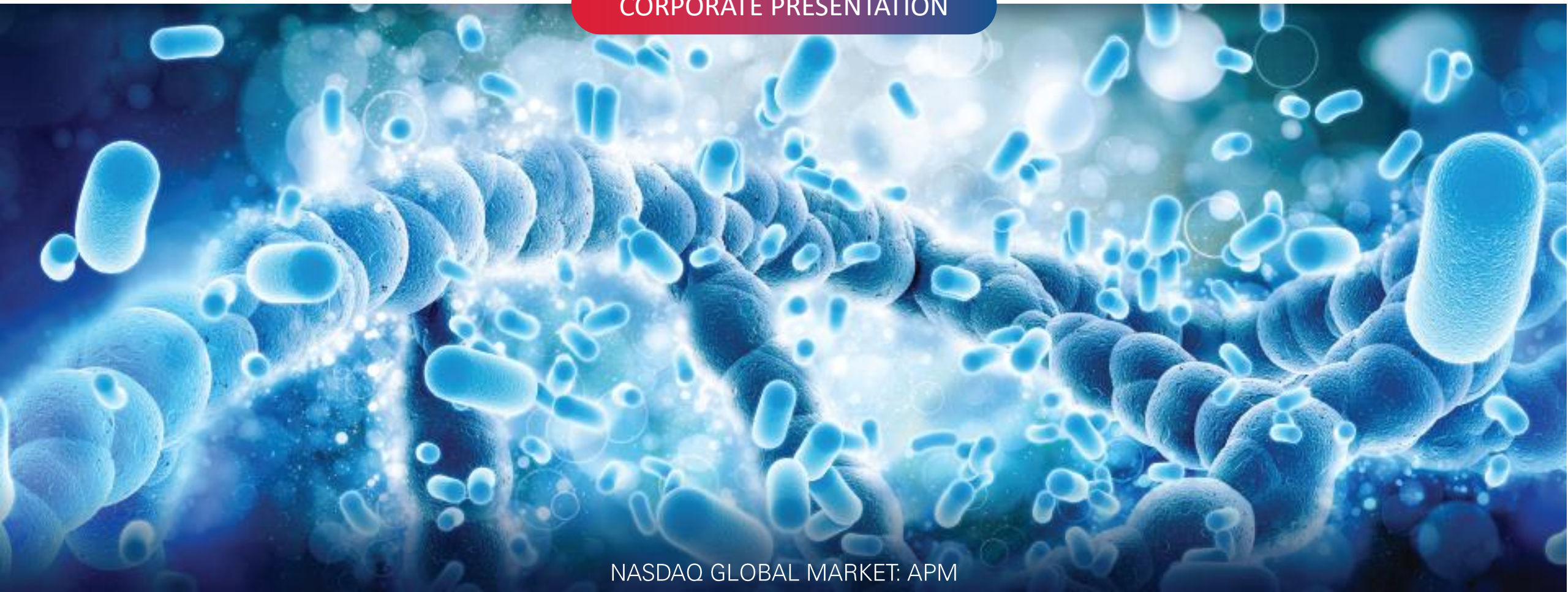
APTORUM

Facilitating Life Science Innovations to Serve Unmet Medical Needs

CORPORATE PRESENTATION



NASDAQ GLOBAL MARKET: APM

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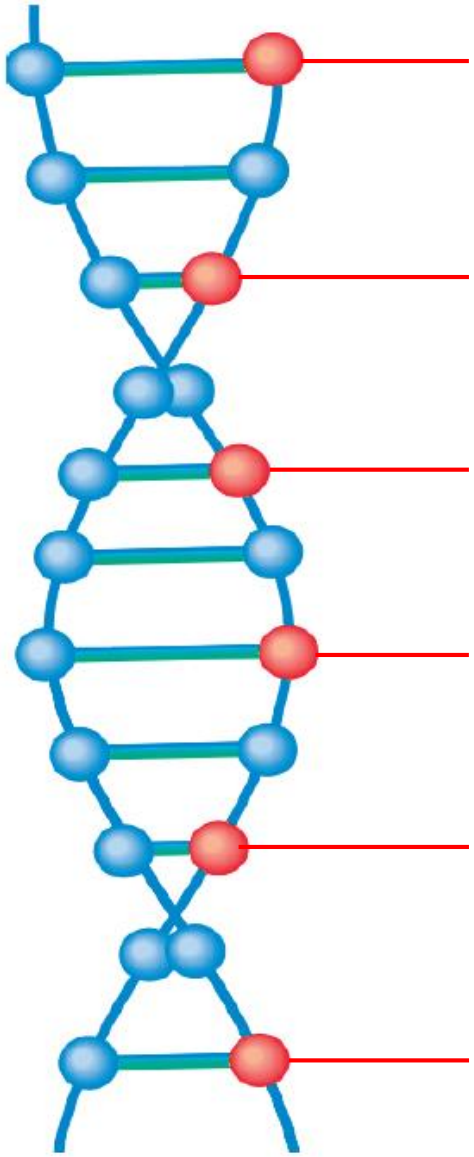
Investment Highlights



Aptorum Group (Nasdaq: APM) is a biopharmaceutical company focused on development of novel therapeutics for unmet medical needs, with a current market capitalization of over USD 400 million

Over 15 therapeutic candidates under development in areas including infectious diseases, gastrointestinal microbiome, drug repurposing for orphan diseases and amongst others

3 therapeutic candidates expected to reach clinical phases over Q2 - Q4 2020. Lead programs for the treatment of (i) neuroblastoma (ii) *S. aureus* (incl MRSA) infections, (iii) obesity

3 major pillars of drug discovery platforms: (i) deploying computational and high throughput screening of FDA approved therapeutics against over 7,000 potential orphan cancer targets (ii) targeting bacterial infections using an anti-virulence (non-bactericidal) approach, and (iii) targeting over 70 potential therapeutic targets via the modulation of the chemical signaling of gut microbiota, and

Over 40 staff, clinical advisors and consultants with vast experience in drug development and clinical trials including US FDA, EMA and NMPA (formerly known as CFDA) purposes

Clinical trials and development sites based in North America and Asia

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Team

Leadership

MR. IAN HUEN

Founder, Chief Executive Officer and Executive Director

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

MR. DARREN LUI

President and Executive Director

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

DR. CLARK CHENG

Chief Medical Officer and Executive Director

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

MISS SABRINA KHAN

Chief Financial Officer

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

DR. THOMAS LEE WAI YIP

Head of Research and Development

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

DR. ANGEL NG SIU YAN

Chief Operating Officer

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

Independent Non-Executive Directors

PROFESSOR DOUGLAS ARNER

Kerry Holdings Professor in Law, HKU

DR. JUSTIN WU

COO of CUHK Medical Centre

DR. MIRKO SCHERER

CEO of CoFes China

MR. CHARLES BATHURST

Founder of Summerhill Advisors Limited

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Team

Pharmaceutical Development Team

DR. KWOK CHOW

Canada Based Development Team and Advisor

- President of Covar Pharmaceuticals Inc. and Powder Pharma Coating Inc
- Former Senior Director at Global PDS Technology and Alliances at Patheon Inc.
- Formerly employed at Glaxo
- B.S. in Pharmacy, the University of Minnesota;
- Ph.D. in Industrial Pharmacy, the University of Toronto

MR. AUSTIN FREEDMAN

Canada Based Development Team and Advisor

- Executive Director of Pharmaceutical Development at Covar Pharmaceuticals Inc.
- Formerly employed at Glaxo, Apotex and Patheon
- Member of the Royal Pharmaceutical Society
- B.Pharm. (Hons.), the University of London

DR. HERMAN LAM

Canada Based Development Team and Advisor

- Director of Analytical Development at Covar Pharmaceuticals Inc.
- CEO of Powder Coating Pharma, Inc.
- Former Principle Investigator at Glaxosmithkline
- B.Sc. in Chemistry, the University of Toronto; Ph.D. in Chemistry, York University, Canada.

DR. MARY MAZUR MELNYK

Canada Based Development Team and Advisor

- Regulatory Consultant
- M.Sc. in Medical Sciences/ cell and Microbiology,
- McMaster University; Ph.D. in Molecular Biology/Biochemistry/Toxicology, York University, U.S.

DR. ALBERT CHOW

Chief Executive Officer & Executive Director at Aptorum Pharmaceutical Development Ltd.

- Former professor at School of Pharmacy, CUHK
- Former independent Non-Executive Director, Jacobson Pharma Group
- M.Sc. in Pharmaceutical Chemistry, and Ph.D. in Physical Pharmaceutics,
- University of Toronto

DR. CHUEN YAN LEUNG

Senior Associate

- Expertise in stem cell biology and molecular biology
- Former lead scientist at Procella therapeutics
- Croucher Research Fellow at the Karolinska Institute, Sweden
- Ph.D. in stem cells and embryology, University of Cambridge

DR. JOHN LI

Associate Director

MChem, The University of Sheffield; Ph.D. in Organic Chemistry, The University of Leeds

DR. DANIEL POON

Senior Technical Manager

B.Sc in Chemistry, HKUST; Ph.D. in Pharmacy, CUHK

DR. YANNY CHAN

Senior Scientist (Pharmaceutics)

M.Sc. in Materials Science and Nanotechnology; Ph.D. in Biology and Chemistry, CUHK

DR. SOPHIA TSANG

Senior Scientist (Chemistry)

B.Sc (Hons) in Chemistry, The University of Auckland; Ph.D. in Organic Chemistry, The University of Auckland

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Team

Clinical Advisor

DR. NISHANT AGRAWAL

Senior Clinical Advisor

- Professor of Surgery, School of Medicine, University of Chicago

DR. HENRY CHAN LIK YUEN

Senior Advisor

- Associate Dean, Faculty of Medicine, CUHK

DR. PHILIP W.Y. CHIU

Senior Advisor

- Professor, Department of Surgery, Institute of Digestive Disease, CUHK

DR. VINCENT MOK CHUN TONG

Senior Advisor

- Head of Division of Neurology, Dept of Medicine & Therapeutics, CUHK

Consultants, Advisors and Principal Investigators

DR. KEITH CHAN

Consultant

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

DR. LAWRENCE BAUM

Senior Scientific Advisor

- Hon. Asso. Professor, Department of Psychiatry, The University of Hong Kong

DR. FRANCIS SZELE

Senior Scientific Advisor

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

MR. WILLIAM WEISS

Consultant

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

DR. RICHARD KAO

Principal Investigator

- Asso. Professor, Department of Microbiology, The University of Hong Kong

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Team

Technology Assessment Committee

DR. KENNY YU

Committee Member

- Research Associate, Tabar Lab, Memorial Sloan Kettering Cancer Center, New York City, New York, USA

DR. KA-WAI KWOK

Committee Member

- Asst. Professor, Department of Mechanical Engineering, The University of Hong Kong

DR. OWEN KO HO

Committee Member

- Asst. Professor, Department of Medicine and Therapeutics, CUHK

DR. SUNNY WONG

Committee Member

- Asst. Professor, Department of Medicine and Therapeutics, CUHK

DR. JASON Y.K. CHAN

Committee Member

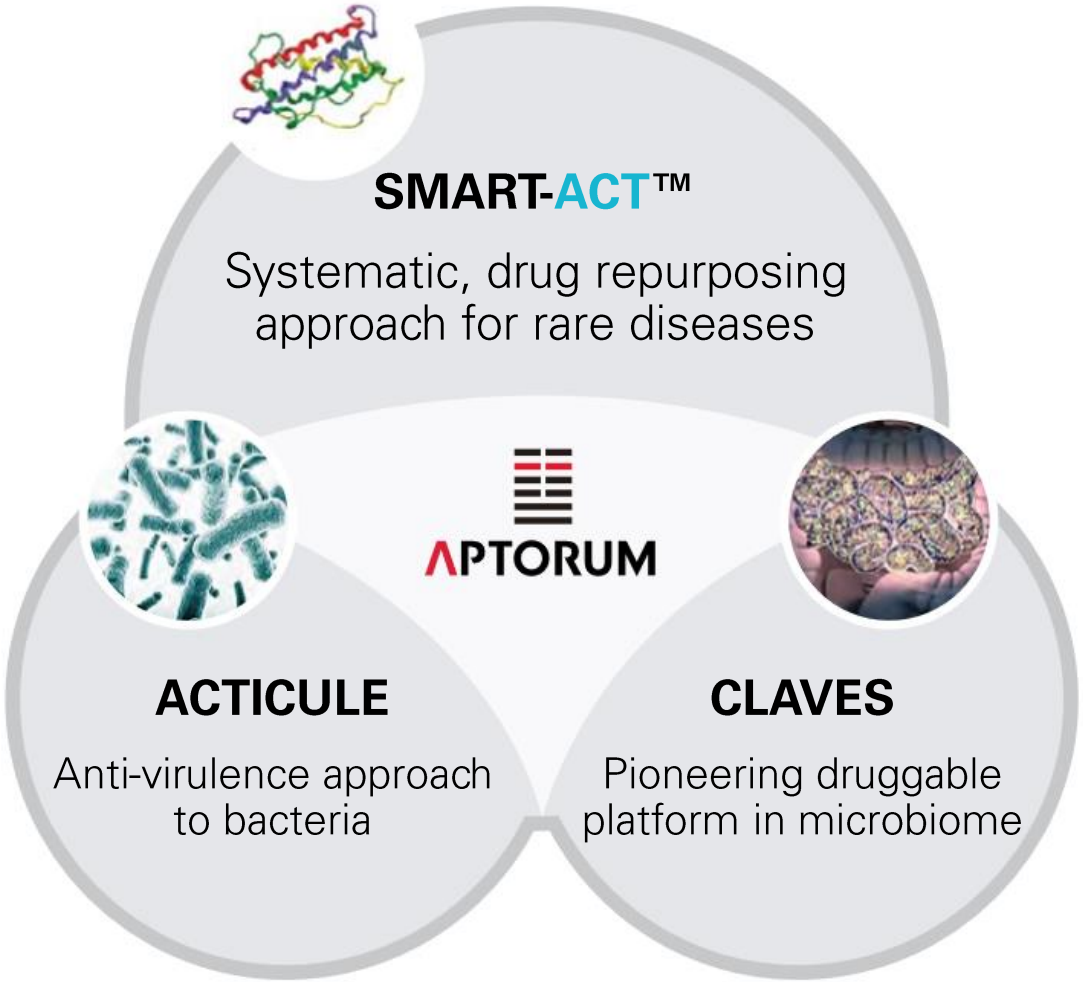
- Asst. Professor, Department of Otorhinolaryngology, CUHK

DR. WILLIAM WU KA KEI

Committee Member

- Asso. Professor, Department of Anaesthesia and Intensive Care, CUHK

Aptorum's 3 Core Pillars



- Aptorum's 3 core pillars of therapeutic discovery and development, focused on novel therapeutics for unmet medical needs
- Ever expanding universe of proprietary intellectual property in relation to our pipeline products

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Project Portfolio (3 Major Pillars)

Current progress of pipeline programs: Lead Projects | Device Candidates | Other Candidates | Projected timeline[1]

Pillar 1: SMART-ACT™ (SACT series) – Orphan diseases drug repurposing platform

Over 7,000 orphan diseases to be screened in the next 5 years

IND 505(b)(2) filing[3]

Program	Indication	Computational discovery	*In vitro* validation	Existing PhI/II clinical safety data[2]	*In vivo* validation	Bridging studies	Phase II/III with limited population[4]
SACT – 1	Neuroblastoma				Q4 2019		Ready for clinical trial 2H 2020
SACT – 2	To be disclosed						
SACT – 3	To be disclosed						

Pillar 2: Acticule (ALS series) – Infectious diseases

Small molecule, anti-virulence and non-bactericidal approach

IND NDA

Program	Indication	Discovery	Lead optimization	IND enabling	Phase I	Phase II/III based on LPAD pathway[5]
ALS – 4	Anti *S. aureus* (incl. MRSA)			oral formulation Q3 2019	2H 2020	
ALS – 1	Anti influenza A			Q4 2020		
ALS – 2	Gram+ bacteria					
ALS – 3	Gram+ bacteria					

Hybrid study
- Volunteers + patients
- Initial efficacy readout

Pillar 3: Claves (CLS series) - Microbiota

Large molecule approach. Over 70 targets / indications

IND NDA

Program	Indication	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					

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 domain 4. Subject to FDA's approval 5. 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

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Project Portfolio (Others)

Program	Modality	Indication	Formulation	Commercialization
DOI (NLS – 2)	Supplement	Menopausal symptoms		Q1 2020

Program	Modality	Indication	Discovery	Lead optimization
NLS – 1	Small molecule	Endometriosis		
VLS – 2	Small molecule	Alzheimer's & Parkinson's disease		
SPLS – 1	Small molecule	Liver cancer		

Program	Modality	Indication	Lab-based phantom trial	Animal trial
SLS – 1	Robotic catheter platform for intra-operative MRI-guided cardiac catheterization	Heart rhythm disorders		

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Overview of Our Lead Projects

SACT-1

Small molecule repurposed drugs targeting three important therapeutic target proteins related to poor prognosis of neuroblastoma.

Population affected:

In the US, approximately **700** children and adolescents younger than 20 years of age are diagnosed with tumors of the sympathetic nervous system each year, of which approximately **650** are neuroblastomas[1]

The incidence of neuroblastoma is **10.2 cases per million children** under 15 years of age[2]

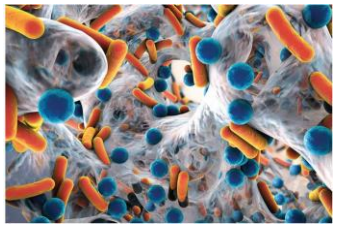
Neuroblastoma accounts for approximately **15%** of all cancer-related deaths in the pediatric population[2]

Market Size:

Global Market Size in 2017: **USD 2.6 billion[3]**

Expected Global Market Size by 2023: approx. **USD 3.23 billion[3]** (at CAGR of 3.7%)

1. Cancer Incidence and Survival among Children and Adolescents: United States SEER Program: 1975-1995, https://seer.cancer.gov/archive/publications/childhood/childhood-monograph.pdf; 2. Neuroblastoma, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3668791; 3. Neuroblastoma Market Global Industry Perspective, Comprehensive Analysis, Size, Share, Growth, Trends, and Forecast 2019 – 2023, https://www.medgadget.com/2019/06/neuroblastoma-market-global-industryperspective-comprehensive-analysis-size-share-growth-trends-and-forecast-2019-2023.html



ALS-4

A small molecule anti-virulence (non-bactericidal) drug for the treatment of infections caused by Staphylococcus aureus including MRSA. It disarms the bacteria by inhibition of the production of staphyloxanthin, the golden pigment covering the bacteria, which makes it resistant to attack from reactive oxygen species (ROS) employed by phagocytic cells and neutrophils. Without the pigment, the bacteria are highly susceptible to host immune clearance.

Population affected:

53 million people worldwide carry MRSA[1].

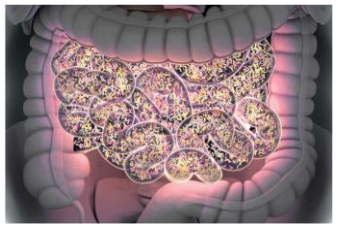
For example, in U.S., **~126,000** hospitalizations are due to MRSA yearly, where severe infections occur in **~94,000** people each year and are associated with **~19,000** deaths[2]

Market Size:

Global Market Size in 2016: **USD 2.97 billion[3]**

Expected Global Market Size by 2025: **USD 3.91 billion[3]**

1. Roche Annual report 2017, https://www.roche.com/dam/jcr:78519d71-10af-4e02-b490-7b4648a5edb8/en/ar17e.pdf; 2. emedicinehealth: MRSA https://www.emedicinehealth.com/mrsa_infection/article_em.htm#how_common_is_mrsa 3. Healthcare Drive: Global Methicillin-resistant Staphylococcus Aureus (MRSA) Drugs Market Analysis and Forecast Predictions, https://www.healthcaredive.com/press-release/20180405-global-methicillin-resistant-staphylococcus-aureus-mrsadrugs-market-anal/



CLS-1

A macromolecule that modulates the chemical signaling of gut microbiota for the treatment of obesity. CLS-1 is an orally administered non-absorbable macromolecule that binds a metabolite excreted by gut microbiota with high affinity and specificity. In this way, the absorption of this particular metabolite, which is linked to obesity, can be inhibited.

Population affected:

Obesity is known to be a major worldwide public health problem that affects more than 1.9 billion adults in 2018, which means **39% of adults** are considered obesity and overweight[1]

By 2025, global obesity prevalence will reach **18%** in men and surpass **21%** in women; severe obesity will surpass **6%** in men and **9%** in women[1]

Market Size:

Global Market Size in 2018: **USD 6.14 billion[2]**

Expected Global Market Size by 2026: **USD 9.9 billion[2]**

1. The Gut Microbiome Profile in Obesity: A Systematic Review, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5933040; 2. Obesity Treatment Market To Reach USD 19.90 Billion By 2026, https://www.globenewswire.com/newsrelease/2019/06/06/1865530/0/en/Obesity-Treatment-Market-To-Reach-USD-19-90-Billion-By-2026-Reports-And-Data.html

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Overview of Our Lead Projects

ALS-1

A small molecule that targets nucleoproteins for the treatment of infections caused by Influenza A. Influenza A nucleoprotein is an essential protein for the proliferation of the influenza virus. ALS-1 causes the aggregation of nucleoprotein and this prevents the aggregated nucleoprotein from entering the nucleus and triggers the replication of the virus.

Population affected:

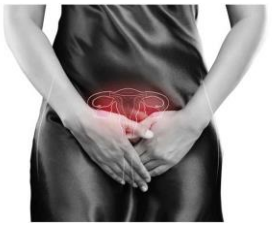
Annual epidemics estimated to result in **~3-5 million** cases of serious influenza infections, causing about **290,000-650,000 deaths** each year[1], around **50-80%** of influenza infections are type A[2]

Market Size:

Global Market Size in 2016: **USD 0.60 billion**[3]

Expected Global Market Size by 2025: **USD 1.2 billion**[3]

1. WHO: Influenza (Seasonal), http://www.who.int/en/news-room/fact-sheets/detail/influenza-(seasonal); 2. WHO Global circulation of influenza viruses, http://apps.who.int/flumart/Default?ReportNo=6; 3. Bloomberg: New Drugs Are Coming to Fight Nasty Flu Seasons (9 Feb 2018), https://www.bloomberg.com/news/articles/2018-02-08/flu-relief-is-coming-as-successors-to-aging-tamiflu-near-market



NLS-1

An anti-angiogenic small molecule derived from green tea for non-hormonal treatment of endometriosis. NLS-1 inhibits the formation of blood vessels resulting in inhibition of development, growth, angiogenesis of endometriosis.

Population affected:

~176 million women globally (≈1 in 10 women during their reproductive years)[1]

~30-40% of women with endometriosis are subject to risk of infertility and may develop complications during pregnancy[2]

Market Size:

Market Size in 2015: **USD 1.72 billion** (across the 7 major countries)[3]

Expected Market Size by 2025: just over **USD 2 billion** (across the 7 major countries)[3]

1. Endometriosis.org: Facts about endometriosis, http://endometriosis.org/resources/articles/facts-about-endometriosis; 2. Washington University Physicians", Endometriosis", https://fertility.wustl.edu/getting-started-infertility/infertility-factors/endometriosis, J. Fisher M. Kirkman", Endometriosis and fertility: women's accounts of healthcare", Human Reproduction, Volume 31, Issue 3, March 1, 2016, Pages 554–562, January 11, 2016, https://doi.org/10.1093/humrep/dev337; 3. R&D: Endometriosis Market Expected to Surpass $2 Billion by 2025 (11 Nov 2016) – By Global Data. List of 7 major countries: the US, France, Germany, Italy, Spain, the UK and Japan, https://www.rdmag.com/news/2016/11/endometriosis-marketexpected-surpass-2-billion-2025

NLS-2

A natural supplement derived from Chinese yam for the relief of menopausal symptoms. NLS-2 was shown to stimulate estradiol biosynthesis and induce estradiol and progesterone secretion. It counteracts the progression of osteoporosis and augment bone mineral density; and improve cognitive functioning.

Population affected:

1.2 billion postmenopausal women projected by the year 2030[1]

85% of postmenopausal women experience menopause-related symptoms in their lifetime[2]

Market Size:

Global Market Size in 2019: **USD 17.1 billion**[3]

Expected Global Market Size by 2025: **USD 50.1 billion**[3]

1. Cancer Incidence and Survival among Children and Adolescents: United States SEER Program: 1975-1995, https://seer.cancer.gov/archive/publications/childhood/childhood-monograph.pdf; 2. Neuroblastoma, https://www.ncbi.nlm.nih.gov/ pmc/articles/PMC3668791; 3. Neuroblastoma Market Global Industry Perspective, Comprehensive Analysis, Size, Share, Growth, Trends, and Forecast 2019 – 2023, https://www.medgadget.com/2019/06/neuroblastoma-market-globalindustryperspective-comprehensive-analysis-size-share-growth-trends-and-forecast-2019-2023.html

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Focus on Unmet Medical Needs and Orphan Diseases

	Unmet medical needs	Orphan (rare) diseases
FDA criteria	"Filling an unmet medical need is defined as providing a therapy where none exists or providing a therapy which may be potentially better than available therapy"[1]	"defined as those intended for the safe and effective treatment, diagnosis or prevention of rare diseases/disorders that affect fewer than 200,000 people in the U.S., or that affect more than 200,000 persons but are not expected to recover the costs of developing and marketing a treatment drug"[2]
Estimated number of cases	Not limited as filing an unmet medical need to the FDA include therapeutics which may be potentially better than available therapy[1]	• An estimated 7,000 orphan diseases[3] • An estimated 25-30 million[3] people in the US are living with an orphan disease[3]
Regulatory incentives	Include Breakthrough Therapy[4] and Fast Track[1] designations in the U.S.; Sakigake designation in Japan[5]; and Priority Medicines (PRIME) scheme[6], accelerated assessment[7], and conditional marketing authorization[8] in Europe **A drug that receives FDA Fast Track designation is eligible for:** • More frequent meetings and communication with FDA[1] • Eligibility for Accelerated Approval and Priority Review[1] • Rolling Review for BLA or NDA[1]	FDA's Orphan Drug Designation Program and Orphan Products Grant Program provides the following incentives[9,10]: • Phase I clinical investigations may receive up to $200,000 per year for up to three years and Phase II and Phase III clinical investigations, may receive up to $400,000 of total costs per year for up to four years • Exclusivity – The first sponsor of a designated orphan drug to obtain FDA marketing approval for the designated rare disease or condition receives seven years of marketing exclusivity • Tax credit – A sponsor may claim as tax credits half of the qualified clinical research costs for a designated orphan product • Waiver of Prescription Drug User Fees – The sponsor's fee as prescribed by the Prescription Drug User Fee Act (PDUFA Fees) at the time of submitting a marketing application to FDA are waived for a designated product
Aptorum's strategic angle	• Aptorum's focus on unmet medical needs and orphan diseases strategically position ourselves to exploit untapped markets without fierce competition • Aptorum's team has expertise and drug development experience in orphan diseases and unmet medical needs • Fast to market as a result of accelerated regulatory approval processes	

1. https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/fast-track; 2. https://www.fda.gov/about-fda/office-special-medical-programs/office-orphan-products-development; 3. https://rarediseases.info.nih.gov/diseases/pages/31/faqs-about-rare-diseases; 4. https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/breakthrough-therapy; 5. https://www.mhlw.go.jp/english/policy/health-medical/pharmaceuticals/140729-01.html; 6. https://www.ema.europa.eu/human-regulatory/research-development/prime-priority-medicines; 7. https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/accelerated-assessment; 8. https://www.ema.europa.eu/human-regulatory/marketing-authorisation/conditional-marketing-authorisation; 9. https://www.fda.gov/industry/developing-products-rare-diseases-conditions/fda-rare-disease-day-february-28-2011. Data from 2011, may have since been updated or changed by the FDA; 10. https://www.fda.gov/about-fda/office-special-medical-programs/office-orphan-products-development.

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Facilitating Life Science Innovations to Serve Unmet Medical Needs

SMART-ACT™ - ORPHAN DRUG DEPURPOSING PLATFORM

SMART-ACT™: Executive Summary

SMART-ACT™

Drug Repurposing

- FDA-approved small molecules
- Expedited Phase I through existing safety data on the approved drug
- Greatly reduces duration of drug development from 12 years to 4 years
- Patent protection through indication, reformulation and combination patents

+

Orphan Diseases

- FDA fast track procedures
- Small scale clinical trials
- 7 years of market exclusivity in parallel to patent protections
- 10% combined incidence in the US
- 95% orphan diseases without treatment
- 7000 orphan diseases & rising

=

Rapid generation of late-stage clinical candidates

Systematic approach to rare disease

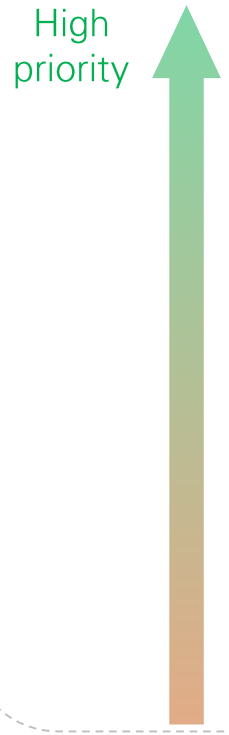
Orphan Disease Selection

7000+ Orphan Diseases

Patient population definition:

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

Disease selection criteria



Life threatening disease

High unmet need

IP protection

Market size

Competitive landscape

Clinical trial design

Paediatric disease

By region

Target selection

Disease knowledge

SMART-ACT™
High Priority
Orphan Diseases

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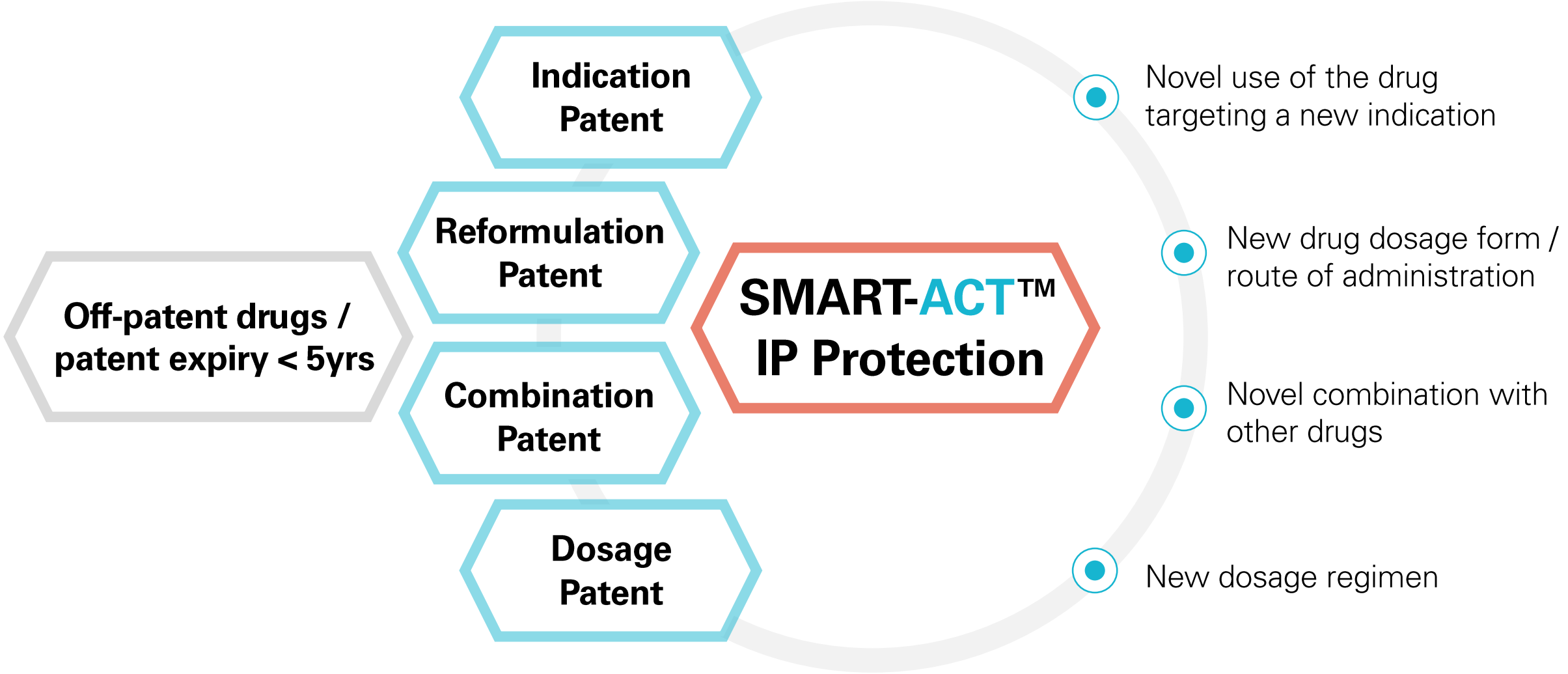
SMART-ACT™: Patent Strategy



SMART-ACT™: Pipeline Workflow

1 New drug indication

- Life threatening disease
- Lack of effective treatment
- Large market size

2 Drug target selection

- Computational mining from literature
- Up to 5 disease drug targets selected

3 1,600 FDA-approved small molecule drugs

Computational

4 In silico generated hits

Wet lab

5 In vitro validation

- Cell line model
- IC_{50}
- Combo treatment standard therapy

6 In vivo validation

- Animal model
- In vivo efficacy

7 IP protection

- Indication patent
- Reformulation
- Combination patent
- Dosage patent

8 Development / out-licensing

- US FDA 505(b)(2) filing
- In-house development or out-licensing with co-development partners

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

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SMART-ACT™: Priority Focus

Deep, prioritised pipeline of orphan diseases to be screened

- 3-5 drugs to reach ph2/3 confirmation study per year

Orphan cancers		
Carcinoma of esophagus	Familial colorectal cancer	Malignant peripheral nerve sheath tumor
Carcinoma of gallbladder and extrahepatic biliary tract	Familial Melanoma	Neuroblastoma
Cholangiocarcinoma	Gastrointestinal stromal tumor	Non-Hodgkin Lymphoma
Epstein-Barr virus-associated gastric carcinoma	Glioblastoma	Rare carcinoma of pancreas
Erdheim-Chester Disease	Hereditary breast and ovarian cancer syndrome	Squamous cell carcinoma of the esophagus/lip
Ewing Sarcoma	Langerhans Cell Histiocytosis	Thyroid carcinoma

Genetic, Immune, Metabolic & Neurological Disorders		
Cystic fibrosis	Mastocytosis	Primary hyperoxaluria type 1
Duchenne Muscular Dystrophy	Primary biliary cholangitis	Autosomal dominant familial amyotrophic lateral sclerosis
Sickle cell disease	Glycogen storage disease type II	Chronic Inflammatory Demyelination Polyneuropathy
Atypical hemolytic uremic syndrome	Mucopolysaccharidosis II	Primary erythromelalgia
Hereditary angioedema	Mucopolysaccharidosis III	Idiopathic arthritis

Repurposing existing drugs with the 505(b)(2) regulatory pathway

FDA 505(b)(2) regulatory pathway

- For new indications, dosage forms, dosing regimens, strength, orphan drug indications and more of an already approved drug[1,2]
- Type of US new drug application (NDA) that can rely in part on the FDA's previous finding on the safety and efficacy of the API as well as data available in the public domain

FDA approved 505(b)(2) reformulation examples[3]

Product (Company)	Formulation technology	Regulatory pathway	Value proposition	Market value
Abraxane for injectable suspension (Celgene)	Nanoparticle albumin-bound paclitaxel or nab-paclitaxel	505(b)(2), new formulation, change from ethanol/surfactant solution to nanosuspension	Enhance of safety, efficacy and PK properties	1.1 billion, 2018
Restasis (Allergen)	Cyclosporine Ophthalmic Emulsion, 0.05%	505(b)(2), new indication, change route of administration	Creation of first line of treatment for dry eye disease	1.4 billion, 2017
Neoral (Sandoz)	Cyclosporine liquid microemulsion (SEDDS)	505(b)(2), new formulation	Enhancement of bioavailability, PK profile and dose reduction	>300 million, 2000
Kaletra (Abbott)	Lopinavir/ritonavir tablets by amorphous solid dispersion	505(b)(1), new formulation (using its own data)	Enhancement of product bioavailability, switch from refrigerated to RT storage, dose reduction	835 million, 2015

1. Guidance for Industry: Applications Covered by section 505(b)(2), https://www.fda.gov/downloads/Drugs/Guidances/ucm079345.pdf 2. Guidance for Industry: Determining Whether to Submit an ANDA or a 505(b)(2) Application; https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM579751.pdf 3. https://drug-dev.com/formulation-forum-revitalization-of-older-drug-products-using-innovative-formulation-technologies-by-505b2-regulatory-pathway/

SACT-1: Development

CURRENT

Computer database of chemical structures of 2,600 approved drugs

Screening against 3 major therapeutic targets for neuroblastoma

Candidate validation on *in vitro* Neuroblastoma model

Q1 2020

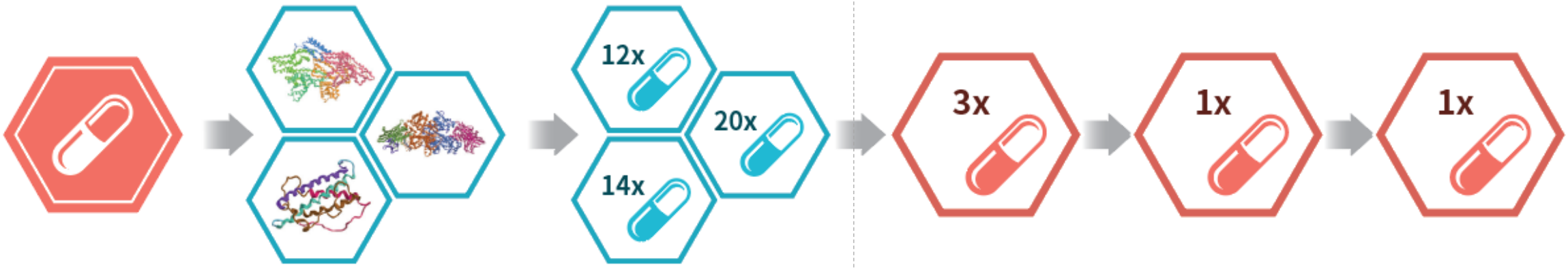
In vivo xenograft efficacy model

Q3/4 2020

Phase 2/3 trial commencement

2024

Regulatory approval



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

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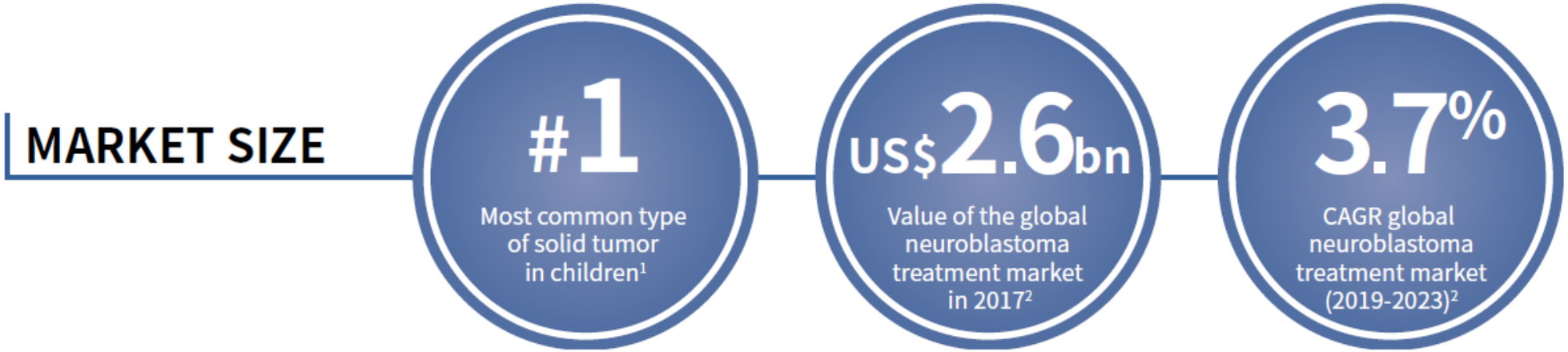
SACT-1 (neuroblastoma): market overview

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



Prevalence

- ~650 cases of neuroblastoma in children each year in the US[3]
- Accounts for ~15% of all cancer-related deaths in the pediatric population[4]

Orphan drug designation[5]

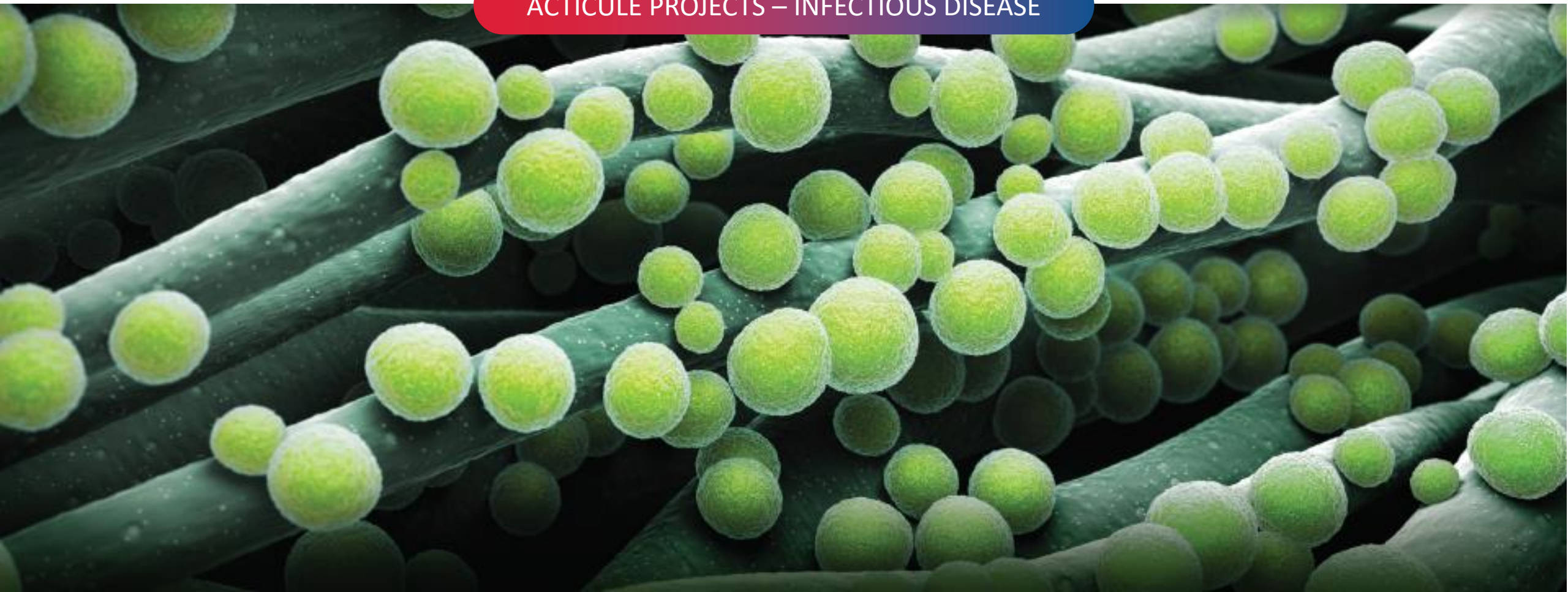
- Neuroblastoma is a rare disease and drugs are qualified for orphan designation by the FDA
- Designated orphan drugs receive 7 years of market exclusivity
- Patents on reformulation, if granted, will provide up to 20 years of patent exclusivity from the application date in parallel to the 7-year market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

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

APTORUM

Facilitating Life Science Innovations to Serve Unmet Medical Needs

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]

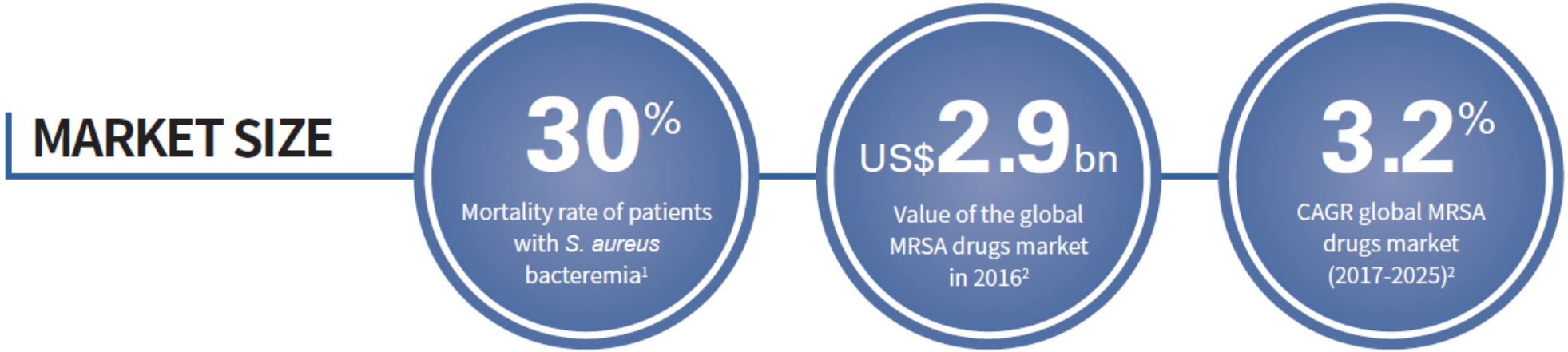
ALS-2/ALS-3

- 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

Market Overview

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



Recent deals in infectious disease

- In 2014, Merck's acquisition of Cubist Pharmaceuticals, a large developer of antibiotics, for USD 8.4bn[3]
- In 2018, Roivant's licensing of Intron's Phase II asset for USD 667.5m in upfront and milestone payments[4]

1. Clin Microbiol Rev. 2012 Apr;25(2):362-86; 2. "Methicillin-resistant Staphylococcus Aureus (MRSA) Drugs Market - Global Industry Analysis, Size, Share, Growth, Trends, and Forecast, 2017-2025" (2018). Transparency market research; 3. https://dealbook.nytimes.com/2014/12/08/merck-agrees-to-acquire-drug-maker-cubist-for-9-5-billion/; 4. https://www.prnewswire.com/news-releases/roivant-sciences-and-intron-bio-sign-licensing-dealfornovel-anti-superbugs-biologic-sal200-300753307.html

ALS-4: Approved Drugs for MRSA Infections

Frequently prescribed antibiotics for MRSA infections[1]

Product (Company)	Antibiotic Class	Indication(s)	RoA	Dose	Cost of Treatment (duration)	Notes
Vancomycin (Generic)	Glycopeptide	Severe infections caused by MRSA	IV / oral*	2g/day	USD 101-144 (7-10 days)	• **Currently, the most frequently prescribed** antibiotic for MRSA suspected infections[1,2] • In clinical use for >60 years[3], **vancomycin-resistant *S. aureus* (VRSA) was first discovered in 2002[4]**
Daptomycin (Merck)	Lipopeptide	ABSSSI, *S. aureus* bacteremia	IV	4-6mg/kg/day	USD 6,736-23,710[5] (14-42 days)	• In clinical use since 2003[6] • **Daptomycin resistance described in S. aureus as early as 2006[7]**
Linezolid (Pfizer)	Oxazolidinone	ABSSSI, CABP, HABP, uSSSI	IV / oral	0.8-1.2g/day	IV: USD 1,920-5,376 Oral: USD 2,978-11,429 (10-14 days)	• In clinical use since 2003[8]. Entirely synthetic, not expected to develop clinical resistance[9], however • **Linezolid resistance encountered clinically since 2010[9]**
Ceftaroline fosamil (Actavis)	Cephalosporin	ABSSSI, CABP	IV	1.2g/day	USD 1,831-5,127 (5-14 days)	• In clinical use since 2010[10] • **Ceftaroline resistance encountered clinically since 2016[11]**
Tigecycline (Pfizer)	Glycycycline	ABSSSI, CABP, CIAI	IV	0.1-0.2mg/day	USD 1,888-4,977 (5-14 days)	• In clinical use since 2005[12] • **Tigecycline resistance encountered clinically in developing countries since 2017[13,14]**
Televancin (Theravance Biopharma)	Lipoglycopeptide	ABSSSI, HABP, VABP	IV	10mg/kg/day	USD 3,002-10,568 (7-21 days)	• In clinical use since 2009[15] • **Vancomycin resistance leads to a 4-8x increase in telavancin MIC** (minimum inhibitory concentration)[16]

ABSSSI: acute bacterial skin and skin structure infection; CABP: community-acquired bacterial pneumonia; HABP: hospital-acquired bacterial pneumonia; CIAI: complicated intra-abdominal infection; VABP: ventilator-associated bacterial pneumonia; * Only for intestinal infections; 1. Reproduced from" Companies Take Aim at MRSA Infections" P T. 2016 Feb; 41(2): 126–128; 2. Clin Infect Dis. 2011 Feb 1;52(3):e18-55; 3. Clin Infect Dis. 2006 Jan 1;42 Suppl 1:S5-12; 4. Centers for Disease Control and Prevention. https://www.cdc.gov/hai/settings/lab/vrsa_lab_search_containment.html; 5. Cost of treatment of Daptomycin for S. aureus bacteremia at a dosage of 6mg/kg; 6. FDA. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2003/21-572_Cubicin.cfm; 7. Int J Antimicrob Agents. 2006 Oct;28(4):280-7; 8. FDA. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2002/21-130s003_21131s003_21132s003_ZyvoxTOC.cfm; 9. Pharmaceuticals (Basel). 2010 Jul; 3(7): 1988–2006; 10. FDA. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2010/200327orig1s000toc.cfm; 11. J Antimicrob Chemother. 2016 Jun; 71(6): 1736–1738; 12. FDA. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2005/21-821_Tygacil.cfm; 13. New Microbes New Infect. 2017 Sep; 19: 8–12; 14. Journal of Microbiology and Infectious Diseases 2017; 7 (4):173-177; 15.FDA. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2009/022110s000TOC.cfm; 16. Clin Infect Dis. 2015 Sep 15;61 Suppl 2:S58-68.

ALS-4: Addressing the Shortfall of Vancomycin

Vancomycin

- Generic antibiotic that is the most frequently prescribed for MRSA-suspected infections[1,2]
- After >60 years[3] of clinical use, its use against *S. aureus* is becoming limited. Vancomycin has been shown to have slow bactericidal activity, poor anti-staphylococcal activity, poor tissue penetration, and high rates of infection relapse[4,5,6,7,8,9]
- The shortcomings of Vancomycin has been compounded since the discovery of vancomycin-resistant S. aureus (VRSA) in 2002[10]
- Vancomycin is not orally bioavailable and must be administered intravenously in order to treat systemic infections[11,12]. Oral vancomycin is only effective for treating local intestinal infections. Therefore, for MRSA-suspected infections oral vancomycin is only indicated for the treatment of pseudomembranous colitis

ALS-4: Potentially a complementary therapeutic to vancomycin

- As a combination therapy to overcome the shortcomings of vancomycin
- ALS-4 can potentially complement other bactericidal antibiotics as well, therefore ALS-4 is not a direct competitor of antibiotics
- Synergistic effects of other drugs with vancomycin against MRSA has been demonstrated previously with β-lactam antibiotics and vancomycin[13]

1. "Companies Take Aim at MRSA Infections" P T. 2016 Feb; 41(2): 126–128; 2. Clin Infect Dis. 2011 Feb 1;52(3):e18-55; 3. Clin Infect Dis. 2006 Jan 1;42 Suppl 1:S5-12; 4. Antimicrob Agents Chemother. 2008 Jan;52(1):192-7; 5. Clin Infect Dis. 2007 Jan 15;44(2):190-6; 6. Clin Infect Dis. 2007 Sep 1;45(5):601-8; 7. J Clin Microbiol. 2011 Oct;49(10):3669-72; 8. Clin Infect Dis. 2007 Sep 15;45 Suppl 3:S191-5; 9. J Clin Microbiol. 2004 Jun;42(6):2398-402; 10. Centers for Disease Control and Prevention. https://www.cdc.gov/hai/settings/lab/vrsa_lab_search_containment.html; 11. J Infect. 2018 Dec;77(6):489-495; 12. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019-2018 Nov 18; 13. J Clin Microbiol. 2016 Mar; 54(3): 565–568

ALS-4: Value Proposition

ALS-4 is uniquely poised to tackle multidrug-resistant *S. aureus*

Antibiotics


Brilacidin
(Phase II)


Lefamulin


Afabicin
(Phase II)


Delafloxacin


Omadacycline


Exebacase
(Phase II)

Prone to resistance

- Bactericidal reagents creates strong selective pressure for resistance
- Antibiotics/bactericides leaked into the ecosystem creates a continuous selective pressure for bacterial resistance

New modalities

Symbiotics© Treatment

(Gene therapy for bacteria to inactivate antibiotic sensitivity)

Likely extremely costly

- S. aureus has a doubling time of 30 minutes[1]. To perform efficient gene therapy on bacteria will likely be prohibited by cost
- Can only design therapy for known antibiotic resistant mechanisms

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ALS-4

(Anti-virulent drug candidate)

Not prone to resistance

- Disables bacterial virulence to facilitate host immune clearance
- Not bactericidal on its own, if exposed to the ecosystem the selective pressure to develop resistance is less significant
- Oral formulation opens up ALS-4 to the preventive market and maintenance therapy. Mainstay of current antibiotic treatments have no oral form for systemic infection
- Does not directly compete with antibiotics

1. Todar's online textbook of bacteriology: http://textbookofbacteriology.net/growth_3.html

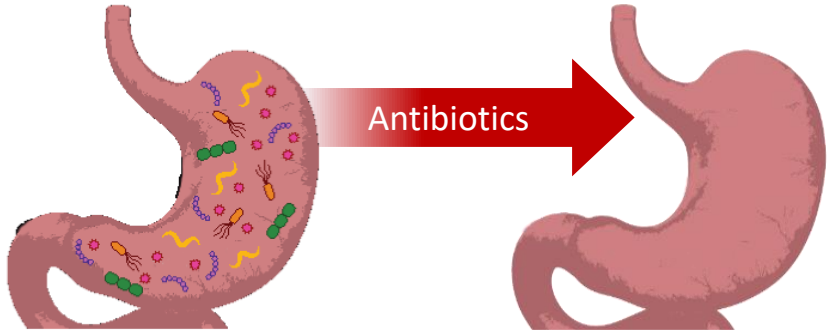
The description of ALS-4 and related conclusory statements on ALS-4 on this slide are based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing.

ALS-4: Value Proposition

Antibiotic

- Antibiotic resistance in S. aureus has been discovered in most prescribed antibiotics for MRSA[1]
- Broad spectrum and indiscriminate[2]
- Commonly affect normal flora, may lead to superinfection in case of drug resistance[3]

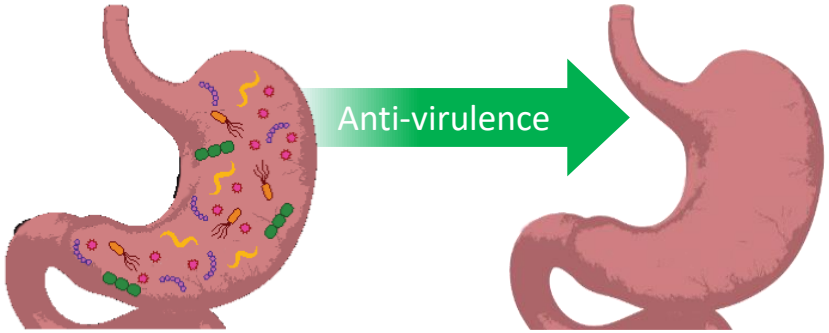
Indiscriminate clearance



Anti-virulence (ALS-4)

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

Directed against pathogen



1. Refer to "ALS-4: Approved Drugs for MRSA Infections" for complete set of sources; 2. P T. 2016 Feb; 41(2): 126–128; 3. J Infect Dis. 2018 Jan 30;217(4):628-636; 4. Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing; 5. MBio. 2017 Sep 5;8(5). pii: e01224-17; 6. J Exp Med. 2005 Jul 18;202(2):209-15.

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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.

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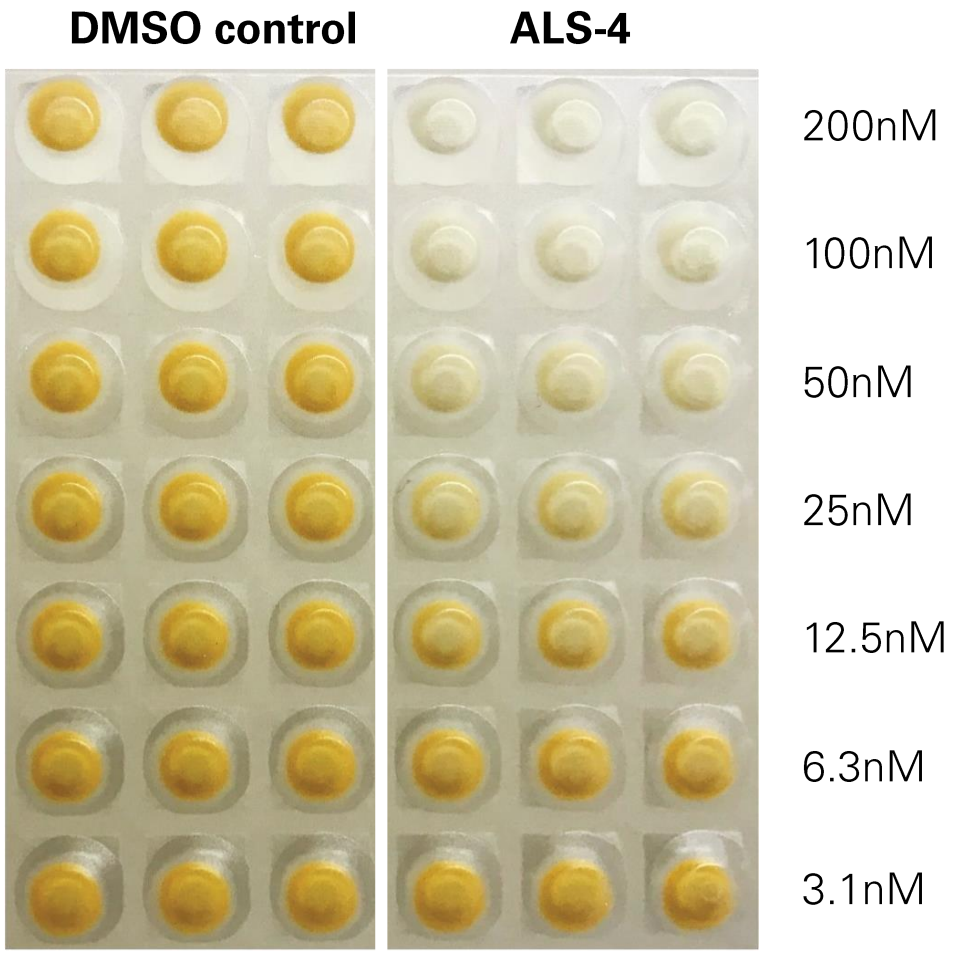
ALS-4: Mechanism of Action

ALS-4

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

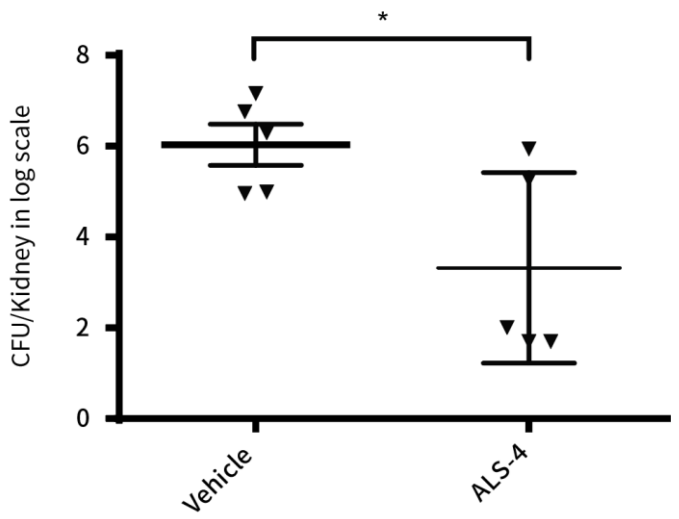


Based on Aptorum's internal tests/experimentation and has not yet been verified by clinical trials or third party testing. Applies to all content on this slide.

ALS-4: *In Vivo* Efficacy

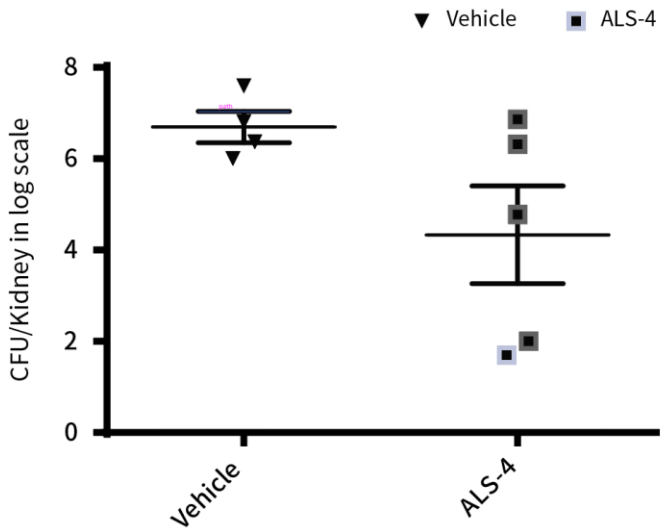
ALS-4 inhibits *S. aureus* pigment production with an IC_{50} = 20nM

Acute treatment



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

Delayed treatment



ALS-4 concentration: 1 mM
Inoculum: 2 X 10^7 per mouse
Treatment: twice for first 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.

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Unique Opportunity to Tackle Infectious Disease

Revolutionary Anti-virulence Approach

Award-winning approach to tackle a huge global unmet need: bacterial infections caused by *Staphylococcus aureus* including MRSA

Excellent Traction Towards IND Filing

Good progress on IND-enabling studies, with the expected IND filing in Q3/4 2020

1st place, Innovation Academy Category, ICPIC 2017

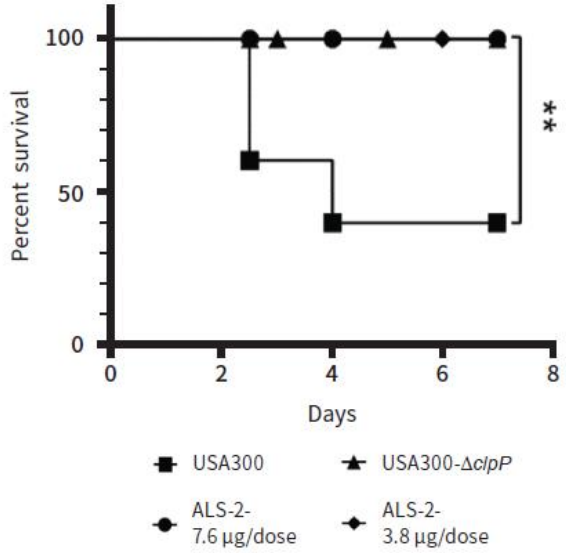
- Awarded to the Company's Hong Kong team, led by Dr. Richard KAO
- For the revolutionary concept of applying chemical genetics to tackle MRSA infection, which forms the scientific basis of ALS-2, ALS-3 and ALS-4

ALS-2 & ALS-3

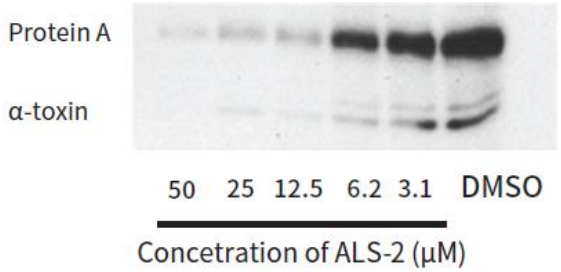
Additional anti-virulence, non-bactericidal therapeutics for the treatment of infections caused by Gram Positive bacteria

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

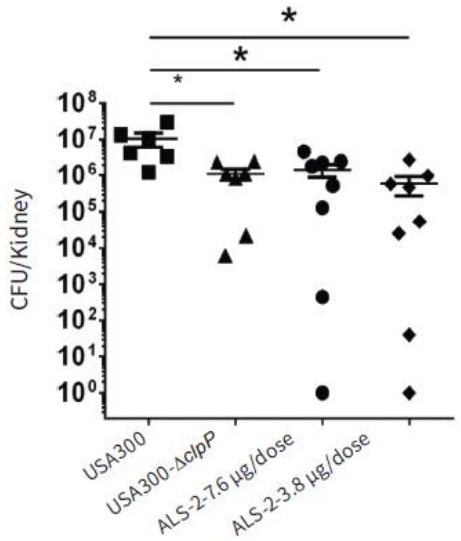
ALS-2 rescues mice from MRSA infection[1]



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

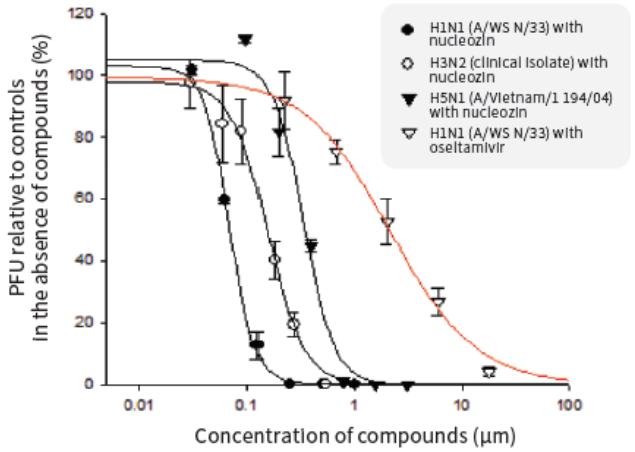
1. Proc Natl Acad Sci U S A. 2018 Jul 31;115(31):8003-8008

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

ALS-1 inhibits influenza A nucleoprotein (NP)

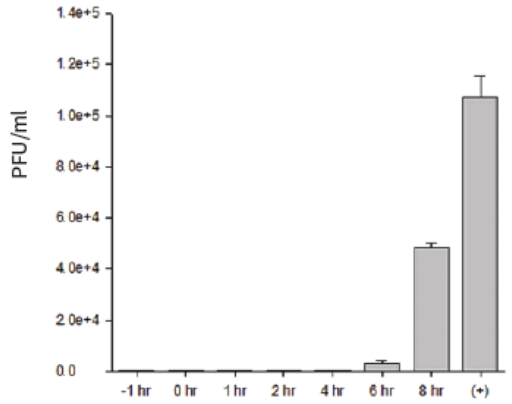
- NP is the most abundantly expressed protein during the course of an infection[1]. Its primary function is to encapsidate the virus genome for RNA transcription, replication and packaging. It is also a key adapter molecule between virus and host processes[1]
- ALS-1, by targeting NPs, acts upstream 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[3]

ALS-1 outperforms Tamiflu® (oseltamivir, in red) in vitro with a lower IC50[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; 3. Refer to the next slide "ALS-1: A Unique Antiviral Therapeutic Against Influenza A".

ALS-1: A Unique Antiviral Therapeutic Against Influenza A

Influenza A

- WHO estimates ~1 billion people are infected and up to 500,000 people die from influenza each year[1]
- There are four types of influenza viruses: influenza A, B, C, D. Influenza A causes the most serious disease in humans and is the most common cause of seasonal flu epidemics and pandemics[1]

Treatments for influenza A

	Drug (trade name)	Class	Mechanism	Route of administration	Notes
Recommended by the CDC for the 18/19 season	Oseltamivir (Tamiflu)	Neuraminidase inhibitor	Prevents viral release from host cell	Oral	• Most commonly prescribed, oseltamivir (Tamiflu) was approved in 19993. Almost 100% of the 08/09 seasonal H1N1 viruses in the US were resistant to oseltamivir[4,5,6,7,8,9]
	Zanamivir (Relenza)			Inhalation / IV	• Resistance against other neuraminidase inhibitors are rapidly rising[10]
	Peramivir (Rapivab)			IV	
	Baloxavir marboxil (Xofluza)	Cap-dependent endonuclease inhibitor	Prevents viral RNA replication	Oral	• Recently approved in October 201811. According to FDA, baloxavir beat placebo but not oseltamivir (Tamiflu) on the alleviation of symptoms[12]
	Adamantanes incl. amantadines and rimantadines	M2 inhibitor	Prevents intracellular uncoating of the virus's shell	Oral	• Not recommended due to >99% resistance among circulating viruses[2]

1. World Health Organization. Influenza (seasonal)—Fact sheet No 211. 2014. www.who.int/mediacentre/factsheets/fs211/en; 2. Influenza Antiviral Medications: Summary for Clinicians. CDC. https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm; 3. https://www.accessdata.fda.gov/drugsatfda_docs/nda/99/21087_Tamiflu.cfm; 4. N Engl J Med. 2006 Nov 23;355(21):2174-7; 5. Science. 2006 Apr 21;312(5772):389-91; 6. N Engl J Med. 2009 Mar 5;360(10):953-6; 7. JAMA. 2009 Mar 11;301(10):1034-41; 8. Science. 2009 Mar 20;323(5921):1560-1; 9. Curr Opin Infect Dis. 2008 Dec;21(6):626-38; 10. Acta Biochim Pol. 2014;61(3):505-8; 11. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/210854Orig1s000TOC.cfm; 12. https://www.fda.gov/news-events/press-announcements/fda-approves-new-drug-treat-influenza.

APTORUM

Facilitating Life Science Innovations to Serve Unmet Medical Needs

CLAVES PROJECTS

Executive Summary

Human Microbiota

- We live in constant symbiosis with our gut bacteria, and dysbiosis can be the cause to numerous diseases[1]

Claves Technology

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

CLS-1: Lead Program Targeting Obesity

- CLS-1 is the lead program in the Claves projects, intended to target metabolites secreted by the microbiota linked to obesity[2]
- CLS-1 is also shown to modulate gut microbiota population linked to obesity[2,3]
- CLS-1 achieves significant weight loss in a mouse model without affecting the gut mucosa, inflammation, and the functions of the liver and kidneys[2,3]
- Non-absorbable nature of the Claves therapeutics may expedite traditional toxicological studies[2]
- US FDA IND submission and Phase 1 studies expected to commence in Q4 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

Landscape Overview: The Human Gut Microbiota

- Contains **100s of species of microbes**
- Constantly producing **1000s of active metabolites**
- Some metabolites provides immunological and metabolic benefits
- **Dysbiosis (microbial imbalance) is a significant factor in disease**

Source: Lancet. 2003 Feb 8;361(9356):512-9; 2. Science. 2012 Jun 8;336(6086):1268-73; 3. Gastroenterology. 2014 May;146(6):1547-53

CLS-1: Unmet Medical Needs in Obesity Treatment

Obesity Treatment

- First-line intervention for obesity such as dietary change and increased physical activity often fail in the long term[1]
- No consensus regarding the optimal therapy, and existing pharmacotherapy has limited effectiveness and an imperfect safety record[1]
- Gastric bypass surgery is still considered the "gold standard" due to its effectiveness, but only a small fraction of the qualifying population undergoes these procedures because of the associated risks[1,2]

FDA-approved anti-obesity medications (trade name, company)	Mechanism	Common side effects	Other complications
Orlistat (Xenical, Roche)	Reduces fat absorption in the gut	Diarrhea, gas, leakage of oily stools, stomach pain	Rare cases of sever liver injury
Lorcaserin (Belviq, Arena)	Suppressing appetite	Constipation, cough, dizziness, dry mouth, feeling tired, headaches, nausea	May cause complications when taken with antidepressants
Phentermine-topiramate (Qsymia, Vivus)		Constipation, dizziness, dry mouth, taste changes, tingling of hands and feet, insomnia	May lead to birth defects
Naltrexone-bupropion (Contrave, Nalpropion)		Constipation, diarrhea, dizziness, dry mouth, headache, increased blood pressure, increased heart rate, insomnia, liver damage, nausea, vomiting	May not use in conjunction with a variety of medications
Liraglutide (Saxenda, Novo Nordisk)		Constipation, diarrhea, nausea, abdominal pain, headache, increased heart rate	May increase chance of developing pancreatitis
Others (phentermine, benzphetamine, diethylpropion, phendimetrazine)		Dry mouth, constipation, insomnia, dizziness, restlessness, headache, raised blood pressure, increased heart rate, feeling nervous	May not use in conjunction with a variety of medications

1. Obes Surg. 2012 Jun;22(6):956-66; 2. J Am Assoc Nurse Pract. 2017 Oct;29(S1):S30-S42; 3. National Institute of Diabetes and Digestive and Kidney Diseases https://www.niddk.nih.gov/health-information/weight-management/prescription-medications-treat-overweight-obesity

CLS-1: Value Proposition

CLS-1

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

Claves Platform

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

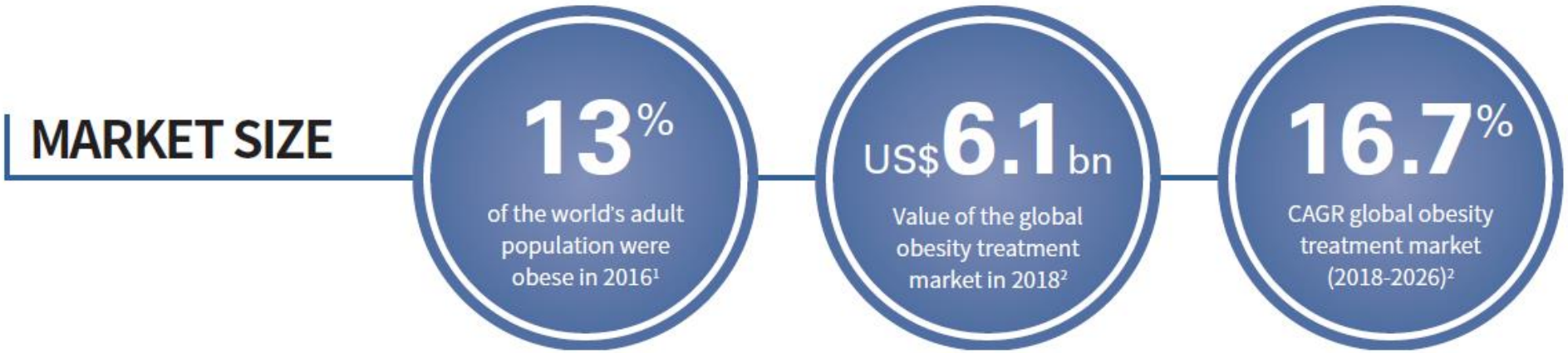
POSSIBLE INDICATIONS

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

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

CLS-1: Market Overview

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



Recent Deals in Obesity Treatment

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

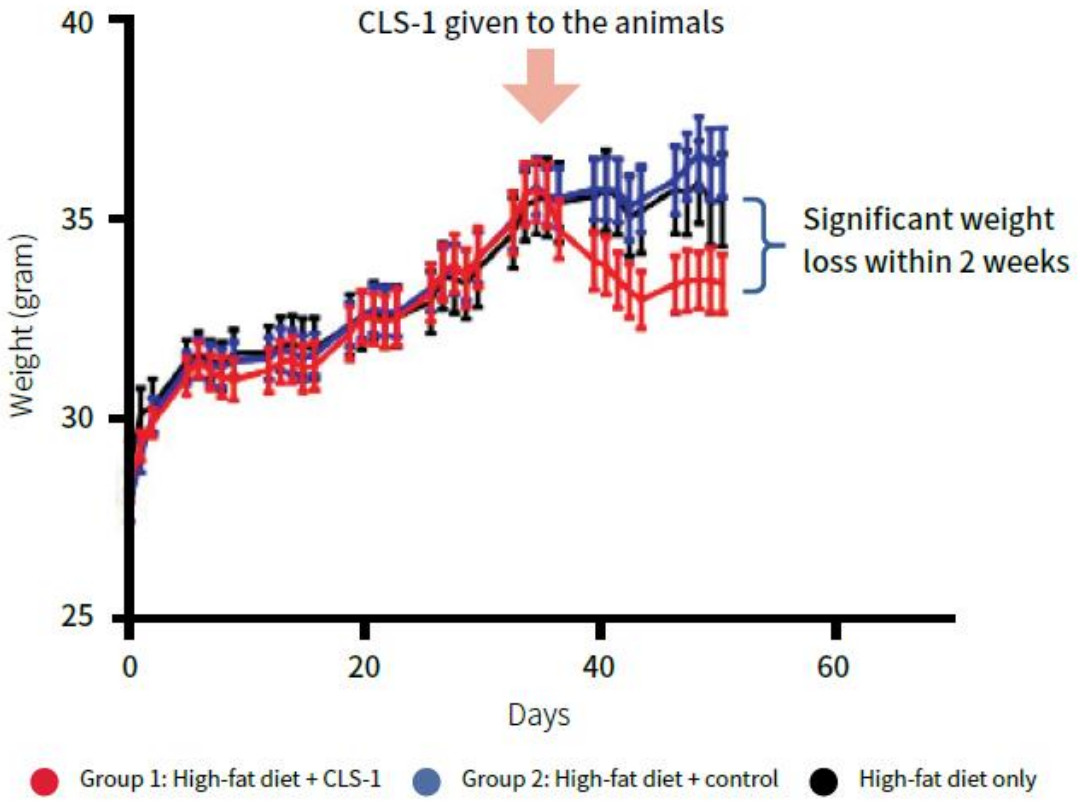
Competing Drugs

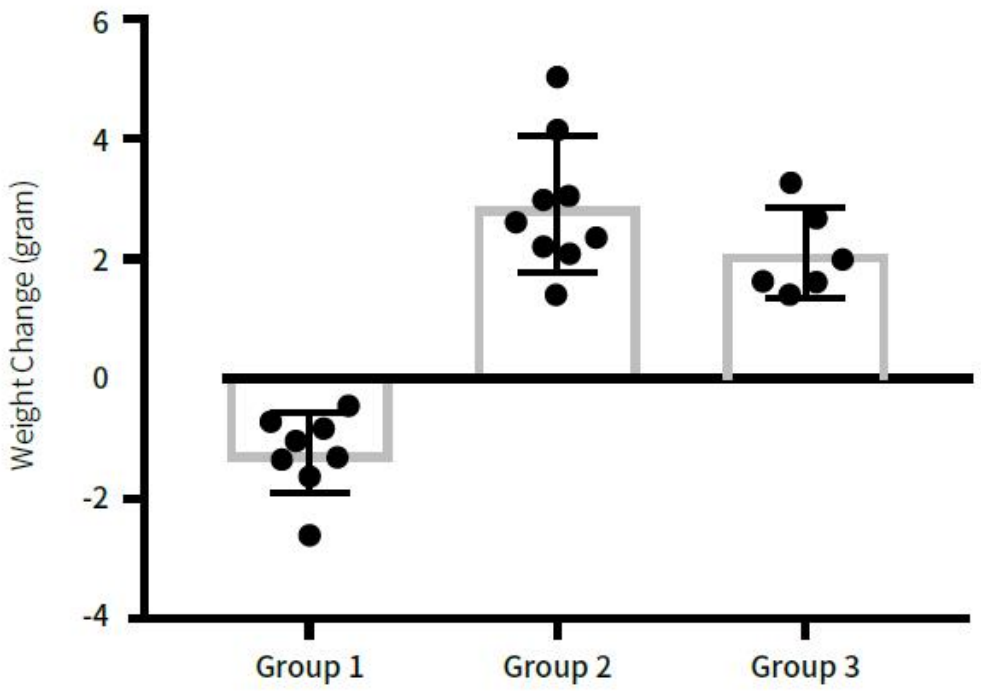
- CLS-1 is a drug candidate for obesity treatment that achieves its effect by modulating the chemical signaling of gut microbiota. There are no obesity treatment drugs on the market using similar mechanism[3].

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

CLS-1: Efficacy in a Mouse Model

CLS-1 treatment significantly reduces body weight in mice





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

APTORUM

Facilitating Life Science Innovations to Serve Unmet Medical Needs

DIETARY SUPPLEMENT FOR MENOPAUSAL SYMPTOMS (NLS-2)

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	Commercialization
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

Landscape Overview and Value Proposition

Menopausal syndrome

- Symptoms include hot flashes, mood disorders, night sweats, depression, nervous tension, and insomnia
- Menopause also puts women at increased risk of cardiovascular disease and osteoporosis

Hormone replacement therapy (HRT)

- Hormone replacement therapy restores endogenous estrogen levels using exogenous estrogen and progestin[1,2,3,4]
- Effective in relieving menopausal symptoms, however HRT is associated with:
- Breast cancer[5,6,7]
- Ovarian cancer[5]
- Venous thromboembolism[8]
- Stroke[8]
- Endometrial cancer[9]
- Current crisis in shortage of HRT supplies highlights urgent need for alternative treatments[10,11]

Currently available dietary supplements

- A widely-marketed type of dietary supplement for menopausal symptoms are plant-based phytoestrogens (a class of isoflavones)[12,] commonly derived from soy, black cohosh and red clover[12]
- Evidence for relief of menopausal symptoms is weak, with a large placebo effect observed in most clinical trials[13,14,15,16]
- "Among nonprescription remedies, clinical trial results are insufficient to either support or refute efficacy for soy foods and isoflavone supplements (from either soy or red clover), black cohosh, or vitamin E." -2004 statement from the North American Menopause Society[17]

APTORUM DOI supplement

- DOI is a non-toxic novel compound. Proof-of-concept studies demonstrated that DOI stimulated estrogen production via a non-hormonal, tissue-specific mechanism[18]
- Aptorum is developing formulation as dietary supplement containing DOI

1. Obstet Gynecol. 2002 Dec;100(6):1209-18; 2. Obstet Gynecol. 2004 Nov;104(5 Pt 1):1042-50; 3. Journal of internal medicine. 256, 361–374. 4. Lancet. 2003; 362:419–427; 5. Womens Health (Lond). 2013 Jan;9(1):59-67; 6. JAMA. 2000; 283:485–491; 7. Lancet. 2003; 362:419–427; 8. J Intern Med. 2004 Nov;256(5):361-74; 9. Obstet Gynecol. 1995 Feb;85(2):304-13; 10. https://www.theguardian.com/society/2019/aug/24/hrt-shortage-ukwomen; 11. https://www.bbc.com/news/health-49304163; 12. Front Neuroendocrinol. 2010 Oct; 31(4): 400–419; 13. Mol. Nutr. Food Res. 2009; 53:1084–1097; 14. Inflammopharmacology. 2008; 16:227–229; 15. Expert. Opin. Pharmacother. 2009; 10:1133–1144; 16. J. Nutr. 2003; 133:1983S–1986S; 17. Menopause. 2004; 11:11–33; 18. Sci. Rep. 5, 10179; doi: 10.1038/srep10179 (2015).

Market Overview

1.2bn

- postmenopausal women projected by the year 2030[1]
- **85%** of postmenopausal women experience menopause-related symptoms in their lifetime[2]

USD **2.5** bn

Value of the global menopause treatment market in 2019[3]

USD **17.1** bn

Value of the global isoflavone supplement market in 2019[4]

4.2%

CAGR global menopause treatment market (2017-2023)[3]

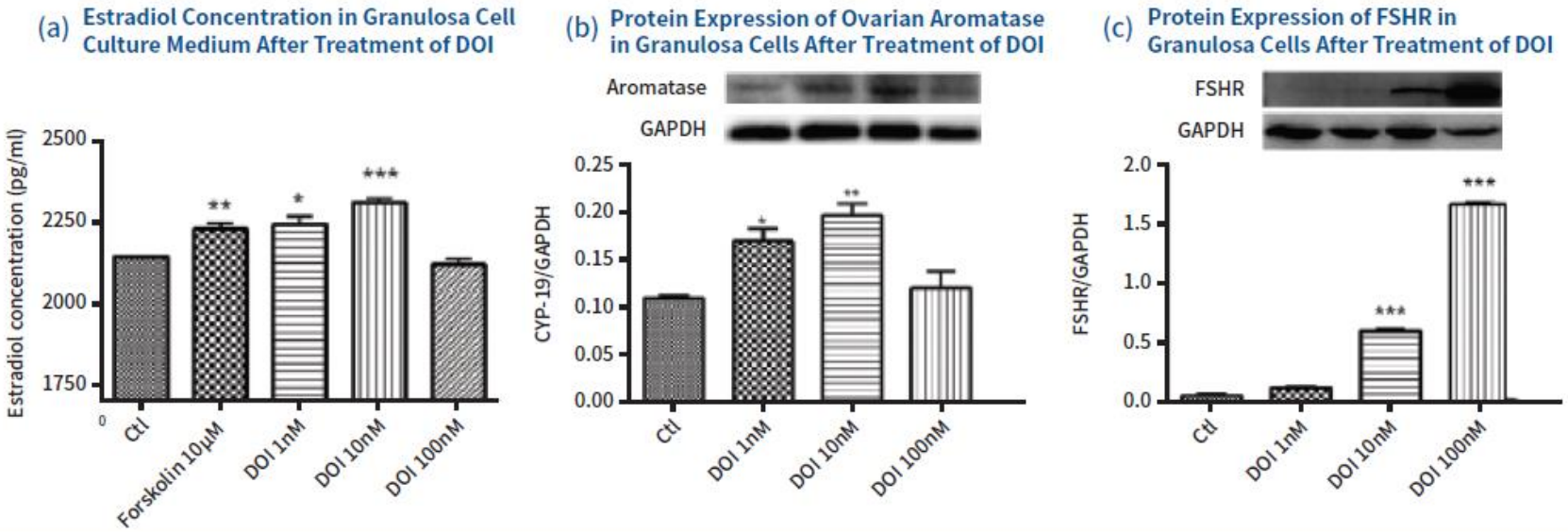
1. World Health Technical Report Series . Research on the Menopause in the 1990's, https://apps.who.int/iris/bitstream/handle/10665/41841/WHO_TRS_866.pdf?sequence=1&isAllowed=y; 2. Symptoms during the perimenopause: prevalence, severity, trajectory, and significance in women's lives, https://www.amjmed.com/article/S0002-9343(05)00885-5/fulltext; 3. Calculated based on the forecasted market size of USD 3bn by 2023 and a forecasted CAGR of 4.2% between 2017-2023. Menopause Treatment Market 2019: https://www.reuters.com/brandfeatures/venture-capital/article?id=119980; 4. Isoflavones Market Size To Reach USD 50.06 Billion By 2025. https://www.grandviewresearch.com/press-release/global-isoflavones-market. (Isoflavones are naturally occurring compounds found in a wide variety of plants. The isoflavones supplement market is the main menopausal supplement market.)

DOI- A Chinese Yam Extract To Address Menopausal Syndrome

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.**



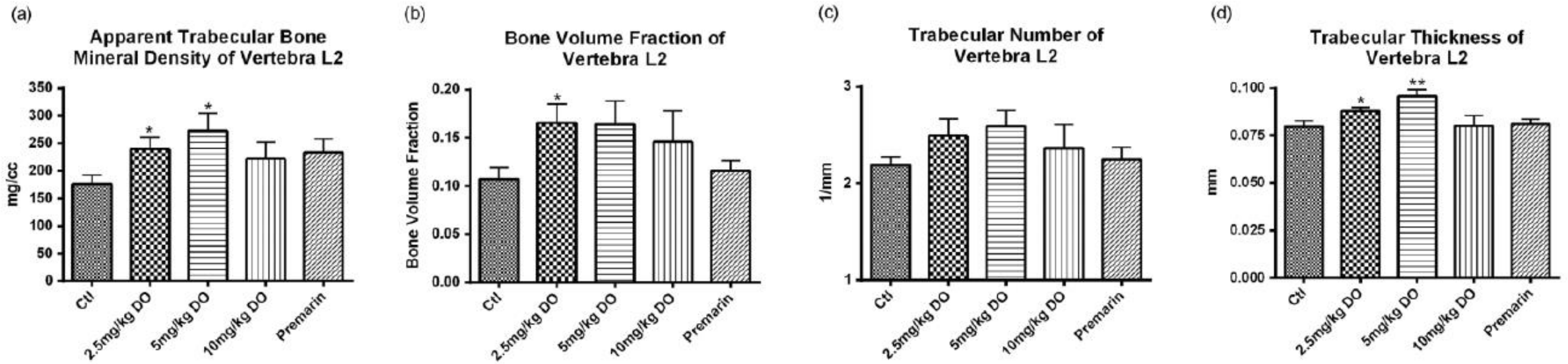
(a) Stimulatory activity of DOI on estrogen biosynthesis in granulosa cells. Protein expression of (b) aromatase and (c) follicle-stimulating hormone receptor (FSHR) in ovarian granulosa cells. Results are expressed as means ± SEM (n = 3). *P < 0.05, **P < 0.01, ***P < 0.001 compared with the control 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 Syndrome

DOI and bone density[1]

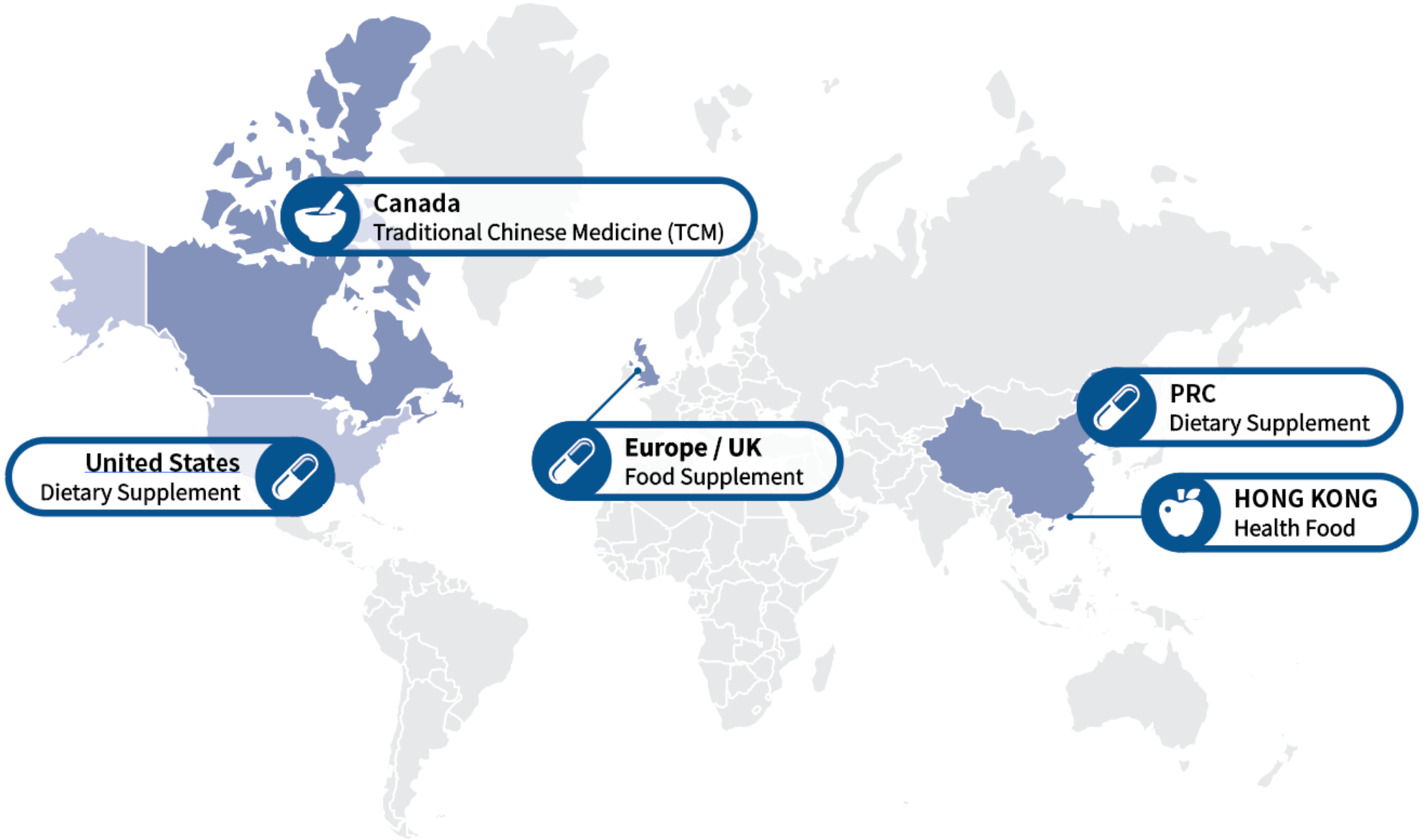
- DOI in old female SD rats demonstrated an increase in the apparent bone mineral density, bone volume fraction and trabecular thickness by microCT scanning



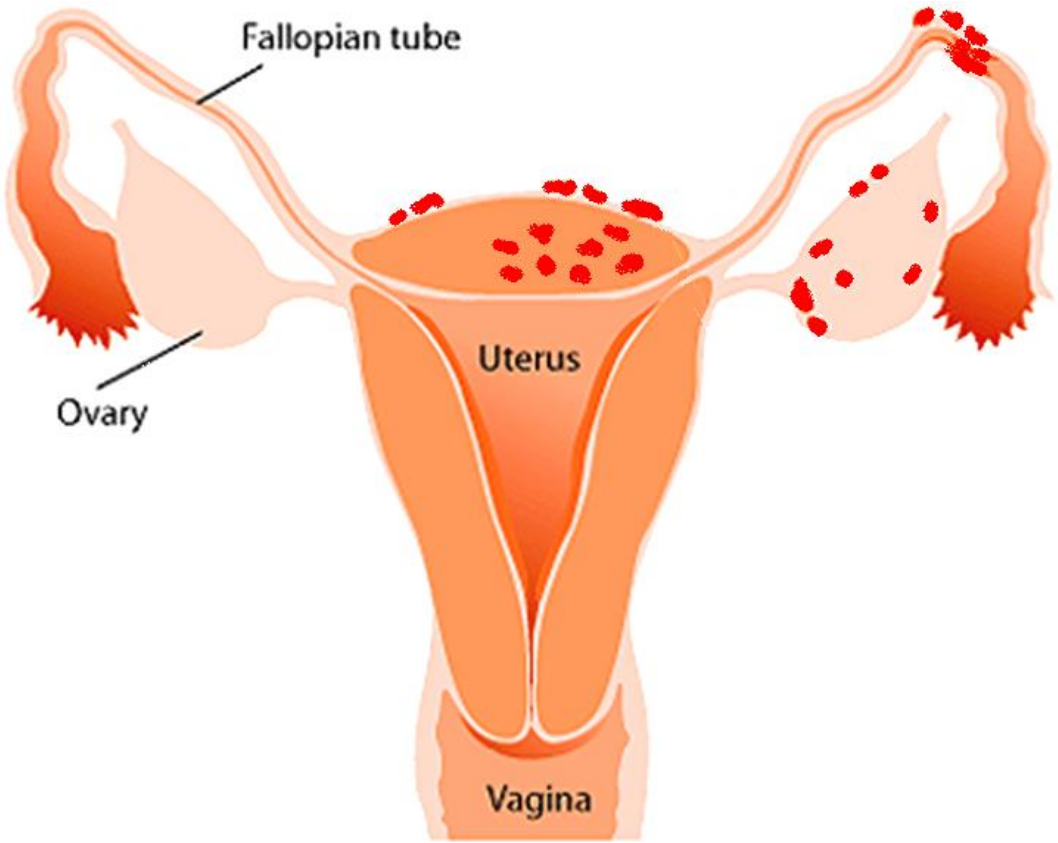
(a) Serum estradiol, (b) apparent trabecular bone mineral density, (c) bone volume fraction of Sprague Dawley rats after treatment with DOI for 2, 4, and 6 weeks. Results are expressed as means ± SEM (n = 6; except Premarin group, where n = 3). *p < 0.05, **p < 0.01 compared with the control group (unpaired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

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

Regulatory Information



NLS-1: Treatment of Endometriosis with a Non-Hormonal Approach



Endometrium outside the uterine cavity

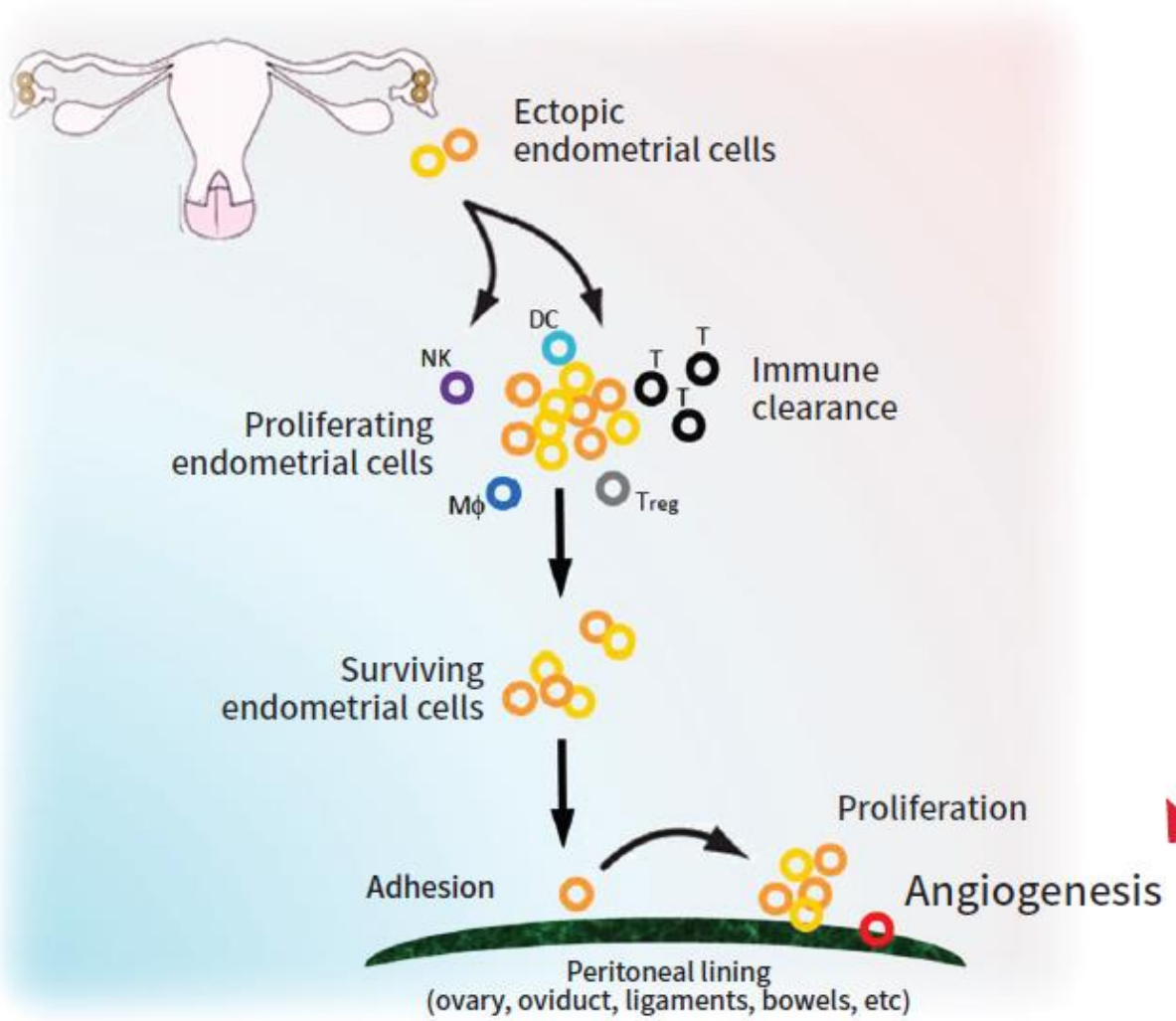
A chronic gynecological disorder affecting 10% of woman during reproductive ages with 176 million known cases worldwide[1]

Medical Problems[2]

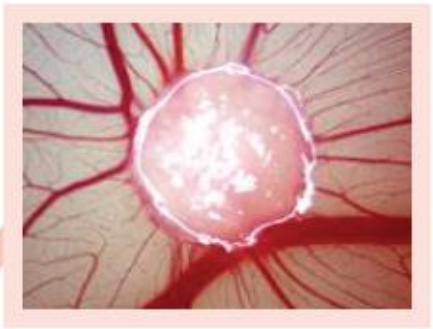
- chronic pelvic pain
- dysmenorrhea
- infertility ectopic pregnancy
- miscarriage

1. Endometriosis.org: Facts about endometriosis, http://endometriosis.org/resources/articles/facts-about-endometriosis; 2. J Assist Reprod Genet. 2010 Aug;27(8):441-7.

NLS-1: Pathophysiology

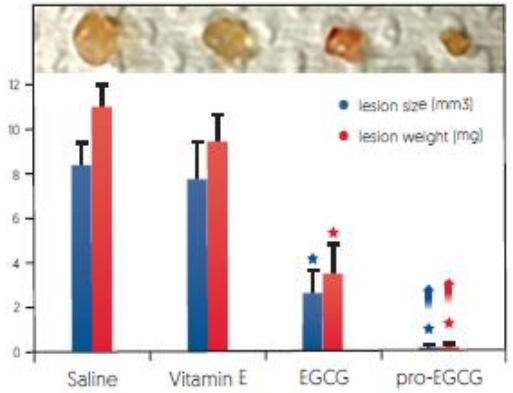


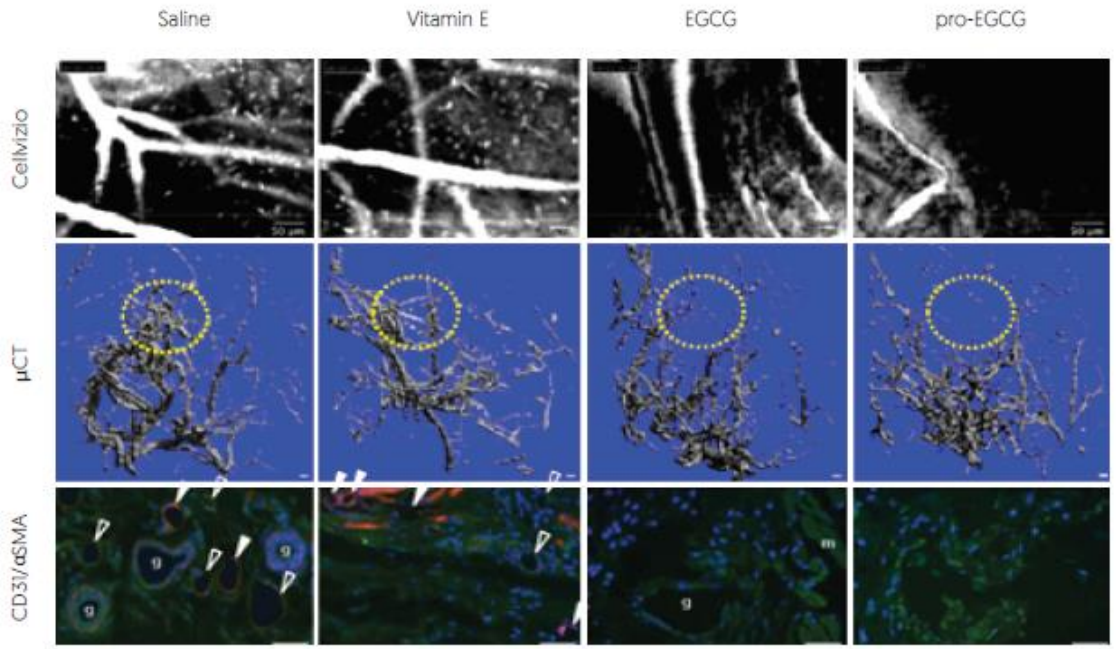
The areas of endometriosis bleed, resulting in inflammation and scarring[2]



1. The figure is modified from Hum Reprod Update. 2011 Nov-Dec;17(6):829-47; 2. J Assist Reprod Genet. 2010 Aug;27(8):441-7.

NLS-1: A Potent Anti-Angiogenesis Agent for Endometriosis in Mice



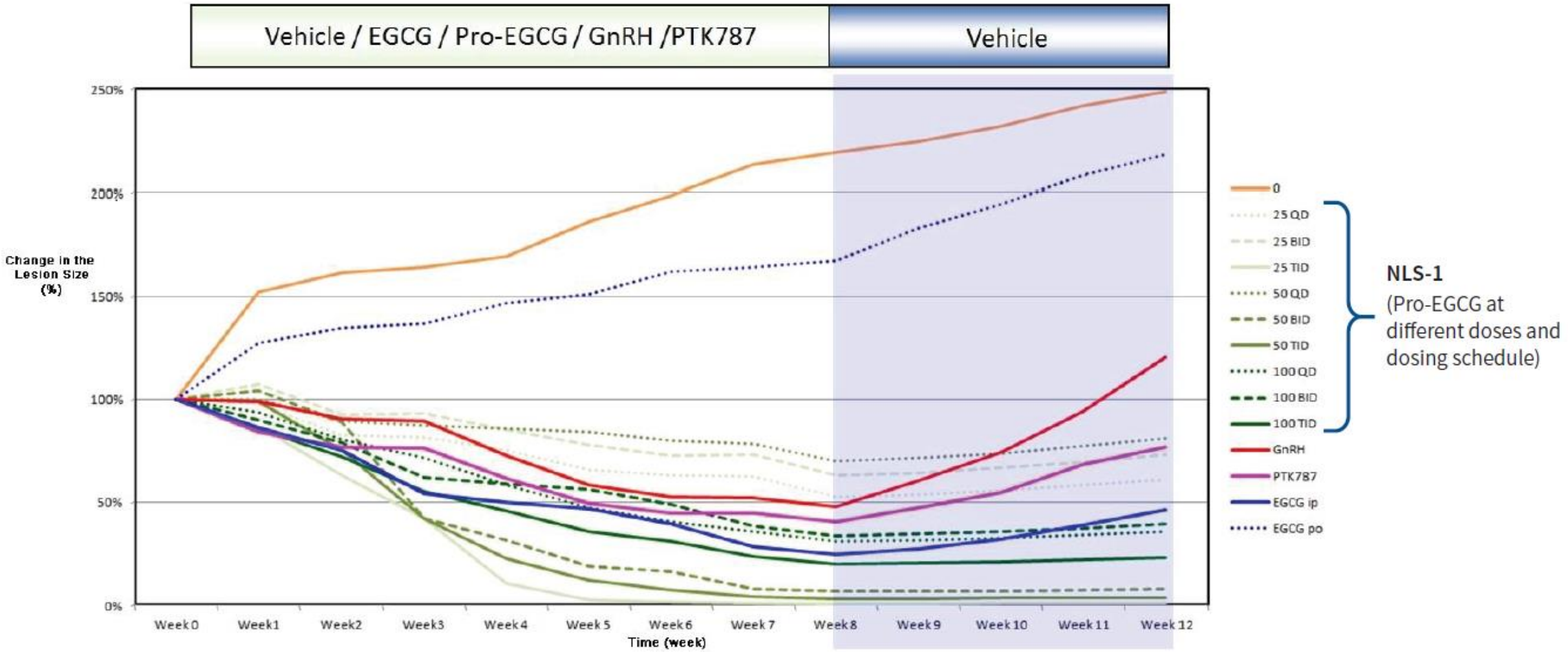


Studies utilizing mouse endometriosis models demonstrated that administration of NLS-1 resulted in greater reductions in the size and weight of lesions than Vitamin E, EGCG or the control without any treatment molecule.

Studies utilizing mouse endometriosis models demonstrated that administration of NLS-1 resulted in greater reductions in angiogenesis than Vitamin E, EGCG or the control without any treatment molecule.

All content on this slide is adapted from Angiogenesis. 2013 Jan;16(1):59-69.

NLS-1: Efficacy in an Animal Model



Comparison of the efficacy of different treatment in an experimental endometriosis model

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


APPENDIX

Recent Business Update

SEPTEMBER 9, 2019	Aptorum Group has initiated IND-enabling studies for its ALS-4 small molecule candidate against *S. aureus* including MRSA Aptorum Group commenced the preclinical development of two novel drug candidates, CLS-1 and SACT-1, for indications in Obesity and Neuroblastoma respectively
May 6, 2019	Aptorum Group's Subsidiary, Claves Life Sciences Limited, established a novel therapeutic platform for treatment of various diseases via modulation of the chemical signaling relating to gut microbiota
April 24, 2019	Aptorum Group, Aeneas Capital Limited, and A*ccelerate Technologies Pte Ltd, the enterprise office of the Agency for Science, Technology and Research (A*STAR), signed a USD 90 million agreement to co-create local deep tech start-ups in the healthcare and life sciences sector
April 24, 2019	Aptorum Group established Smart Pharma to focus on computational repurposed drug discovery for orphan and unmet diseases

ALS-4: Projected Sales

A highly-specific, anti-virulent drug candidate[1], ALS-4's pricing will be in contrast with the low pricing of generic antibiotics (e.g. vancomycin)[2]

Invasive MRSA[3]	US	EU	PRC	JP	RoW	Global
Infection rate	0.029%	0.029%	0.029%	0.029%	0.029%	0.029%
Treatment penetration rate	100%	100%	80%	100%	30%	50%
Peak patient volume share	80%	70%	50%	80%	50%	57%
ASP at launch (USD)	20,000	10,000	6,000	10,000	3,000	7,705
Patients covered at peak sales ('000)	86	159	222	28	266	762
Peak sales (USDm)	1,716	1,594	1,335	284	799	5,722

S. Aureus excl. invasive MRSA[3]	US	EU	PRC	JP	RoW	Global
Infection rate	0.036%	0.036%	0.036%	0.036%	0.036%	0.036%
Treatment penetration rate	100%	100%	80%	100%	30%	50%
Peak patient volume share	20%	15%	10%	20%	5%	10%
ASP at launch (USD)	20,000	10,000	6,000	10,000	3,000	9,067
Patients covered at peak sales ('000)	26	42	55	9	33	165
Peak sales (USDm)	529	421	329	87	99	1,465

1. MBio. 2017 Sep 5;8(5). pii: e01224-17 and 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. All projected figures on this slide are internal estimates.

Income Statement Summary (U.S. GAAP)[1]

	SIX MONTHS ENDED JUNE 30 (UNAUDITED)		YEAR ENDED DECEMBER 31, 2018	MARCH 1, 2017 THROUGH DECEMBER 31, 2017
	2019	2018		
	USD	USD	USD	USD
Revenue	239,792	26,662	383,450	-
Research and development expenses	(2,714,217)	(1,342,179)	(3,101,432)	(2,560,323)
General and administrative fees	(3,232,916)	(2,238,025)	(4,919,626)	(1,480,093)
Legal and professional fees	(2,008,774)	(1,063,032)	(1,811,770)	(1,395,490)
Net loss attributable to Aptorum Group Limited	(9,088,471)	(5,488,372)	(14,831,723)	(2,547,462)
Net loss per share – basic and diluted	(0.31)	(0.20)	(0.53)	(0.09)
Interest (expense) income, net[2]	(3,678,566)	(301,362)	(4,458,191)	44,269
Depreciation and amortization	(585,701)	(209,267)	(682,902)	(58,903)
Share based compensation expenses	(593,806)	-	-	-

Notes:

1. The following slide contains selected information for the Company's income statement. Please see the Company's most recently filed Form 20-F and Form-1/A for the Company's complete financial statements.

2. During the six months ended June 30, 2019 and year ended December 31, 2018, the net interest expenses included USD 3.1 M and USD 2.4 M, respectively, amortization of beneficial conversion feature which are non-cash items.

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

	June 30 2019 (unaudited)	December 31 2018	December 31 2017
	USD	USD	USD
Cash, restricted cash and marketable securities	6,135,837	27,121,576	18,698,455
Total current assets	7,742,644	28,722,941	20,283,399
Property, plant and equipment, net	5,777,657	4,260,602	346,587
Total assets	24,730,370	45,074,640	31,559,982
Convertible debts	-	(10,107,306)	(480,000)
Warrant liabilities	-	(753,118)	-
Total current liabilities	(597,141)	(12,184,865)	(1,330,734)
Total liabilities	(718,082)	(12,328,738)	(1,330,734)
Total equity attributable to the shareholders of Aptorum Group Limited	24,942,586	33,114,435	30,243,293
Working Capital[2,3]	7,145,503	16,538,076	18,952,665

Notes:

1. The following slide contains selected information for the Company's balance sheets. Please see the Company's most recently filed form 20-F and Form F-1/A for the Company's complete financial statements.

2. Current assets less current liabilities.

3. As of September 2019, Aptorum Group has access to over USD15m in working capital from shareholder support

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