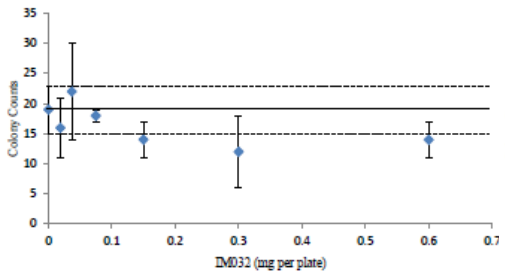


Figure 6. (TA1535, +S9) - Mean colony counts ± SD were plotted against the test item concentration.

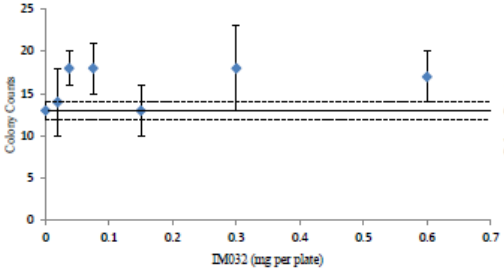


Figure 8. (TA1537, +S9) - Mean colony counts ± SD were plotted against the test item concentration.

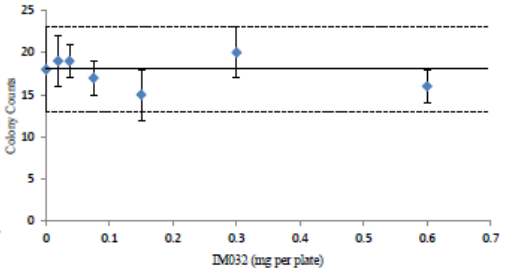


Figure 10. (WP2 *uvrA*, +S9) - Mean colony counts ± SD were plotted against the test item concentration.

- 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

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

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ALS-4: chemistry, manufacturing and controls

ALS-4 properties

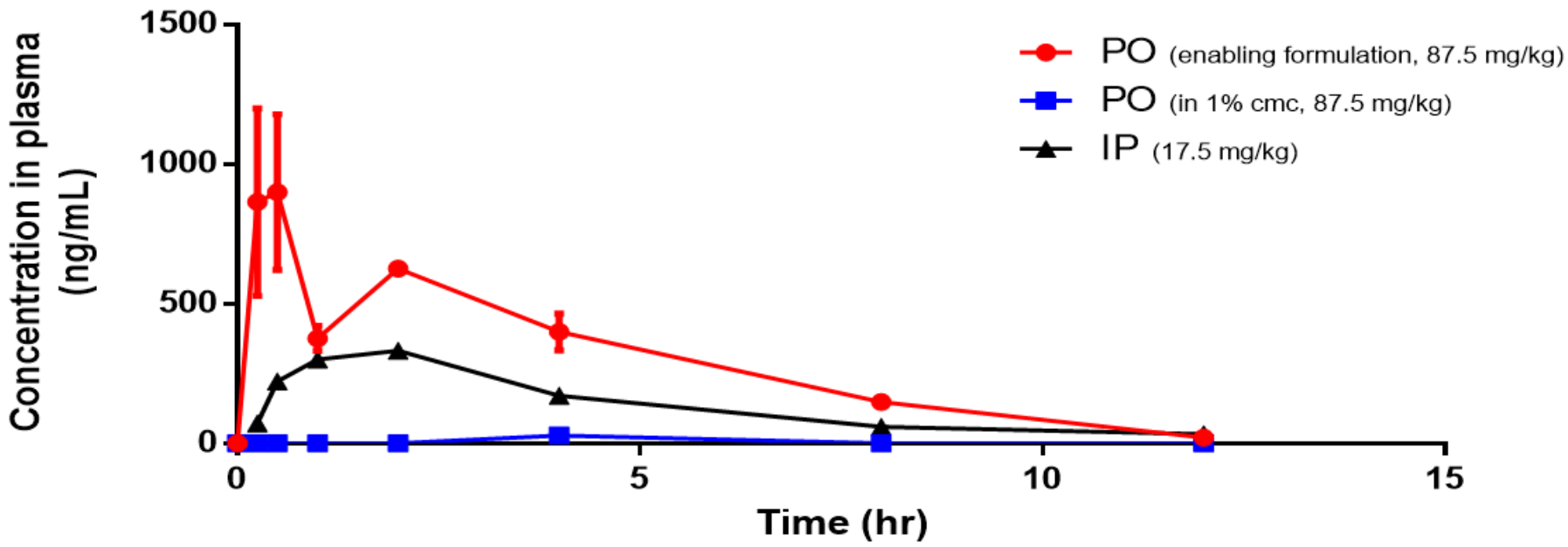
Molecular weight (g/mol)	449.36
LogD[1] pH7.4	4.43
pka(s)[1]	14.5
Caco-2 permeability	2.27 x 10^{-4} cm/s (non-pgp substrate)
Permeability (Human jejunum, pH 6.5)	7.39 x 10^{-4} cm/s
In vitro CL (human, monkey, dog, rat, mouse liver microsomes)	94.97, 335.4, 170.92, 145.8, 180 (µL/min/mg)
Plasma protein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

[1]Calculated properties using ACD/Labs (Release 2017.2.1)

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

ALS-4: chemistry, manufacturing and controls

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

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

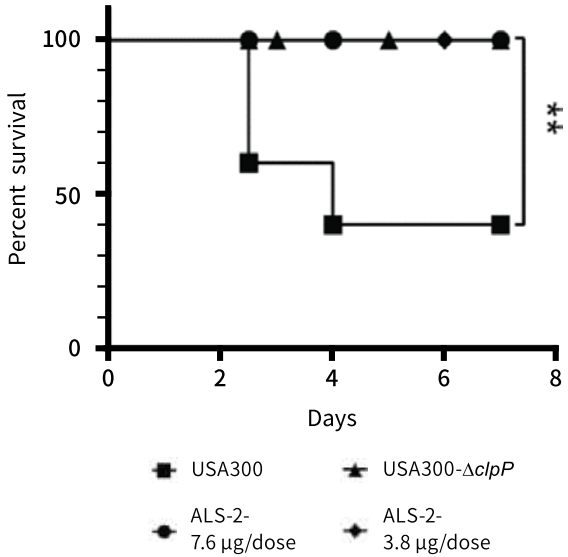
The above data is based on Aptorum's internal tests and has not yet been verified by clinical trials or third party testing

ALS-2 & ALS-3

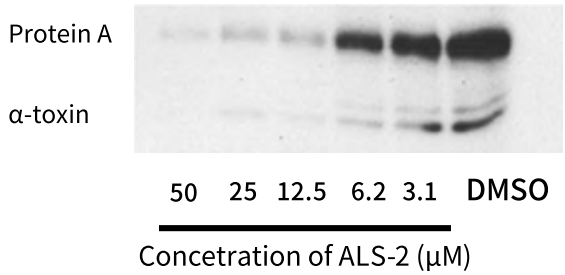
Additional anti-virulence, non-bactericidal therapeutics for the treatment of infections caused by Gram Positive bacteria

ALS-2 Anti-virulence compound that suppresses multiple unrelated virulence factors in *S. aureus*[1]

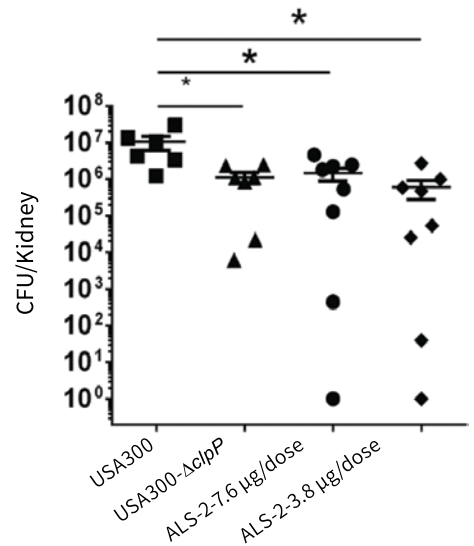
ALS-2 rescues mice from MRSA infection[1]



ALS-2 reduces virulence gene production[1]



ALS-2 reduces bacterial load in mice[1]



ALS-3 Antibiotic-potentiating compound by using a non-bactericidal approach

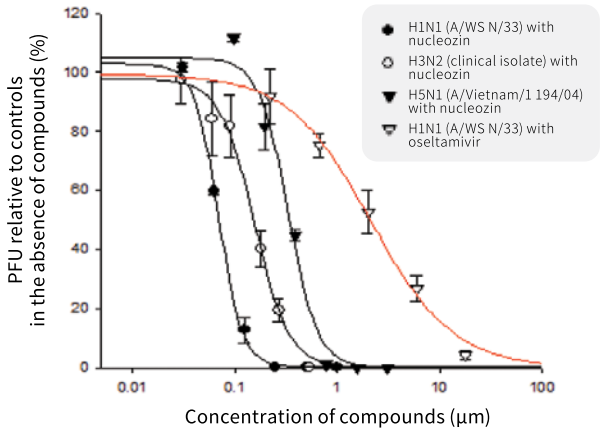
1. Proc Natl Acad Sci U S A. 2018 Jul 31;115(31):8003-8008

ALS-1: targetting a novel druggable target for influenza A

ALS-1 INHIBITS INFLUENZA A NUCLEOPROTEIN (NP)

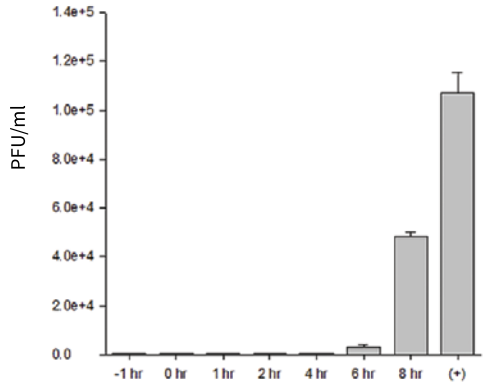
- NP is the most abundantly expressed protein during the course of an infection[1]. Its primary function is to encapsidate the virus genome for RNA transcription, replication and packaging. It is also a key adapter molecule between virus and host processes[1]
- ALS-1, by targeting NPs, acts upstream of Neuraminidase inhibitors such as Tamiflu, which target the last stage (budding) of the viral life cycle[2]. This novel mechanism distinguishes ALS-1 from all other currently marketed antiviral drugs

ALS-1 outperforms Tamiflu®
(oseltamivir, in red) *in vitro* with a lower IC_{50}[2]



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 IC_{50} 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 events[2]



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

APTORUM

Facilitating Life Science Innovations to Serve Unmet Medical Needs

CLAVES PROJECTS

Claves pipeline overview

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

Pillar 2 : Claves (CLS series) - Microbiota

Large molecule approach. Over 70 targets / indications

IND **NDA**

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

- CLS-2 & CLS-3 are additional Claves assets targeting diseases with unmet needs

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

CLS-1: binding to therapeutic target

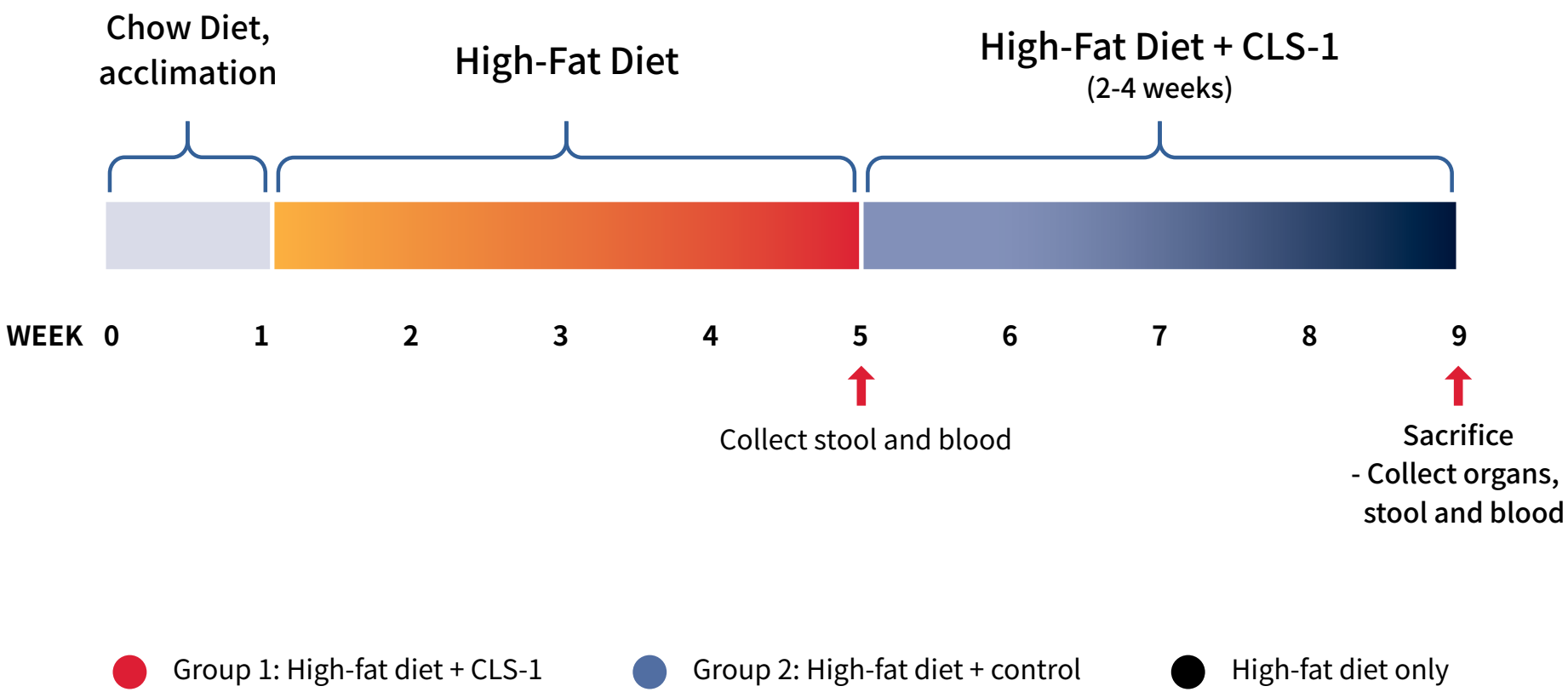
- Identified key microbiota metabolite linked to obesity (therapeutic target)
- Screened different candidates using the Claves platform to target obesity-linked metabolite, by testing the binding capacity of different CLS-1 candidates (with different compositions) to the target metabolites
- A7 was selected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

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

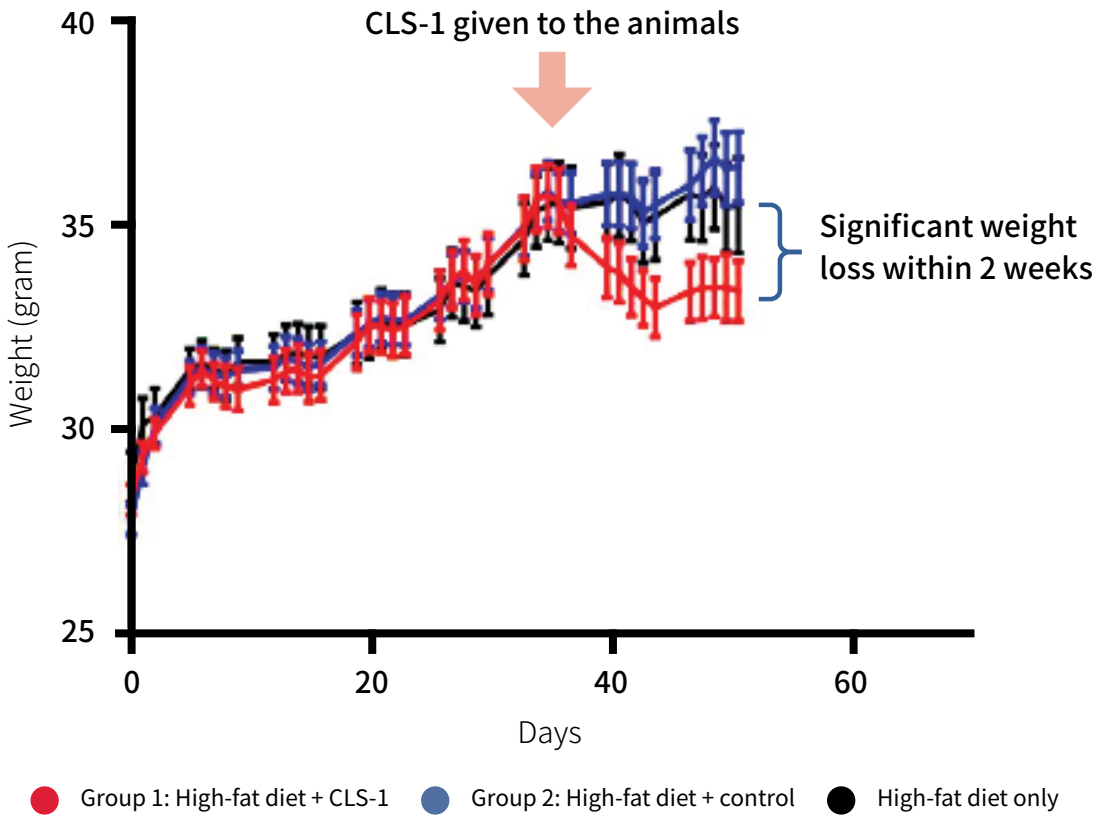
CLS-1: efficacy in a mouse model

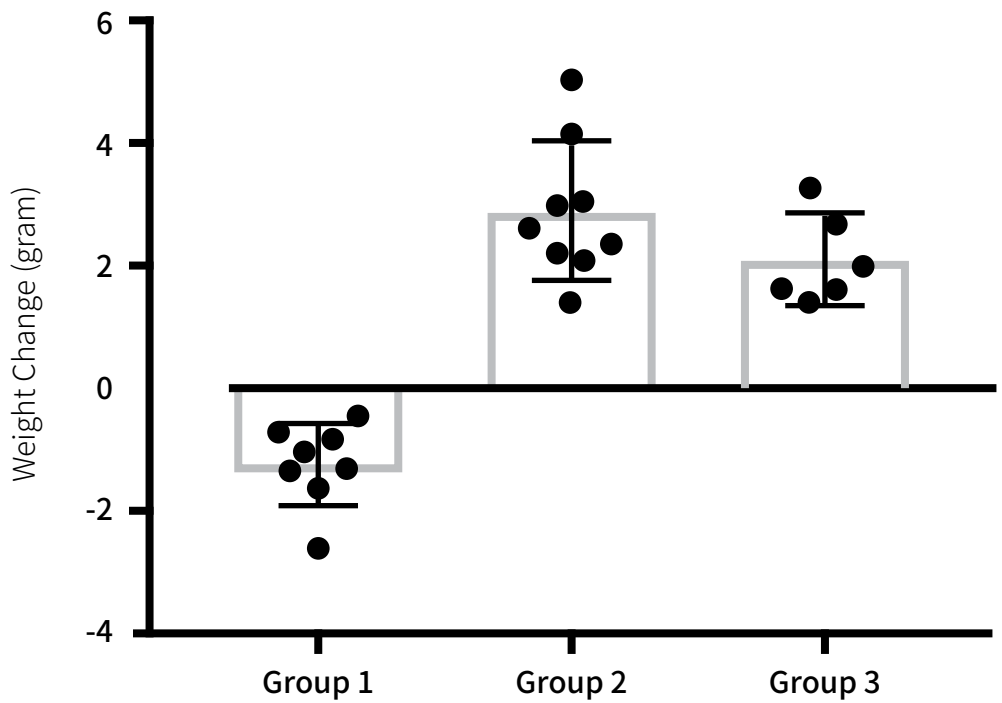
Experimental outline to test efficacy of CLS-1 treatment (orally available, non-absorbable) in mice on a high-fat diet



CLS-1: efficacy in a mouse model

CLS-1 treatment significantly reduces body weight in mice





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

For illustrative purposes only. There is no guarantee of any project being completed or having a specific outcome.

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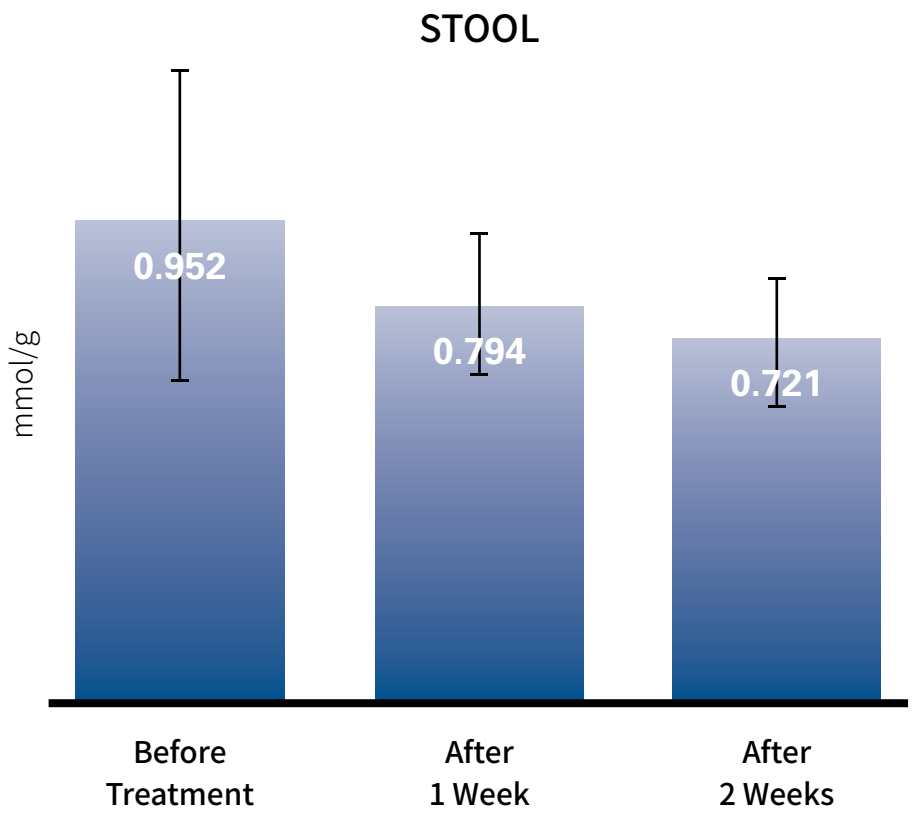
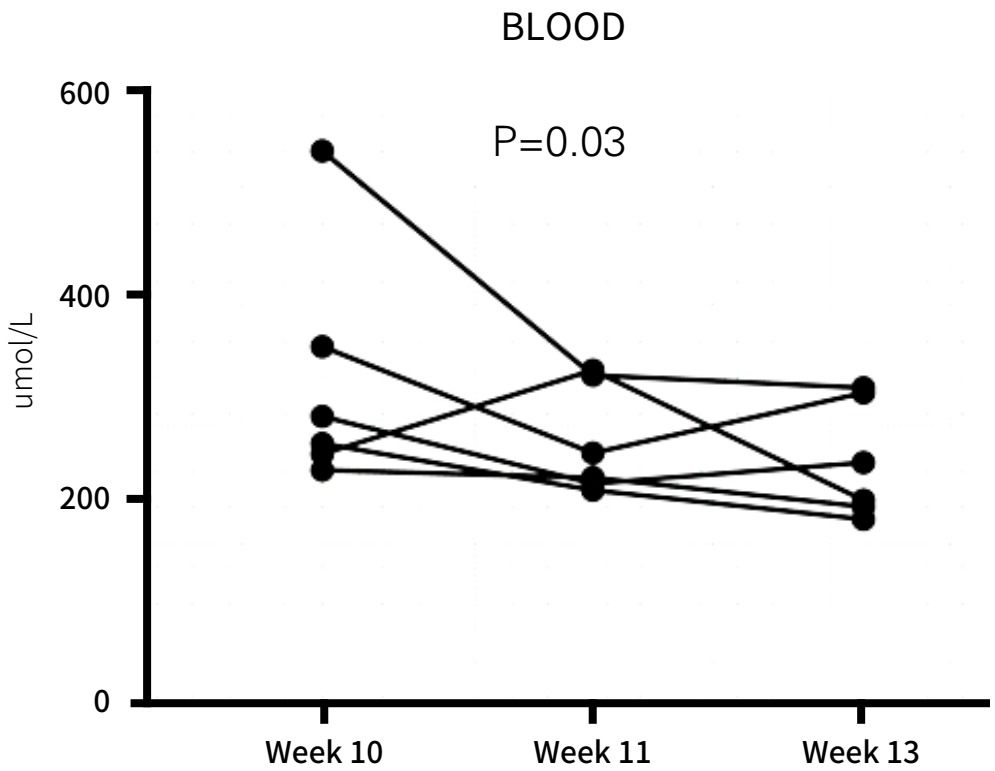
CLS-1: pharmacodynamics

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

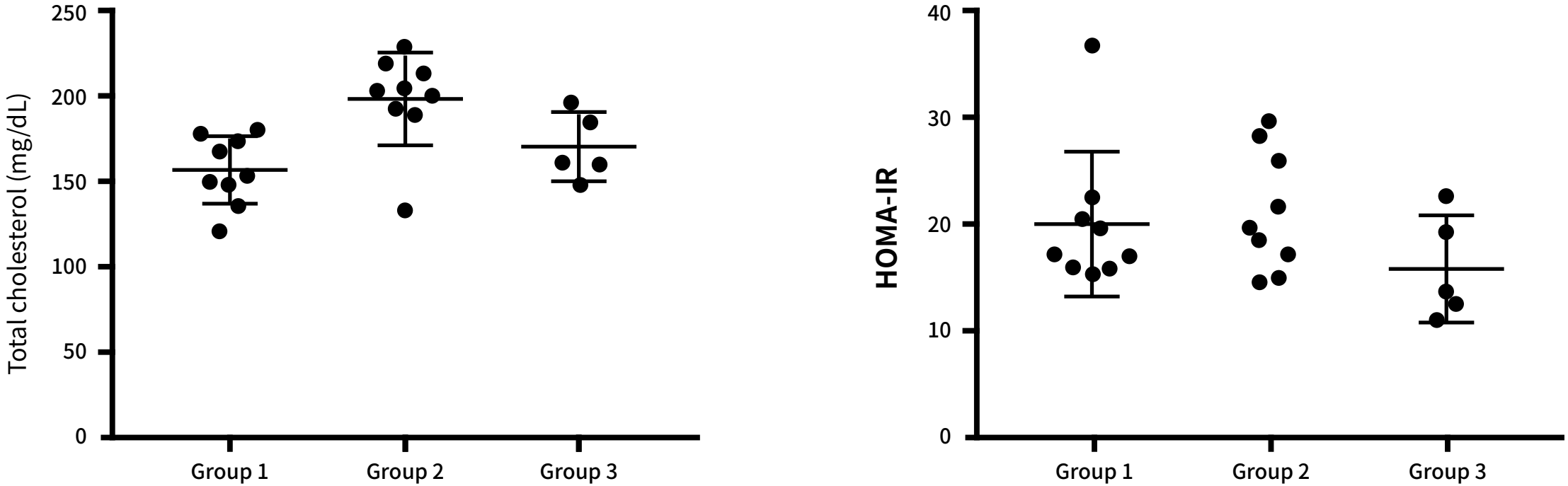




The above data are based on Aptorum's internal tests and has not yet been verified by clinical trials or third party testing.

CLS-1: pharmacodynamics

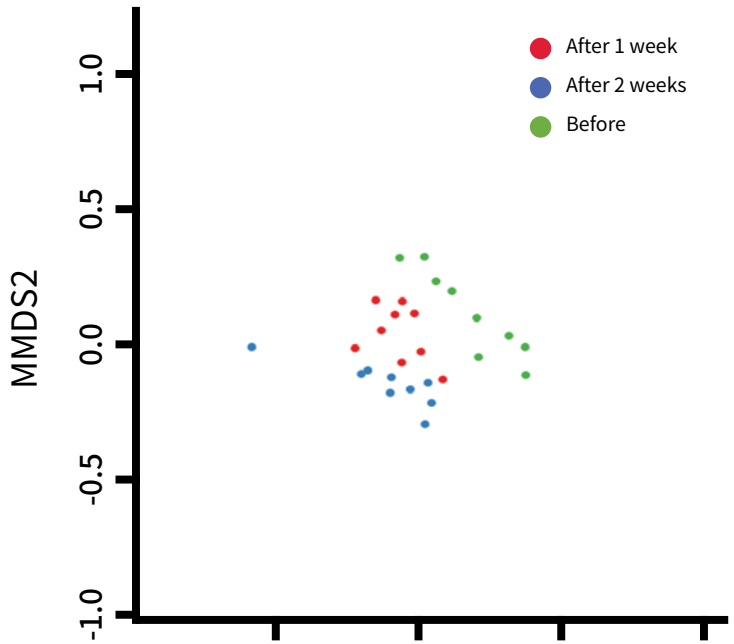
Cholesterol and Insulin Resistance



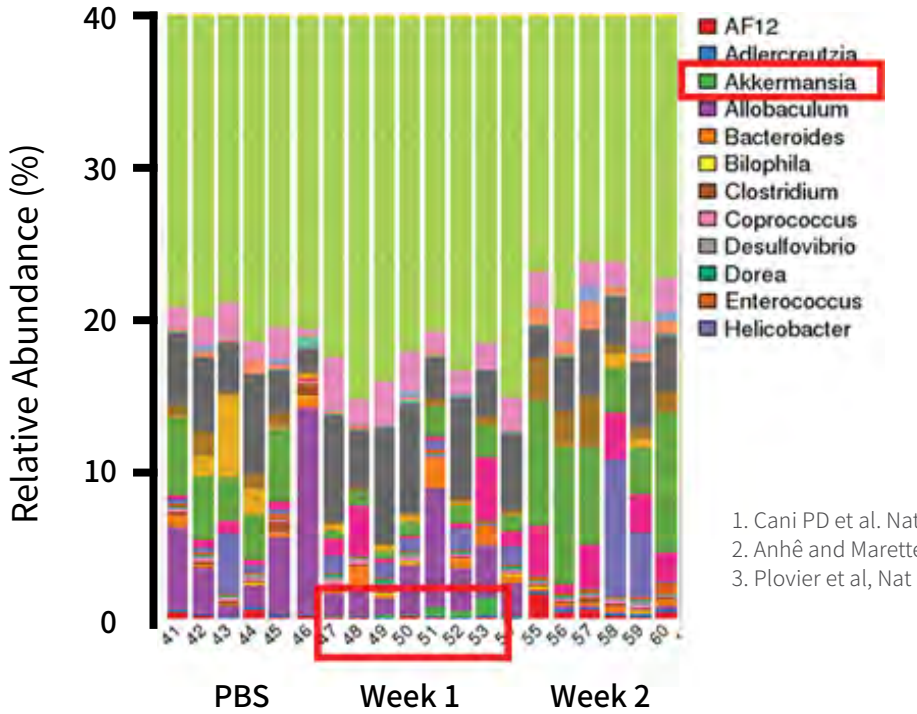
The above data are based on Aptorum' s internal tests and has not yet been verified by clinical trials or third party testing.

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]



1. Cani PD et al. Nat Rev Endocrinol 2014
2. Anhê and Marette. Nat Med 2017
3. Plovier et al, Nat Med 2017

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

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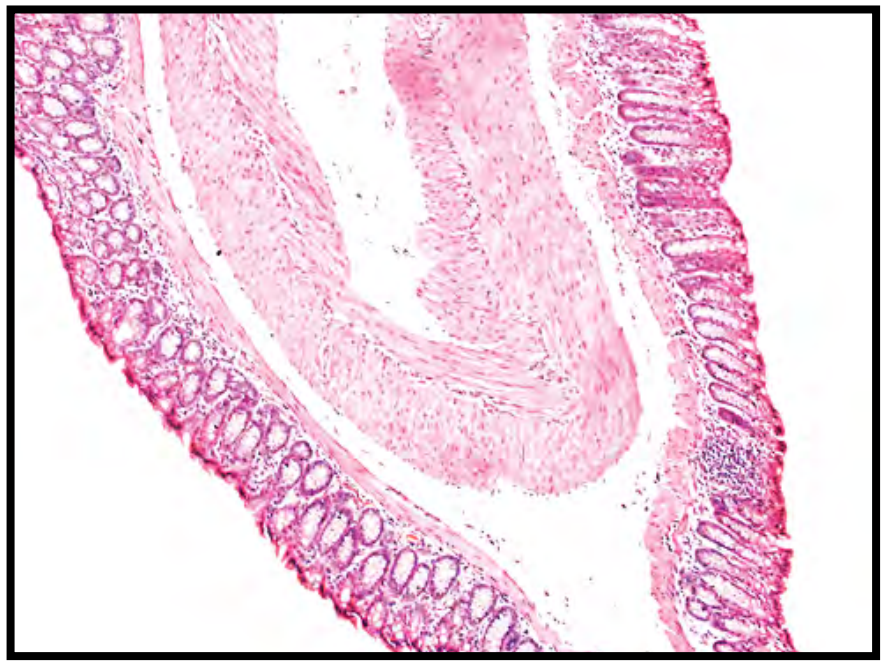
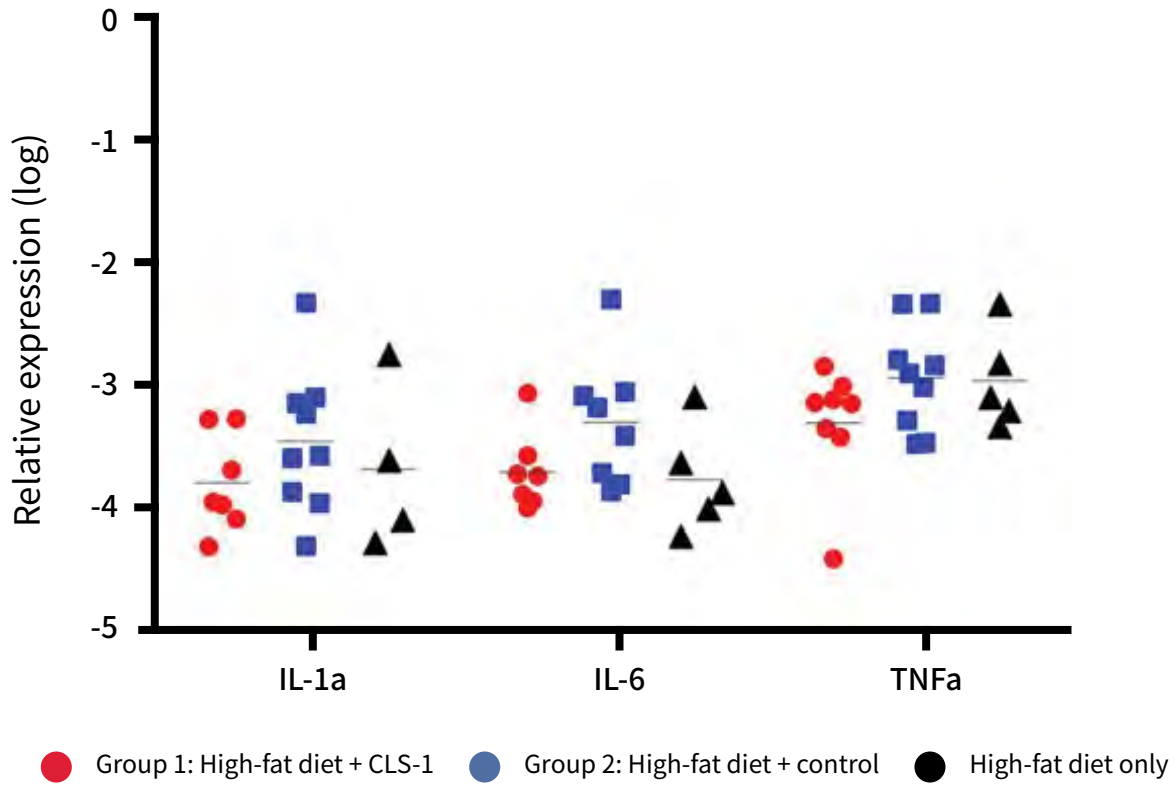
CLS-1: toxicology (gut histology and inflammatory markers)

Mucosa and Inflammatory Markers





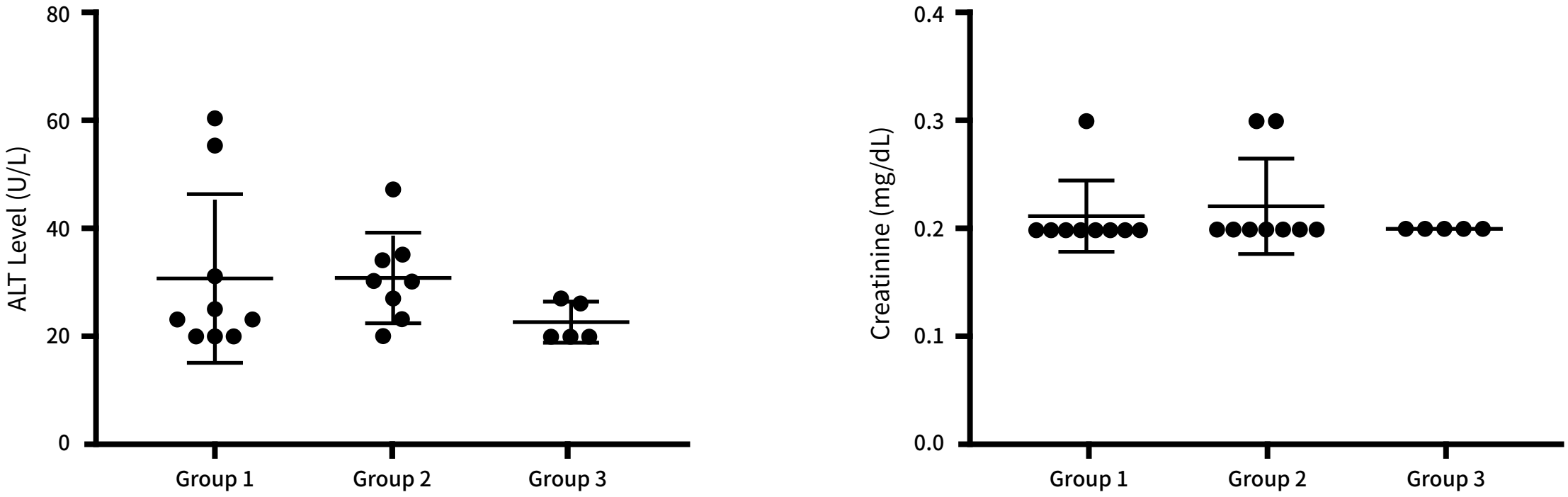
CLS-1 does not upregulate inflammatory markers

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

APTORUM

CLS-1: toxicology (liver and renal functions)

Liver and Renal Functions



CLS-1 does not interfere with liver and renal functions

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

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CLS-1: towards clinical trials

PHARMACOLOGY & PHARMACOKINETICS

- In vivo non-absorbability and mass balance testing is ongoing

TOXICOLOGY

- GLP toxicology (Ames test) and GLP manufacturing is under planning

CHEMISTRY, MANUFACTURING & CONTROL

- CLS-1 is likely a non-absorbable macromolecule
- Not soluble in the gastrointestinal tract
- API manufacturing process has been scaled up to 100 g

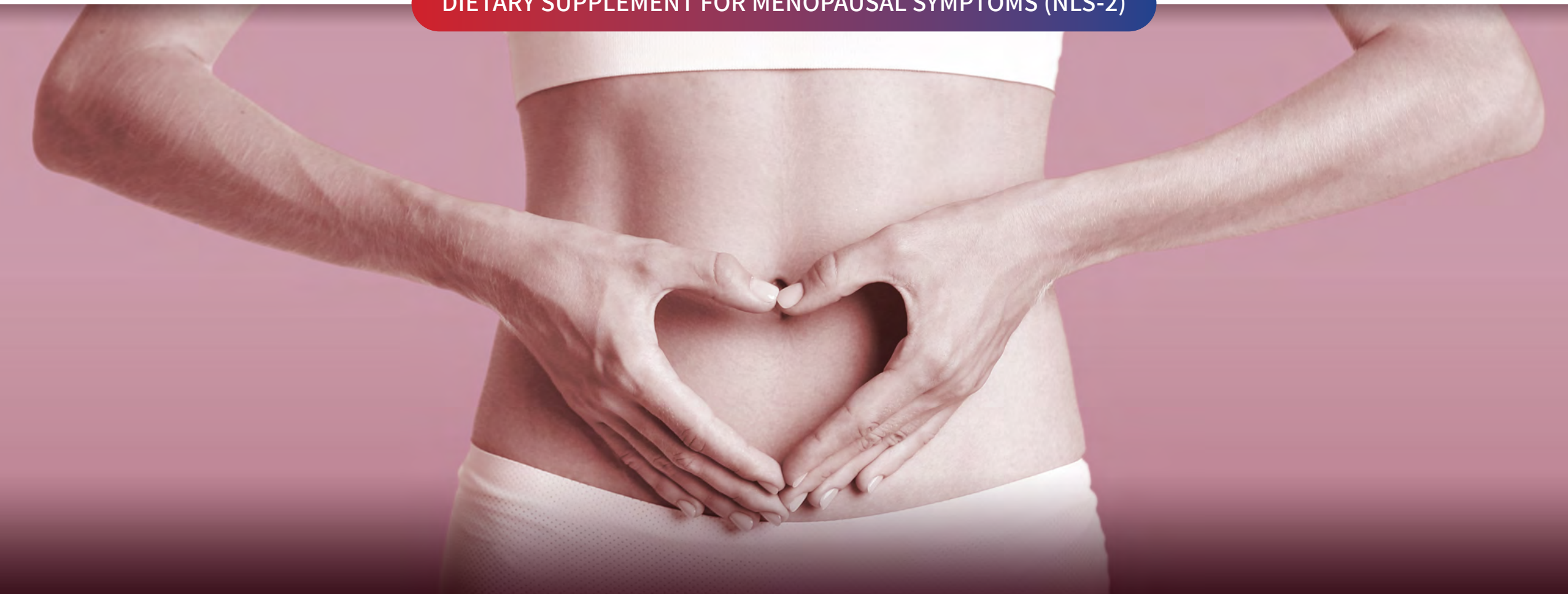
CLINICAL TRIAL STRATEGY & PROTOCOL

- Plan to conduct a hybrid Ph 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

APTORUM

Facilitating Life Science Innovations to Serve Unmet Medical Needs

DIETARY SUPPLEMENT FOR MENOPAUSAL SYMPTOMS (NLS-2)



Executive summary

NLS-2[1]

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

TIMELINE

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

Program	Modality	Indication	Formulation	Commercialisation
DOI (NLS-2)	Supplement	Menopausal symptoms	→	Q1 2020 →

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

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

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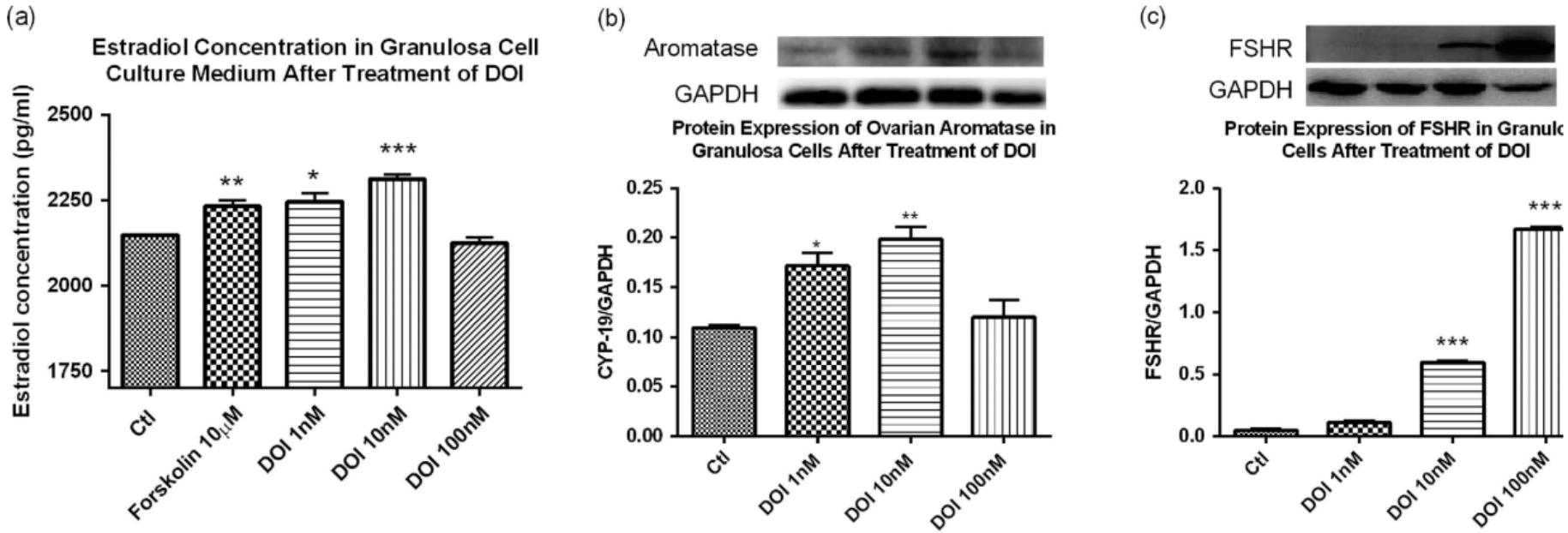
DOI - a Chinese yam extract to address menopausal symptoms

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

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

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

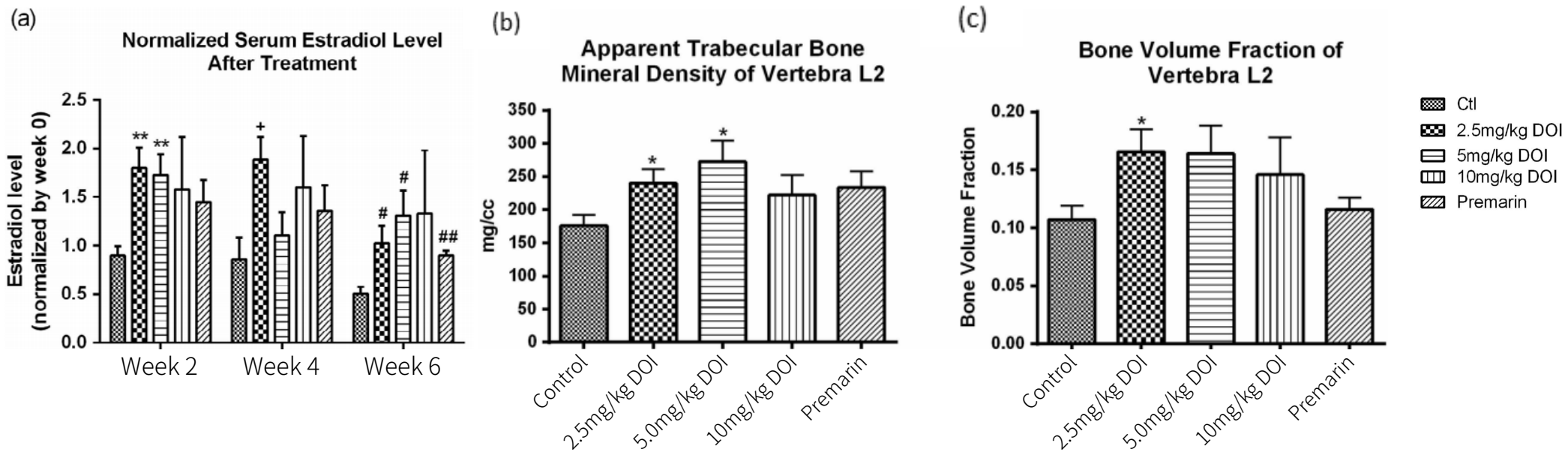


(a) Stimulatory activity of DOI on estrogen biosynthesis in granulosa cells. Protein expression of (b) aromatase and (c) follicle-stimulating hormone receptor (FSHR) in ovarian granulosa cells. Results are expressed as means ± SEM (n = 3). *P < 0.05, **P < 0.01, ***P < 0.001 compared with the control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

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

DOI - a Chinese yam extract to address menopausal symptoms

In *in vivo* rat models, DOI is shown to stimulate estradiol level and induce estrogen-related gene expressions[1]



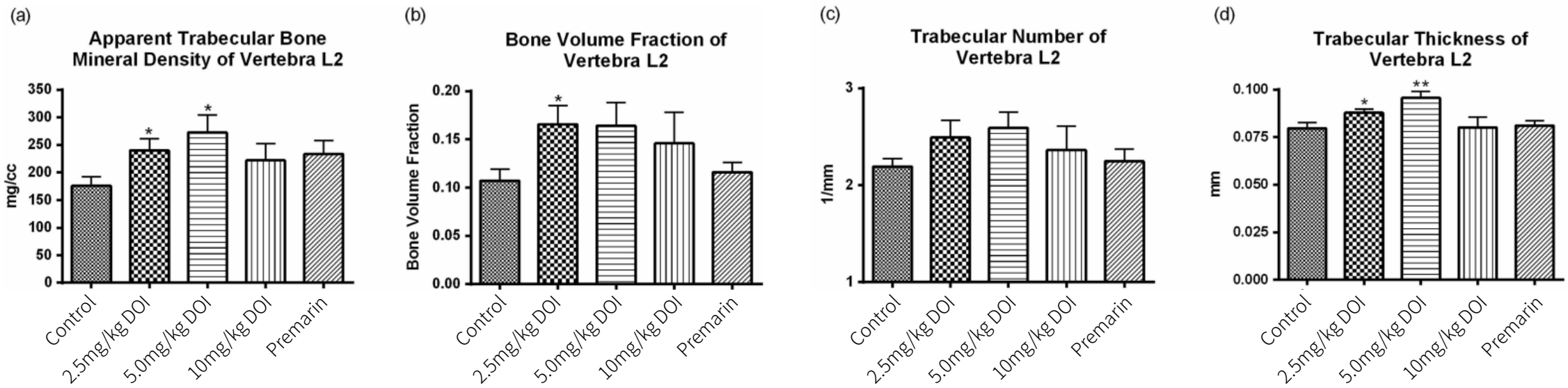
(a) Serum estradiol, (b) apparent trabecular bone mineral density, (c) bone volume fraction of Sprague Dawley rats after treatment with DOI for 2, 4, and 6 weeks. Results are expressed as means ± SEM (n = 6; except Premarin group, where n = 3). *p < 0.05, **p < 0.01 compared with the control group (unpaired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

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

DOI - a Chinese yam extract to address menopausal symptoms

DOI and bone density[1]

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



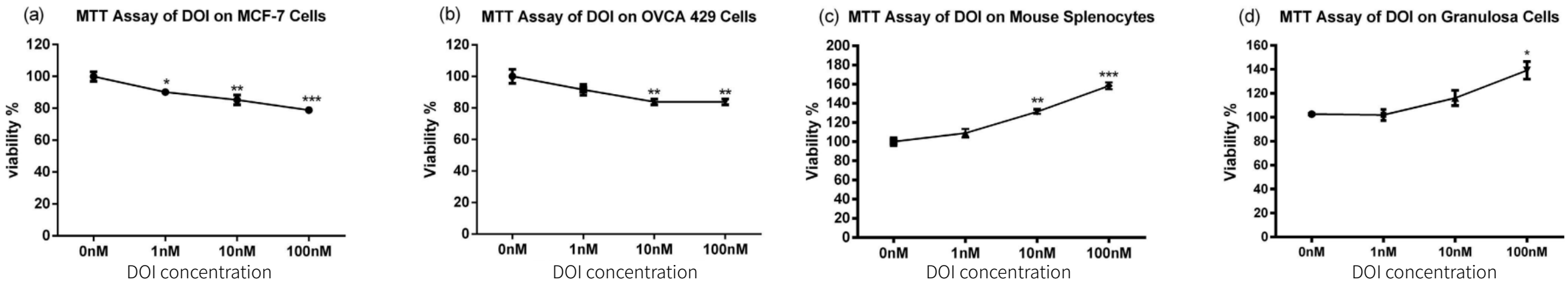
(a) Serum estradiol, (b) apparent trabecular bone mineral density, (c) bone volume fraction of Sprague Dawley rats after treatment with DOI for 2, 4, and 6 weeks. Results are expressed as means ± SEM (n = 6; except Premarin group, where n = 3). *p < 0.05, **p < 0.01 compared with the control group (unpaired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

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

DOI - a Chinese yam extract to address menopausal symptoms

DOI does not cause toxicity in vitro based on cell viability in the MTT assay [1]

- 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

APTORUM GROUP LIMITED

investor.relations@aptorumgroup.com

T +852 2117 6611

F +852 2850 7286