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

FORM 20-F/A
(Amendment No. 1)

☐ REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934

OR

☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2018

OR

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

OR

☐ SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Date of event requiring this shell company report

For the transition period from _____ to _____

Commission file number: 001-38764

APTORUM GROUP LIMITED
(Exact Name of Registrant as Specified in its Charter)

N/A
(Translation of Registrant's Name into English)

Cayman Islands
(Jurisdiction of Incorporation or Organization)

Ian Huen, Chief Executive Officer
Aptorum Group Limited
17/F Guangdong Investment Tower, 148 Connaught Road Central, Hong Kong
Tel: +(852) 2117 6611
Fax: (852) 2850 7286
(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

Securities registered or to be registered pursuant to Section 12(b) of the Act:

Title of Each Class	Name of Each Exchange on Which Registered
Class A Ordinary shares, par value $1.00	NASDAQ Global Market

Securities registered or to be registered pursuant to Section 12(g) of the Act:

None
(Title of Class)

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act:

None
(Title of Class)

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the annual report.

Class A Ordinary Shares: 6,537,269
Class B Ordinary Shares: 22,437,754

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934. Yes ☐ No ☒

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or an emerging growth company. See definition of "large accelerated filer," accelerated filer," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Emerging growth company	☒

If an emerging growth company that prepares its financial statements in accordance with U.S. GAAP, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

U.S. GAAP ☒ International Financial Reporting Standards as issued by the International Accounting Standards Board ☐ Other ☐

* If "Other" has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow. Item 17 ¨ Item 18 ¨

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

EXPLANATORY NOTE

This Amendment No. 1 on Form 20-F/A (the "Amendment") is being filed by Aptorum Group Limited (the "Company," "we," "our," or "us") to amend the Company's Annual Report on Form 20-F for the fiscal year ended December 31, 2018, originally filed with the U.S. Securities Exchange Commission on April 15, 2019 (the "Original Filing"). The Company is filing this Amendment solely to:

1. Include the complete corporate structure diagram included in Item 4. A. Information on the Company, History and Development of the Company (the "Diagram"). The Diagram included in the Original Filing inadvertently did not include the jurisdiction of our subsidiary, Smart Pharmaceutical Development Limited.

2. Include the complete development phase figure included in Item 4. B. Information on the Company, Business Overview, Lead Projects and Other Projects under Development (the "Figure"). The Figure included in the Original Filing inadvertently omitted the arrows showing the stage of development associated with 4 of our, non-lead, projects.

3. Include reference to the XBRL exhibits in the Exhibit Table within Item 19. The XBRL exhibits were filed with the Original Filing, but reference to same was inadvertently omitted from the exhibit table.

This Amendment consists solely of the cover page, this explanatory note, the entirety of Item 4 of Form 20-F – with the completed Figure and Diagram, Item 19, "Exhibits", Exhibits 12.1, 12.2 and 13.1 and a signature page. Except as described above, this Amendment does not amend any information set forth in the Original Filing or reflect any events that occurred subsequent to the filing of the Original Filing on April 15, 2019. Accordingly, this Amendment should be read in conjunction with the Original Filing and with our filings with the U.S. Securities Exchange Commission subsequent to the Original Filing.

Item 4. INFORMATION ON THE COMPANY

A. History and Development of the Company

Aptorum was incorporated under the laws of the Cayman Islands on September 13, 2010. Our share capital is $100,000,000.00 divided into 60,000,000 Class A Ordinary Shares with a nominal or par value of $1.00 each and 40,000,000 Class B Ordinary Shares with a nominal or par value of $1.00 each.

APTUS CAPITAL LIMITED, which has since been renamed to AENEAS CAPITAL LIMITED and which we refer to herein as Aeneas, was always under the direct ownership of Jurchen and not under the ownership chain of Aptorum Group. However, Aptus Asia Financial Holdings Limited ("AAFH"), which has since been renamed to Aeneas Group Limited, was transferred out of the Aptorum Group on November 10, 2017 to be held directly by Jurchen Investment Corporation and that subsequently, APTUS CAPITAL LIMITED was then transferred to be under AAFH.

On May 4, 2017, Mr. Huen transferred all of the ordinary shares in the Company he owned (in the amount of 22,307,596) to Jurchen, a company incorporated in the British Virgin Islands and wholly-owned by Mr. Huen. On October 13, 2017, as part of the Conversions (as defined below) the ordinary shares held by Jurchen were redesignated as 2,230,760 Class A Ordinary Shares and 20,076,836 Class B Ordinary Shares.

On February 21 and March 1, 2017, the Company's board of directors and shareholders resolved to restructure the Company from an investment fund with management shares and non-voting participating redeemable preference shares to a holding company with operating subsidiaries, respectively (the "Restructuring Plan").

According to the Restructuring Plan, the 256,571.12 issued participating shares with par value of $0.01 ("Participating Shares") were redeemed and 4,743,418.88 unissued Participating Shares were cancelled; following such redemption and cancellation, we no longer have any Participating Shares authorized or issued. Additionally, the Company authorized a class of securities consisting of 100,000,000 ordinary shares, par value $1.00 per share ("Ordinary Shares") and issued 25,657,110 Ordinary Shares to our original investors.

During the period March 1, 2017 through October 13, 2017, an aggregate of 2,207,025 Ordinary Shares were issued at a price of approximately $3.90 per share in a private placement we described as a "Series A" offering. Each investor of the Series A offering, in addition to a subscription agreement, signed a shareholder agreement, which set forth the basic governance terms of the Company, as well as our capital structure. The shareholders agreement was terminated in October 2017.

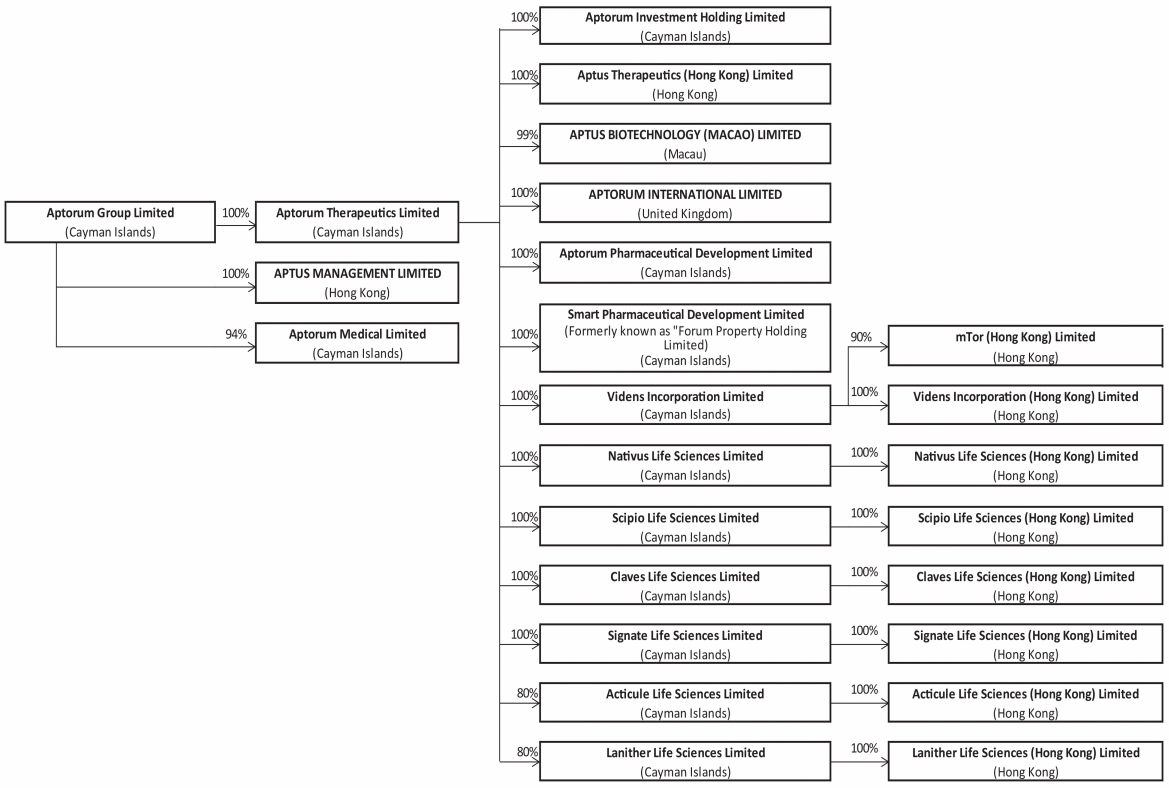
On October 13, 2017, ordinary resolutions were passed at an extraordinary general meeting of the Company approving (the "Conversions"): (i) converting 72,135,865 of authorized but unissued Ordinary Shares into 54,573,620 authorized but unissued Class A ordinary shares, par value of $1.00 per share ("Class A Ordinary Shares") and 17,562,245 authorized but unissued Class B ordinary shares, par value of $1.00 per share ("Class B Ordinary Shares"), respectively; (ii) converting 24,930,839 Ordinary Shares held by three shareholders into an aggregate of 2,493,085 Class A Ordinary Shares and 22,437,754 Class B Ordinary Shares; and (iii) converting 2,933,296 Ordinary Shares held by 24 shareholders into an aggregate 2,933,296 Class A Ordinary Shares. Following these issuances, we had 27 shareholders of record.

On October 19, 2017, we changed our name from APTUS Holdings Limited to our current name, Aptorum Group Limited.

On March 23, 2018, Jurchen transferred 446,152 Class A Ordinary Shares and 4,015,367 Class B Ordinary Shares to CGY Investments Limited, a company incorporated in Hong Kong and which we deem Mr. Darren Lui controls and/or of which he has substantial influence on the disposition rights and voting rights of such shares. Following this transfer, Jurchen owns approximately 33% and 72% of our Class A Ordinary Shares and Class B Ordinary Shares, respectively.

On December 17, 2018, the Company consummated its IPO of 761,419 Class A Ordinary Shares. The Registration Statement was declared effective by the U.S. Securities and Exchange Commission on December 3, 2018 (the "Effective Date"). The shares were sold at a price of $15.80 per share, generating gross proceeds to the Company of approximately $12,030,420. Immediately following the consummation of the IPO and automatic conversion of the Notes and Bonds, there were an aggregate of 6,537,269 Class A Ordinary Shares issued and outstanding.

The following diagram illustrates our corporate structure as of the date of this annual report:



Emerging Growth Company Status

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act (the "JOBS Act"), and we are eligible to take advantage of certain exemptions from various reporting and financial disclosure requirements that are applicable to other public companies, that are not emerging growth companies, including, but not limited to, (1) presenting only two years of audited financial statements and only two years of related management's discussion and analysis of financial condition and results of operations in this annual report, (2) not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, (3) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and (4) exemptions from the requirements of holding a non-binding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. We intend to take advantage of these exemptions.

In addition, Section 107 of the JOBS Act also provides that an emerging growth company can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act, for complying with new or revised accounting standards. As a result, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies.

We could remain an emerging growth company for up to five years, or until the earliest of (1) the last day of the first fiscal year in which our annual gross revenues exceed $1.07 billion, (2) the date that we become a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our Ordinary Shares that is held by non-affiliates exceeds $700 million as of the last business day of our most recently completed second fiscal quarter and we have been publicly reporting for at least 12 months, or (3) the date on which we have issued more than $1 billion in non-convertible debt during the preceding three-year period.

Foreign Private Issuer Status

We are a foreign private issuer within the meaning of the rules under the Exchange. As such, we are exempt from certain provisions applicable to United States domestic public companies. For example:

- we are not required to provide as many Exchange Act reports, or as frequently, as a domestic public company;
- for interim reporting, we are permitted to comply solely with our home country requirements, which are less rigorous than the rules that apply to domestic public companies;
- we are not required to provide the same level of disclosure on certain issues, such as executive compensation;
- we are exempt from provisions of Regulation FD aimed at preventing issuers from making selective disclosures of material information;
- we are not required to comply with the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act; and
- we are not required to comply with Section 16 of the Exchange Act requiring insiders to file public reports of their share ownership and trading activities and establishing insider liability for profits realized from any "short-swing" trading transaction.

B. Business Overview

Overview

We are a Hong Kong based pharmaceutical company currently in the preclinical stage, dedicated to developing and commercializing a broad range of therapeutic and diagnostic technologies to tackle unmet medical needs. We have obtained exclusive licenses for our technologies. In addition, we are also developing certain proprietary technologies as product candidates. We are pursuing therapeutic and diagnostic projects (including projects seeking to use extracts or derivatives from natural substances to treat diseases) in neurology, infectious diseases, gastroenterology, oncology and other disease areas. We also have projects focused on surgical robotics. (See "Item 4. Information on the Company – B. Business Overview – Lead Projects and Other Projects under Development – Lead Projects") Also, we opened a medical clinic, AML Clinic, in June 2018.

Although none of our drug or device candidates has yet been approved for testing in humans, our goal is to develop a broad range of early stage novel therapeutics and diagnostics across a wide range of disease/therapeutic areas. Key components of our strategy for achieving this goal include: (for details of our strategy, See "Item 4. Information on the Company – B. Business Overview – Our Strategy")

- Developing therapeutic and diagnostic innovations across a wide range of disease/therapeutic areas;
- Selectively expanding our portfolio with potential products that may be able to attain orphan drug designation and/or satisfy current unmet medical needs;
- Collaborating with leading academic institutions and CROs;
- Expanding our in-house pharmaceutical development center;
- Leveraging our management's expertise, experience and commercial networks;
- Strategically developing opportunities in Hong Kong to promote access to the PRC market; and
- Obtaining and leveraging government grants to fund project development.

We have devoted a portion of the proceeds from our IPO, to three therapeutic projects ("Lead Projects"). The drug candidates being advanced as the Lead Projects are ALS-1, ALS-4 and NLS-1, described in further detail below. If the results of the remaining preclinical studies of these drug candidates are positive, we expect to be able to submit by 2020 or 2021 an Investigational New Drug Application ("IND") for at least one of these candidates to the U.S. Food and Drug Administration ("FDA") or an equivalent application to the regulatory authorities in one or more other jurisdictions such as the China Food and Drug Administration ("NMPA") and/or the European Medicines Agency ("EMA"). Acceptance of these applications by the relevant regulatory authority would enable the Company to begin testing that drug candidate in humans in that jurisdiction. Our ability to obtain any approval of such applications is entirely dependent upon the results of our preclinical studies, none of which have yet been completed.

Our current business consists of "therapeutics" and "non-therapeutics" segments. However, our focus is on the therapeutics segments. Because of the risks, costs and extended development time required for successful drug development, we have determined to pursue projects within our non-therapeutics segments, such as AML Clinic, to provide some interim revenue and medical robots that may be brought to market and generate revenue more quickly.

Therapeutics Segment. In our therapeutics segment ("Aptorum Therapeutics Group"), we are currently seeking to develop various drug molecules (including projects seeking to use extracts or derivatives from natural substances to treat diseases) and certain technologies for the treatment ("therapeutics") and diagnosis ("diagnostics") of human disease conditions in neurology, infectious diseases, gastroenterology, oncology and other disease areas. In addition, we are seeking to identify additional prospects which may qualify for potential orphan drug designation (e.g., rare types of cancer) or which address other current unmet medical needs. Aptorum Therapeutics Group is operated through Aptorum's wholly-owned subsidiary, Aptorum Therapeutics Limited, a Cayman Islands exempted company with limited liability, whose principal place of business is in Hong Kong and its indirect subsidiary companies (who we sometimes refer to herein as project companies), whose principal places of business are also in Hong Kong.

Non-Therapeutics Segment. The non-therapeutics segment ("Aptorum Non-Therapeutics Group") encompasses two businesses: (i) the development of surgical robotics and medical devices and (ii) AML Clinic. The development of surgical robotics and medical devices business is operated through Signate Life Sciences Limited, a subsidiary of Aptorum Therapeutics Limited. The outpatient clinic is operated through our subsidiary, Aptorum Medical Limited. Effective as of March 2018, we leased office space in Central, Hong Kong as the home to AML Clinic. AML Clinic commenced operations under the name of Talem Medical in June 2018. The estimated general administrative expenses and other operating expenses of the AML Clinic is expected to be no more than USD120,000 per month. The clinic is expected to reach operating profit in 18 months from the clinic reaching its full operating capacity upon (i) the successful recruitment of a minimum of six full time physicians (AML Clinic currently has one full time physician and three part time physicians) and (ii) establishing steady patients flow via brand development. (See "Item 4. Information on the Company – B. Business Overview – Lead Projects and Other Projects under Development – Other Projects under Development – Aptorum Medical Limited - AML Clinic")

The Company has already obtained opportunities resulting in our existing licensing agreements from various contractual relationships that we have entered into, including service/consulting agreements with some of the world's leading specialists and clinicians in our areas of interest, with academic institutions and organizations, and with CROs. We anticipate that these relationships will generate additional licensing opportunities in the future. In addition, we have established and are continuing to expand our in-house research facilities (collectively, the "R&D Center") to develop some of our drug and device candidates internally and to collaborate with third-party researchers.

Prior to March 2017, the Company had pursued passive healthcare related investments in early stage companies primarily in the United States. However, we have since ceased pursuing further passive investment operations and intend to exit all such portfolio investments over an appropriate timeframe to focus resources on our current business.

Our Strategy

Although we plan to continue the development and improvement of a broad range of novel therapeutics and diagnostics across a wide range of disease/therapeutic areas, over the next 24-36 months we plan to concentrate on development of our Lead Projects, while also allocating some resources to develop SLS-1 and maintaining our AML Clinic.

We believe that execution of this strategy will position the Company to catalyze the development and improvement of a broad range of early-staged novel therapeutics and diagnostics across a wide range of disease/therapeutic areas. Failure to achieve positive results in at least one of the programs for a Lead Project could have a material adverse effect on the Company's prospects and business.

To achieve this goal, we are implementing the following strategies:

- **Developing therapeutic and diagnostic innovations across a wide range of disease/therapeutic areas.** We are currently developing drug and device candidates in several disease/therapeutic areas. We believe that by diversifying our research efforts, it would increase the likelihood that at least one of our projects will achieve clinical success and therefore add value to the Company. As of date of this Annual Report, we have obtained 12 exclusively licensed technologies across the areas of neurology, infectious diseases, gastroenterology, oncology, surgical robotics and natural health. Our initial focus will be on developing our Lead Projects, but intend to continue developing our other current projects and seeking new licensing opportunities where we determine that the market potential justifies the additional commitment of our limited resources.

- **Selectively expanding our portfolio with potential products that may be able to attain orphan drug designation and/or satisfy current unmet medical needs.** We have selected innovations for development which we believe are of superior scientific quality, whilst taking into account the potential market size and demand for same, for example, taking into consideration whether the relevant product can satisfy significant unmet medical needs. In particular, Aptorum Group Limited has established a Scientific Advisory Board, which helped us to select our current projects and which we expect will provide input from a scientific perspective towards any future opportunities for acquiring or licensing life science innovations. We intend to continue expanding our line of projects under development, and subject to our financial and other resource limitations, exploring acquisitions or licenses of additional products which may be able to attain orphan drug designations (e.g., rare types of cancer) or satisfy significant unmet medical needs and that show strong preclinical and/or early clinical data to provide promising opportunities for clinical and commercial success.

- **Collaborating with leading academic institutions and CROs.** In building and developing our product portfolio, we believe that accessing external innovation, expertise and technology through collaboration with leading academic institutions and CROs is a vital and cost-efficient strategy. We have established strong relationships with leading academic institutions around the world and expect to continue to strengthen our collaborations by, for example, seeking to provide their affiliated Principal Investigators resources through sponsorship to conduct further research in specialty fields of interest and association with personnel connected to our current project companies, in exchange for obtaining for the Company the first right to negotiate for an exclusive license to any resulting innovations. In addition, we have entered and will continue to actively source arrangements with pharmaceutical companies, in most cases in roles as contract research organizations, to streamline the development of our projects. This may include outsourcing part of the preclinical, clinical studies and clinical supplies manufacturing to externally accredited cGLP, cGMP and cGCP standard contract research organizations or laboratories in order to attain the required studies for submission to the regulatory authorities as part of the clinical development plan. (See "Item 4. Information on the Company – B. Business Overview – Arrangements with Other Parties")

- **Expanding our in-house pharmaceutical development center.** We believe collaborations between the R&D Center operated by APD and the scientists engaged in work for our project companies will enhance clinical and commercial potential of the projects. In addition, APD will assist the project companies by engaging external pharmaceutical companies and/or contract research organizations to outsource any part of the preclinical or clinical development work that cannot be performed by the R&D Center in order to obtain the resources necessary for our development process.

- **Leveraging our management's expertise, experience and commercial networks.** We believe the combination of our management's expertise and experience, with their academic and commercial networks make us an effective platform for advancing healthcare innovations towards clinical studies and commercialization in key global markets. We have assembled a management team with global experience and an extensive record of accomplishments in medical research, consulting and financing, and identification and acquisition of pharmaceutical and biopharmaceutical drug and device candidates. Our Head of Research and Development also has extensive experiences in drug development. We also employ key management personnel with banking and financial experience, which enhances our capability to establish the most efficient financial structure for the development of our programs.

- **Strategically developing opportunities in Hong Kong to provide access to the PRC market.** The PRC is the world's second largest healthcare market (https://seekingalpha.com/article/4038677-opportunities-chinas-healthcare-market) and we plan to market our products there in the future as part of our overall growth strategy. In October 2017, the PRC government announced that the country is planning to accept trial data gathered overseas to speed up drug approvals (https://www.reuters.com/article/us-china-pharmaceuticals/china-to-accept-overseas-trial-data-in-bid-to-speed-up-drug-approvals-idUSKBN1CE080 and http://www.lawinfochina.com/display.aspx?id=26778&lib=law), which is a potential boon for foreign pharmaceutical companies. We believe strategically locating our principal businesses in Hong Kong, as a Special Administrative Region of the PRC, may provide us distinctive advantages in accessing the PRC healthcare market. Two of our key collaborators, The University of Hong Kong (the "HKU") and the Chinese University of Hong Kong (the "CUHK") have received clinical drug trial accreditation by the NMPA for their clinical trial units/centers (http://www.crmo.med.cuhk.edu.hk/en-us/cfdaaccreditation.aspx and https://www.ctc.hku.hk/assurance_cfda.php).

- **Obtaining and leveraging government grants to fund project development.** The Hong Kong government pays close attention to the development of the biotechnology sector in Hong Kong and provides support and funding. We intend to aggressively seek government support from Hong Kong for our product development and to facilitate the development of some of our projects.

Arrangements with Other Parties

As mentioned above, part of our business model includes collaborating with research entities such as academic institutions and CROs, as well as highly regarded experts in their respective fields. We engage these entities and researchers either for purposes of exploring new innovations or advancing preclinical studies of our existing licensed drug candidates. Although the financial cost of these arrangements does not represent a material expense to the Company, the relationships we can access through, specifically, sponsored research arrangements ("SRAs") with academic institutions and organizations can provide significant value for our business; for example, we may decide whether to continue development of certain early-staged projects and/or out-license a project based on the data and results from research governed by SRAs. However, as of the date of this annual report, we do not consider the particulars of any of our SRAs to be material to the success of our current business plans.

Our drug discovery programs are based upon licenses from universities and are mainly conducted in universities via SRAs. As for the development of our drug candidates, our R&D Center conducts part of the CMC work. However, since our current facilities are not cGMP, cGLP or cGCP qualified, we will have to rely on CROs to conduct that type of work, if and when our drug candidates reach the level of development that requires such qualification.

Lead Projects and Other Projects under Development

We are actively operating and managing the development of our drug and device candidates through various subsidiaries. Each candidate is being researched in a subsidiary with a medical/scientific area of focus related to the drug and device candidate in development. We refer to these as our "Project Companies" and their products or areas of focus as either our Lead Projects (i.e., ALS-1, ALS-4 and NLS-1) or Other Projects under Development (as defined below). The selection of a drug and device candidate is based on our estimate of the market potential for that candidate, the scientific expertise required to develop it, and our overall corporate strategy, including our ability to commit personnel and future investment to that candidate.

To pursue a number of our current projects, our Project Companies have entered into standard license agreements with various university and licensing entities customized to the nature of each project. These license agreements largely contain the same terms, as is typically seen in license agreements for an early-stage life science invention; such terms include a worldwide license with licensed field comprising indications in the intended treatment areas, having upfront payments, certain royalty rates, sublicensing royalties, as well as provisions for payments upon occurrence of development and/or regulatory milestones. Under the license agreements, the Project Company must also adhere to certain diligence obligations and may or may not be required to obtain prior consent from the licensor to sublicense the invention. The license terms of our Lead Projects are discussed in detail below.

Generally speaking, pharmaceutical development consists of preclinical and clinical phases. Our immediate efforts would be on the preclinical phase which can further sub-divided into the following stages:

Target Identification & Selection: The target is the naturally existing cellular or modular structure that appears to have an important role in a particular disease pathway and will be targeted by the drug that will subsequently be developed. Target validation techniques for different disease areas can be very different but typically include from in vitro and in silico methods through to the use of whole animal models.

Lead Discovery: Following "Target Identification & Selection," compound screening assays are developed as part of the Lead Discovery. 'Lead' molecules can mean slightly different things to different researches or companies, but in this Annual Report, we refer to Lead Discovery as the process of identifying one or more small molecules with the desired activity against the identified targets. Leads can be identified through one or more approaches, which can depend on the target and what, if any, previous knowledge exists.

Lead Optimization: In this stage of the drug discovery process, the aim is to produce a preclinical drug candidate by maintaining the desired and favorable properties in the lead compounds, while repairing or reducing deficiencies in their structures. For example, to optimize the chemical structures to improve, among others, efficacy, reduce toxicity, improve metabolism, absorption and pharmacokinetic properties.

IND-Enabling Studies: Includes all the essential studies such as GLP toxicology studies, pharmacology and efficacy, pharmacokinetics, in vitro metabolism, CMC studies, and the data of which are used for IND submission.

Drug and Device Candidates

Projects	Candidate / Modality	Indication	Development Stage						
			Target Identification & Selection	Lead Discovery	Lead Optimization	IND-Enabling	Phase 1	Phase 2	Phase 3
Videns' Series									
VLS-1	Curcumin-MNP (Medical Imaging Agent for MRI Diagnosis)	Diagnosis of Alzheimer's Disease							
VLS-2	MITA	Treatment of Alzheimer's & Parkinson's Disease							
VLS-4	Imaging Agent for MRI Diagnosis	Diagnosis of Alzheimer's Disease							
Acticule's Series									
ALS-1	Small molecule	Treatment of viral infections caused by Influenza virus A							
ALS-2	Small molecule	Treatment of bacterial infections caused by Staphylococcus aureus including MRSA							
ALS-3	Small molecule	Reviving existing antibiotics to overcome drug Resistance							
ALS-4	Small molecule	Treatment of bacterial infections caused by Staphylococcus aureus including MRSA							
Nativus' Series									
NLS-1	Small molecule	Treatment of Endometriosis							
NLS-2	An extract from Chinese Yam	Relief of Menopausal Symptoms							
NLS-3	SAC	Treatment of and protection against retinal ischemia/reperfusion injury							
Scipio's Series									
SPLS-1	83b-1 Novel Quinoline Derivative	Treatment of Liver Cancer							

Projects	Candidate / Modality	Indication	Device Development					
			Lab-based Phantom Trial	Animal Trial	IDE Application Approval	Safety/ Feasibility Clinical Study	Pivotal Clinical Study	Process of obtaining PMA
Signate's Series								
SLS-1	Robotic Catheter Platform for Intra-operative MRI-Guided Cardiac Catheterization	Heart Rhythm Disorders by Cardiac Electrophysiology Intervention	On-going					

Lead Projects Candidates Device Candidates

Other Key Projects			
ALS-DDC	Drug Discovery Center + Chemical Library	Drug Discovery by identification and screening of drug molecules for various indications	Setting Up
AML Clinic	Clinic - Talem Medical	Medical Services	Commenced operations in June 2018

Another subsidiary, Aptorum Medical Limited ("AML"),[1] is our vehicle for developing our business of delivering medical services in the form of AML Clinic.

We anticipate allocating approximately 20% of our resources to develop projects other than our Lead Projects (such other projects being referred to herein as "Other Projects under Development"), with a strong focus on SLS-1 and AML Clinic. As a device candidate, SLS-1 may not need to undergo the same regulatory approval process as a drug candidate and therefore we may be able to bring it to market sooner. AML Clinic is expected to provide us with a modest amount of revenue. Even if SLS-1 achieves commercial sales, of which there can be no assurance, revenue from these products alone will not be sufficient for us to carry out all of our plans, but it will assist with name recognition and supplement our income while we develop our Lead Projects.

Lead Projects

Drug and Device Candidates									
Projects	Candidate / Modality	Indication	Development Stage						
			Target Identification & Selection	Lead Discovery	Lead Optimization	IND-Enabling	Phase 1	Phase 2	Phase 3
ALS-1	Small molecule	Treatment of viral infections caused by Influenza virus A							
ALS-4	Small molecule	Treatment of bacterial infections caused by Staphylococcus aureus including MRSA							
NLS-1	Small molecule	Treatment of Endometriosis							

ALS-1: Small molecule intended for the treatment of viral infections caused by Influenza virus A

Professor Richard Kao (Inventor of ALS-1, Founder and Principal Investigator of Acticule) was the first to identify NP as an effective drug target (Nature Biotechnology. 28:600-605). We are exploring ALS-1 as a potential treatment for viral infections caused by Influenza virus A ("IVA").

Two widely prescribed antiviral drug classes for the treatment of influenza are neuraminidase inhibitors ("NI") and M2 protein inhibitors. Zanamivir is a second-generation neuraminidase inhibitor for the treatment of both Influenza A and B in adults and children (5 years old and above). Oseltamivir is a third-generation neuraminidase inhibitor for the treatment of Influenza A and B in individuals older than 1 year of age. Amantadine and rimantadine are M2 membrane protein inhibitors that block the M2 ion channel activity of Influenza A but have no effect on Influenza B. Given the widespread resistance to M2 inhibitors, amantadine and rimantadine are no longer recommended for the treatment of Influenza A.

It is our hypothesis that Influenza A NP is an essential protein for the proliferation of the influenza virus. ALS-1 targets NP and triggers the aggregation of NP and this prevents the aggregated NP from entering the nucleus. In a paper published by the inventor, Prof. Richard Kao, in Nature Biotechnology (28 (6): 600, 2010), ALS-1 inhibited infection of MDCK cells by the Influenza A/WSN/33, H3N2 (clinical isolate) and Vietnam/1194/04 (H5N1) viruses with an IC_{50} (IC_{50} is defined as the concentration of a drug which inhibits half of the maximal response of a biochemical process. In this case, inhibition of the growth of PFU = plaque-forming units is the response) of 0.069 ± 0.003 μM, 0.16 ± 0.01 μM and 0.33 ± 0.04 μM in plaque reduction assay (PRA), respectively (Figure 1A). In this study, oseltamivir (sold under the brand name Tamiflu®) was also included as a control. In this cell culture, ALS-1 outperformed oseltamivir with a lower IC_{50} (Figure 1A). ALS-1 inhibited viral growth even when added within 6 hours after infection of the MDCK cells with the virus (Figure 1B), indicating that the antiviral activities of ALS-1 arise from post-entry and post-nuclear events, suggesting that multiple processes involving NP may be affected, although only the nuclear import process of NP can be readily observed.

In the treatment-free control group, all mice died 7 days after inoculation. After treating with ALS-1, 50% of the mice receiving two doses of ALS-1 (100 μl of 2.3 mg/ml ALS-1) per day for 7 days survived for more than 21 days. Three mice were sacrificed from each treated and untreated group on the 6th day after infection and their lungs tested for live virus by a plaque reduction assay. About a 10x reduction of viral load in the lungs of the ALS-1-treated mice was observed compared to the untreated control group. The animal study results suggest that ALS-1 has the potential to be developed into a useful anti-influenza therapeutic.

[1] Clark Cheng, our Chief Medical Officer and an Executive Director, owns 6% of Aptorum Medical Limited as of the date of this annual report.

ALS-1 is designed to target a broad range of NP variants, a novel therapeutic target. Compared with the currently marketed antiviral drugs for which the viruses have acquired extensive resistance, ALS-1 acts on a completely different therapeutic target. ALS-1 is currently undergoing Lead Optimization to optimize its drug-like properties.

Figure 1A

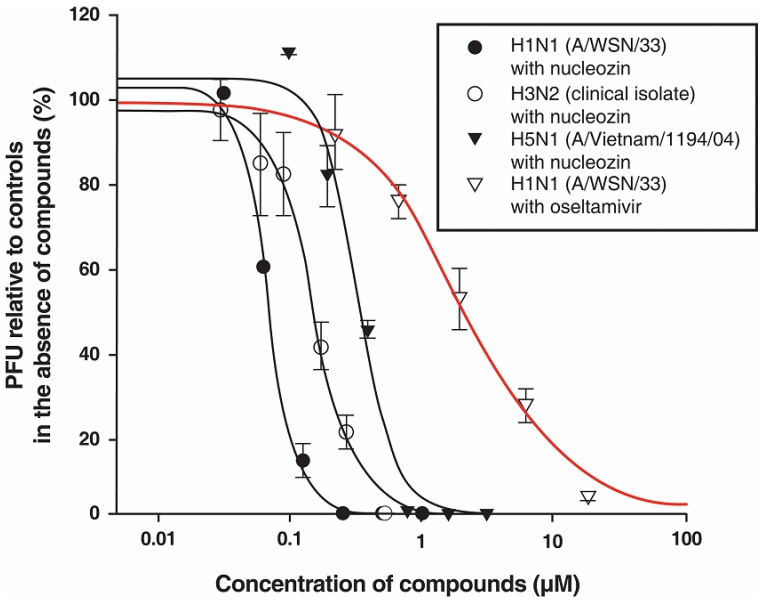


Figure 1B

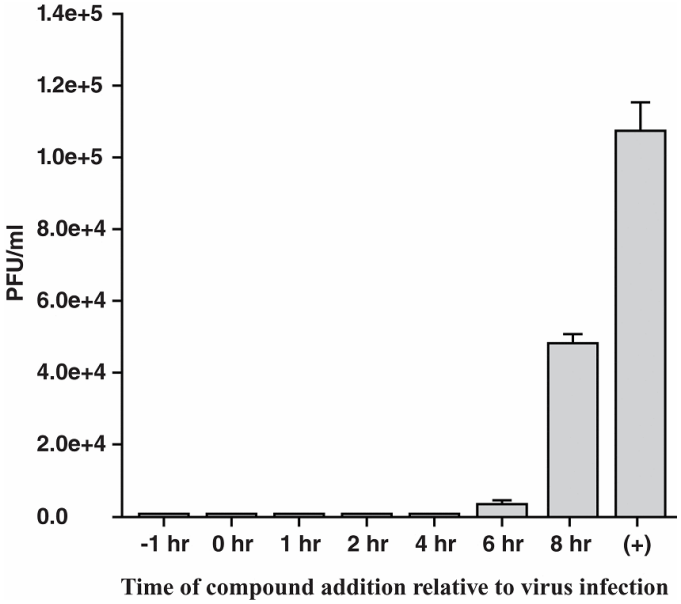


Figure 1A: ALS-1 is shown to cause a greater reduction in the number of infectious virus particles of human H1N1, H3N2 and H5N1 Influenza viruses. MDCK cells were infected with different strains of virus and antiviral activities of different treatments were determined by plaque reduction assay (PRA). Oseltamivir (curve in red) was included for comparisons of in vitro efficacies. The PRA assay was conducted in triplicate and repeated twice for confirmation. PFU = plaque-forming units, a measure of number of infectious virus particles Nucleozin = ALS-1 (Adapted from Nature Biotechnology (28 (6): 600, 2010).

Figure 1B: Efficacies of ALS-1 added at various time points. The experiments were carried out in triplicate and repeated twice for confirmation. The mean value is shown with s.d.; PFU = plaque-forming units, a measure of number of infectious virus particulates (Adapted from Nature Biotechnology (28 (6): 600,2010)).

Patent License

On October 18, 2017, the Company's subsidiary, Acticule, entered into an exclusive license agreement with Versitech Limited, the licensing entity of HKU, for the rights to ALS-1. Subsequently on June 7, 2018, the parties entered into a first amendment to the license agreement.

Under the exclusive license agreement, we were granted an exclusive, royalty-bearing, sublicensable license to develop, make, have made, use, sell, offer for sale and import products that are covered by the licensed patents (as described below). The territory of the license is worldwide and the field of the license is for treatment or prevention of viral infections including influenza.

We paid an upfront fee upon entering into the license agreement. We are required to pay less than 10% of the net sales of the licensed products sold by us or our affiliates as royalties, as well as a low teens percentage of sublicense royalties that we receive from our sublicensees, if any. In addition, we agreed to pay to the licensor aggregate regulatory milestones of up to US$1 million subject to the following achievements: submission of investigational new drug application; completion of phase 1, 2 and 3 clinical trials; and submission of new drug application; grant of regulatory approval. We also agreed to pay to the licensor aggregate sales milestones of up to US$7.8 million subject to the following achievement: first commercial sale; and annual net sales exceeding US$100 million in one jurisdiction.

Pursuant to the license agreement, Acticule became the exclusive licensee of 1 U.S. patent, 1 European Patent, 1 PRC patent and 1 German patent. The claimed invention is described as: "Antiviral Compounds and Methods of Making and Using Thereof."

Acticule has the right to grant sublicenses under the license agreement without prior approval from Versitech Limited and to assign the agreement to any successor to the business related to the license. In the event that Acticule makes an improvement to the licensed technologies, so long as the improvement does not incorporate any licensed patents, Acticule will be the owner of such improvement, subject to a non-exclusive royalty-free license being granted back to Versitech Limited for academic and research purposes only.

The exclusive license agreement shall be in effect until the expiration of all licensed patents (please refer to the patent expiration dates under "Item 4. Information on the Company – B. Business Overview – Intellectual Property"). Acticule may terminate the license at any time with 6-month written notice in advance. Either party may terminate the agreement upon a material breach by other party.

ALS-4: Small molecule for the treatment of bacterial infections caused by Staphylococcus aureus including Methicillin-resistant Staphylococcus aureus ("MRSA")

Just as certain strains of viruses, such as human immunodeficiency virus ("HIV") and influenza have developed resistance to drugs developed to treat them, certain bacteria such as *Staphylococcus aureus*, *Mycobacterium tuberculosis* and *Pseudomonas aeruginosa* have become "superbugs", having developed resistance to many, if not all, of the existing drugs available to treat them, rendering those treatments ineffective in many instances. MRSA is one such bacterium, a gram-positive bacterium that is genetically different from other strains of Staphylococcus aureus. Staphylococcus aureus and MRSA can cause a variety of problems ranging from skin infections and sepsis to pneumonia and bloodstream infections. It is estimated that about one out of every three people (33%) carry Staphylococcus aureus in their nose, usually without any illness; about two in a hundred (2%) carry MRSA (source: https://www.cdc.gov/mrsa/tracking/index.html). Both adults and children may carry MRSA.

Most MRSA infections occur in people who have been in hospital or other health care settings, such as nursing homes and dialysis centers (source: https://www.mayoclinic.org/diseases-conditions/mrsa/symptoms-causes/syc-20375336), which is known as Healthcare-Associated MRSA ("HA-MRSA"). HA-MRSA infections are typically associated with invasive procedures or devices, such as surgeries, intravenous tubing or artificial joints. Another type of MRSA infection, known as Community-Associated MRSA ("CA-MRSA"), has occurred in wider community among healthy people. It often begins as a painful skin boil and spreads by skin-to-skin contact. About 85% of serious, invasive MRSA infections are healthcare associated infections (https://www.cdc.gov/media/pressrel/2007/r071016.htm). The incidence of CA-MRSA varies according to population and geographic location. In the U.S., more than 94,000 people develop serious MRSA infection and about 19,000 patients die as a result each year (https://www.cdc.gov/media/pressrel/2007/r071016.htm). According to the US Centers for Disease Control and Prevention ("CDC"), Staphylococcus aureus, including MRSA, caused about 11% of healthcare-associated infections in 2011 (source: http://www.healthcommunities.com/mrsa-infection/incidence.shtml). Each year in the U.S., around one out of every twenty-five hospitalized patients contracts at least one infection in the hospital (N Engl J Med. 2014, 27;370(13):1198-208). In the U.S., there were over 80,000 invasive MRSA infections and 11,285 related deaths in 2011 (source: https://edition.cnn.com/2013/06/28/us/mrsa-fast-facts/index.html). Indeed, severe MRSA infections most commonly occur during or soon after inpatient medical care. More than 290,000 hospitalized patients are infected with Staphylococcus aureus and of these staphylococcal infections, approximately 126,000 are related to MRSA (source: http://www.healthcommunities.com/mrsa-infection/incidence.shtml).

ALS-4 is a small drug molecule which appears to target the products produced by bacterial genes that facilitate the successful colonization and survival of the bacterium in the body or that cause damage to the body's systems. These products of bacterial genes are referred to as "virulence expression." Targeting bacterial virulence is an alternative approach to antimicrobial therapy that offers promising opportunities to overcome the emergence and increasing prevalence of antibiotic-resistant bacteria.

Professor Richard Kao from The University of Hong Kong (who is also the Founder and Principal Investigator of Acticule and Inventor of ALS-2, ALS-3 and ALS-4) initiated a high throughput approach for screening compounds which are active against virulence expression, which resulted in the discovery of ALS-2, ALS-3 and ALS-4.

ALS-4 targets an enzyme essential for Staphylococcus aureus (including MRSA) survival in vivo. This enzyme is involved in the production of Staphyloxanthin, a carotenoid pigment produced by Staphylococcus aureus including MRSA, and is responsible for the characteristic golden color. This pigment has proven to be an important factor in promoting bacterial invasion as well as rendering the bacteria resistant to attack from reactive oxygen species (ROS) and neutrophils. In other words, pigmented bacteria have increased resistance to the host's immune defenses. ALS-4 may have particular value if it can be shown to be an effective therapy in situations where a Staphylococcus aureus infection is resistant to available antibiotics (i.e., where the pathogen is MRSA).

In a recent study by the inventor, Prof. Richard Kao, ALS-4 demonstrates potent activity against Staphylococcus aureus pigment formation in vitro, as indicated in Figure 2, with an IC_{50} (IC_{50} is defined as the concentration of a drug which inhibits half of the maximal response of a biochemical process. In this case, inhibition of the formation of the golden pigment is the response) equal to 20 nM.

Figure 2

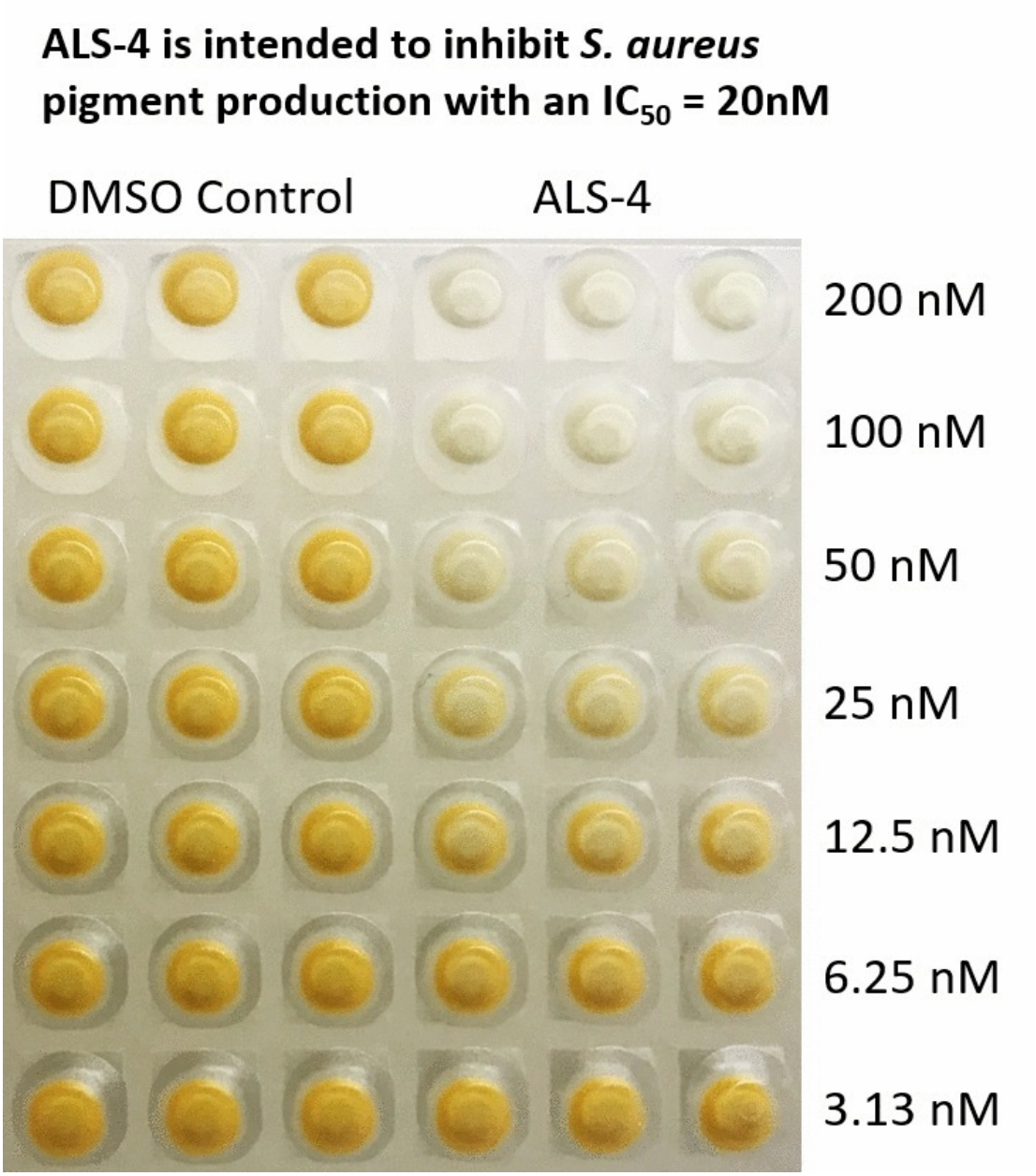


Figure 2: In vitro pigment inhibition by compound ALS-4.
(A) Inhibition of wild-type (WT) Staphylococcus aureus pigmentation in the presence of increasing concentrations of ALS-4.
(B) Pigment inhibition by ALS-4; the IC_{50} for pigment formation is roughly 300 nM.
All data represent mean values ± SD.
NP16 = ALS-4
This assay was conducted in triplicate and repeated twice for confirmation
(Adapted from mBio (8(5): e01224, 2017))

By employing a systemic Staphylococcus aureus mouse infection model, the treatment (1mM of ALS-4 twice daily) and control groups (vehicle) were compared. In both acute treatment and delayed treatment groups, the bacterial counts in the kidneys of mice treated with compound ALS-4 were significantly lower than those of the no treatment group.

Figure 3

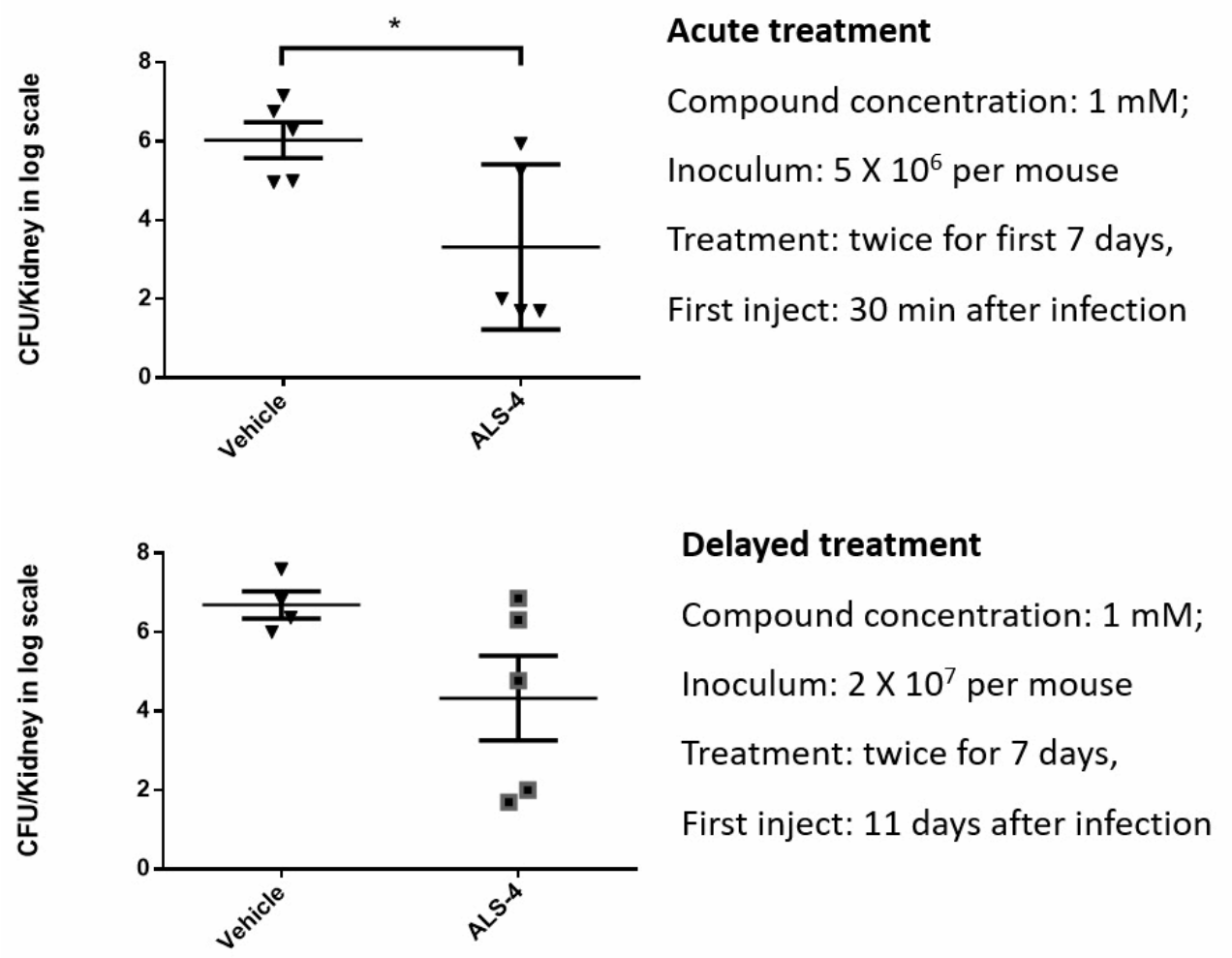


Figure 3: ALS-4 is observed to reduce bacterial load in mice

CFU = Colony Forming Unit, a unit used to estimate the number of viable bacteria in a sample
ALS-4 is currently undergoing Lead Optimization to optimize its drug-like properties.

Patent License

On October 18, 2017, the Company's subsidiary, Acticule, entered into an exclusive license agreement with Versitech Limited, the licensing entity of HKU, for ALS-4. Subsequently on June 7, 2018, the parties entered into a first amendment to the exclusive license agreement.

On January 11, 2019, Acticule and Versitech Limited entered into a second license agreement for ALS-4, where Acticule exclusively licensed the intellectual property rights on certain HKU-owned improvements to the original licensed invention.

Under the exclusive license agreements, we were granted an exclusive, royalty-bearing, sublicensable licenses to develop, make, have made, use, sell, offer for sale and import products that are covered by the licensed patents (as described below). The territory of the licenses is worldwide and the field of the licenses is for treatment or prevention of bacterial infections caused by Staphylococcus aureus including MRSA and bacterial virulence.

We paid an upfront fee upon entering into the license agreements. We are required to pay less than 10% of the net sales of the licensed products sold by us or our affiliates as royalties, as well as a low teens percentage of sublicense royalties that we receive from our sublicensees, if any. In addition, we agreed to pay to the licensor aggregate regulatory milestones of up to US$1 million subject to the following achievements: submission of investigational new drug application; completion of phase 1, 2 and 3 clinical trials; and submission of new drug application; grant of regulatory approval. We also agreed to pay to the licensor aggregate sales milestones of up to US$7.8 million subject to the following achievement: first commercial sale; and annual net sales exceeding US$100 million in one jurisdiction.

Pursuant to the license agreements, Acticule became the exclusive licensee of 2 pending U.S. non-provisional patent applications and 2 PCT applications. With respect to the PCT applications, we plan to enter national phase in member states of the EPO, in PRC and other jurisdictions before the deadline on January 23, 2021. The claimed inventions are described as: "Compounds Affecting Pigment Production and Methods for Treatment of Bacterial Diseases."

Acticule has the right to grant sublicenses to third parties under the license agreements without prior approval from Versitech Limited and to assign the agreements to any successor to the business related to the licenses. In the event that Acticule makes an improvement to the licensed technologies, so long as the improvement does not incorporate any licensed patents, Acticule will be the owner to such improvement, subject to a non-exclusive royalty-free license being granted back to Versitech Limited for academic and research purposes only.

The exclusive license agreements shall be in effect until the expiration of all licensed patents (please refer to the patent expiration dates under "Item 4. Information on the Company – B. Business Overview – Intellectual Property"). Acticule may terminate the licenses at any time with 6-month written notice in advance. Either party may terminate the agreements upon a material breach by other party.

NLS-1: A Derivative of Epigallocatechin-3-Gallate ("Pro-EGCG") for the treatment of Endometriosis

NLS-1, a drug molecule derived from natural products (green tea), is currently under development for the treatment of endometriosis, a disease in which the tissue that normally lines the uterus (endometrium) grows outside the uterus. It can grow on the ovaries, fallopian tubes, bowels, or bladder. Rarely, it grows in other parts of the body. Many studies have assessed the applications of EGCG, a naturally occurring molecule extracted from green tea, for the treatment of endometriosis *in vitro* and in animal models (Hum Reprod. 2014 29(8):1677; Hum Reprod. 2013 28(1):178; Fertil Steril. 2011 96(4):1021). For example, in a mouse model, Ricci et al (Hum Reprod. 2013 28(1):178) demonstrated that EGCG brought a statistically significant reduction in the mean number and the volume of established lesions compared with the control group without treatment. The treatment diminished cell proliferation in a statistically significant manner, reduced vascular density and increased apoptosis within the lesions. EGCG induced reduction in human EEC proliferation and increased apoptosis in primary cultures. Matsuzaki and Darcha (Hum Reprod. 2014 29(8):1677) also showed that EGCG prevented the progression of fibrosis in endometriosis in an animal model.

However, the attractiveness of epigallocatechin-3-gallate as a drug candidate has been diminished by its chemical and metabolic instability (Hum Reprod. 2014 29(8):1677; Angiogenesis. 2013 16(1):59). The Company's drug candidate, NLS-1 or EGCG octaacetate, is supposed to overcome these challenges. NLS-1 is an EGCG derivative synthesized by acetylation of the reactive hydroxyl groups, which appears to prevent generation of reactive phenoxide anions and radicals for dimerization and metabolism, thereby overcoming the chemical and metabolic instability of EGCG.

Despite different hypotheses proposed for the pathogenesis of endometriosis, it is widely accepted that endometriosis is an angiogenesis-dependent disorder, and that angiogenesis plays an essential role in the growth and survival of endometriotic lesions. Endometriotic lesions require new vessel formation to deliver oxygen and nutrients that are essential to the development and progression of endometriosis. Dense vascularization is a typical pathological feature of endometriosis. Numerous peritoneal blood vessels can be observed around the endometriotic lesions during laparoscopy, and ectopic endometrium is highly vascularized under histological examination. Researchers have confirmed in animal models that angiogenesis occurs in endometriosis, by demonstrating the development of adjacent blood vessels from the surrounding vasculature into the endometriotic implants. Anti-angiogenesis therapy offers a potential novel treatment of endometriosis.

In a paper published by the inventors in Angiogenesis (16:59, 2013), NLS-1 brought a statistically significantly reduction in the lesion size and weight compared with EGCG and the control without any treatment in an experimental endometriosis mouse model (Student t-test, $p < 0.05$) (Figure 4A & B). In addition, the inhibition by NLS-1 in all of the angiogenesis parameters was statistically significantly greater than that by EGCG (Student t-test, $p < 0.05$) (Figure 5A & B). In addition, NLS-1 significantly (Student t-test, $p < 0.05$) reduces the lesion size in both prevention and treatment group compared with both saline and EGCG groups (Figure 6). Moreover, NLS-1 also had better bioavailability and greater antioxidation and anti-angiogenesis capacities compared with EGCG.

In addition, regarding a safety study in mice, no signs of stress to NLS-1 administration were observed during the treatment period. No significant weight change was observed over the course of the experiment. Histological examination revealed no obvious reproductive effects on ovarian follicles and endometrial glands under NLS-1 treatments (Figure 7). Also, vascularization of the ovaries and the uterus was not affected in the NLS-1 treatment group.

Figure 4

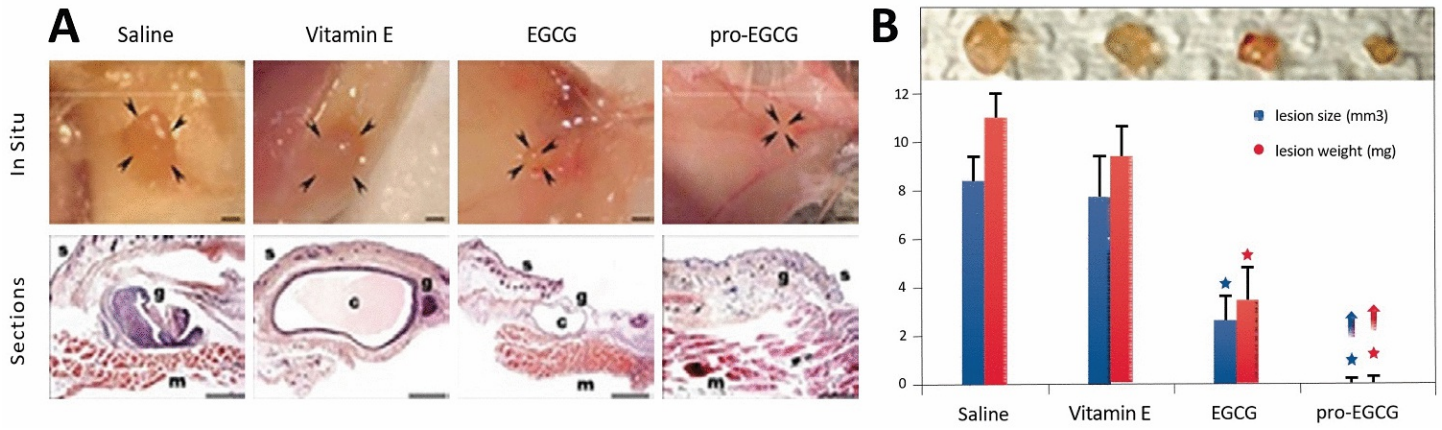


Figure 4A & B
NLS-1 (Pro-EGCG) limits the development of experimental endometriosis in mice. Upper panels show the endometrial implants developed in the right ventral abdominal wall under laparotomy. Arrows indicate the greatest length and perpendicular width of the lesions for lesion size calculation. Lower panels show the sandwich structures of outer skin and subcutaneous layers (s), middle endometriotic lesions with endometrial glands (g) and endometrial cyst-like structures (c), and inner abdominal muscle and peritoneum (m). Scale bars: 0.5 mm. b Bar charts of the lesion size and weight in different groups and representative lesion pictures are shown. Mean ± SEM, student's t test, $*P < 0.05$ compared with saline group; $P < 0.05$ compared with EGCG group.
The sample size was 4 (N=4) for each group.
(Adapted from Angiogenesis (16:59, 2013))

Figure 5

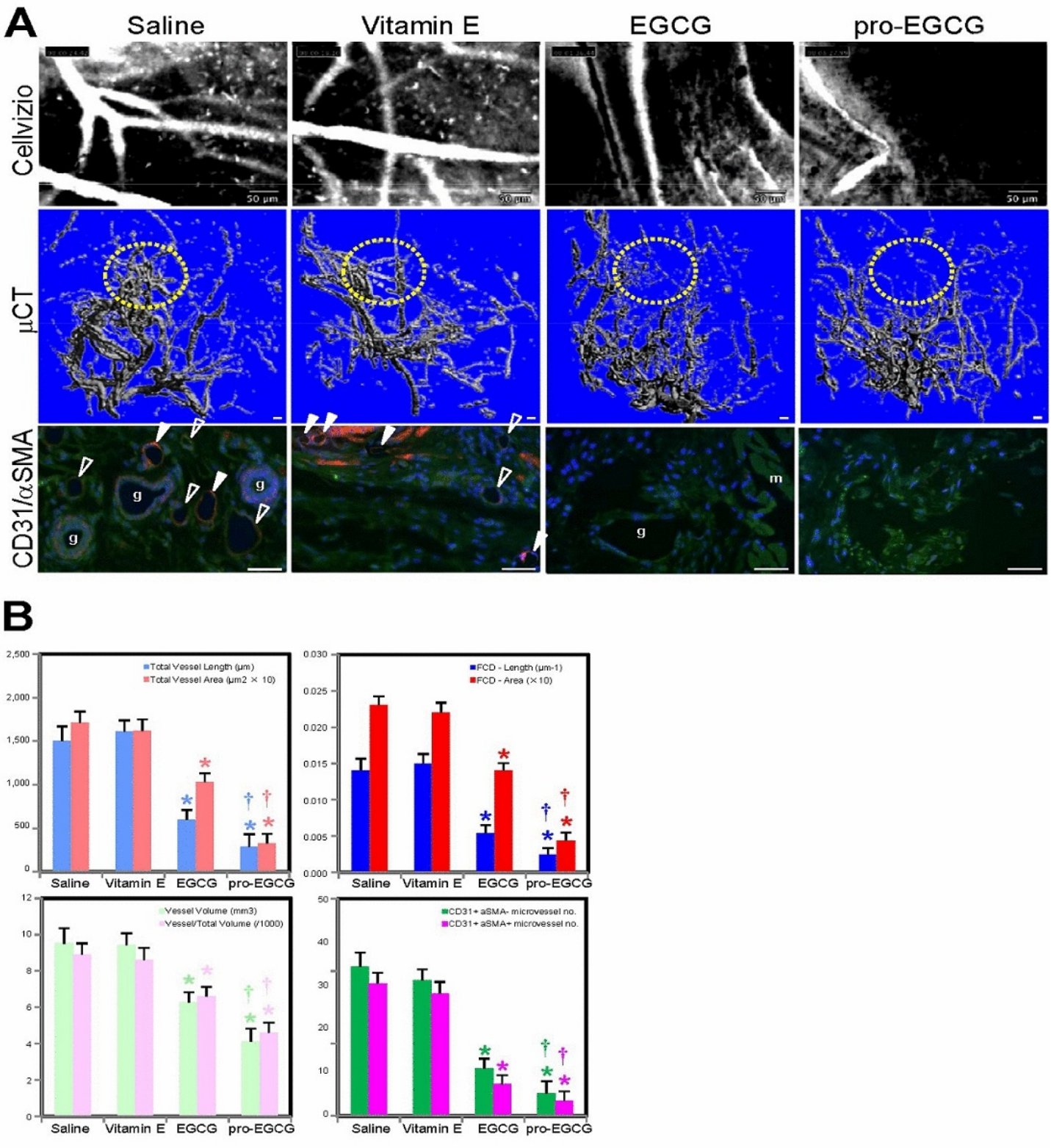


Figure 5A & B

NLS-1 inhibits the angiogenesis of experimental endometriosis in mice. Upper panels: Microvessels in the endometriotic implants were perfused with FITC-Dextran and captured by Cellvizio (white colour) (N=8). Middle panels: Microvessel architectures surrounding the lesions and within the lesions were perfused with microfil contrast medium and captured by lCT (yellow dots) (N=4). Lower panels: Microvessels in the endometriotic lesions were determined by specific antimouse antibodies CD31 for endothelial cells in red, aSMA for smooth muscles in green, and DAPI for nuclei in blue (N=4). New microvessels are CD31-positively and aSMA-negatively stained (closed arrows), old microvessels are CD31-positively and aSMA-positively stained (opened arrows). g: endometrial glands; c: endometrial cyst-like structures; m: abdominal muscle. Representative images in different groups are shown. Scale bars: 10 lm. b Bar charts of the lesion microvessel parameters in different groups are presented. Mean ± - SEM,

student's t test, *P < 0.05 compared with saline group; P < 0.05 compared with EGCG group. (Adapted from Angiogenesis (16:59, 2013)). In addition, NLS-1 significantly ($p < 0.05$) reduces the lesion size in both prevention and treatment group compared with both saline and EGCG groups.

Figure 6

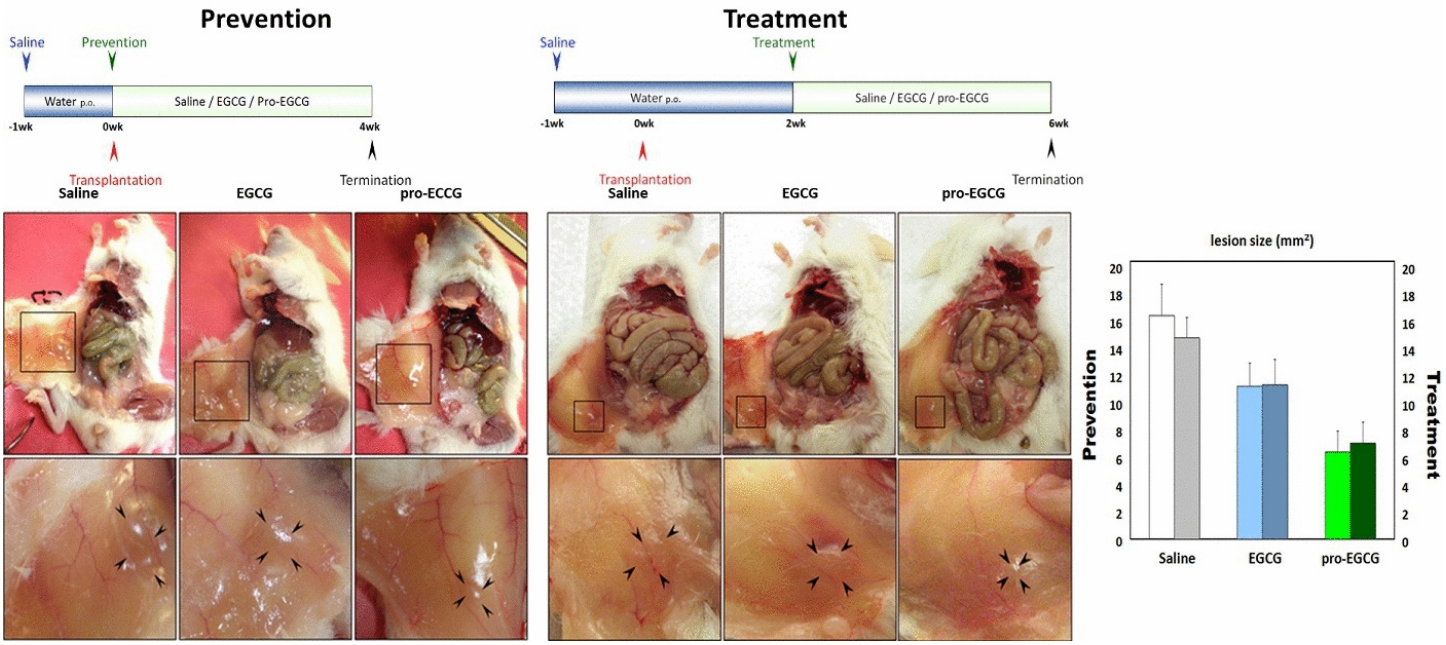


Figure 6: NLS-1 reduces the lesion size in both prevention and treatment groups

Figure 7

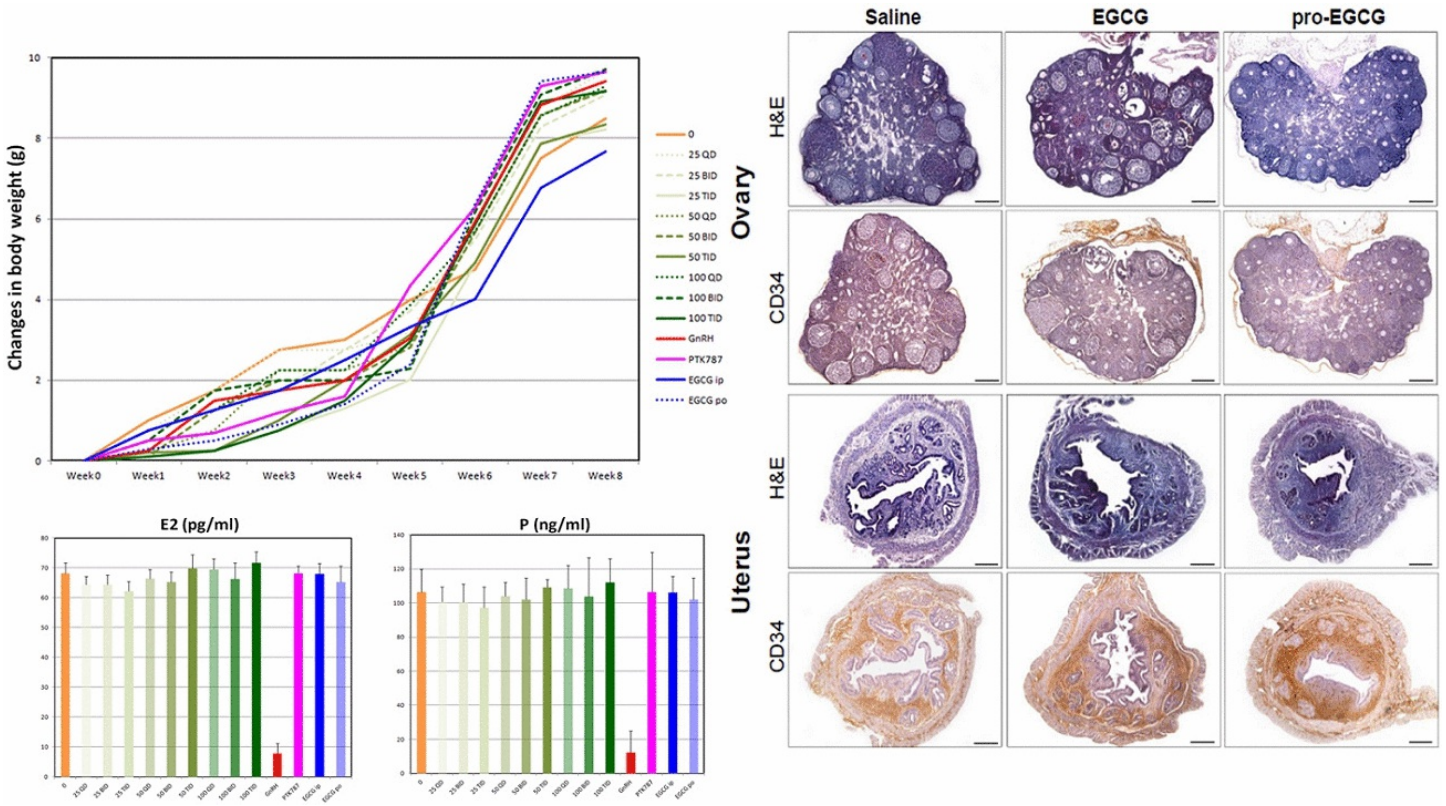


Figure 7
NLS-1 does not cause any weight loss in mice (Upper figure in the left)
NLS-1 does not reduce any estrogen and progesterone level in mice (Lower figures in the left) NLS-1 preserves normal ovarian follicles and endometrial glands. Ovarian follicles and endometrial glands were determined by H&E staining and microvessels in ovarian and endometrial stroma were determined by anti-mouse CD34 immunostaining in ovaries (upper panels in the right) and uterus (lower panels in the right). Representative images in different groups are shown. Scale bars: 0.5 mm.
N=8 was conducted for each group.
(Adapted from Angiogenesis (16:59, 2013)).

As a follow-up study in an animal model of endometriosis, orally administered NLS-1 reduced the lesion size significantly better than oral EGCG ($p<0.05$-0.001 at week 3- 8, ANOVA) and other hormone-based therapy such as intramuscular GnRH analog ($p<0.05$ at week 4-8, ANOVA) and other synthetic anti-angiogenesis agents such as intraperitoneal PTK787 ($p<0.05$-0.01 at week 4-8, ANOVA), as reflected in Figure 8.

Figure 8

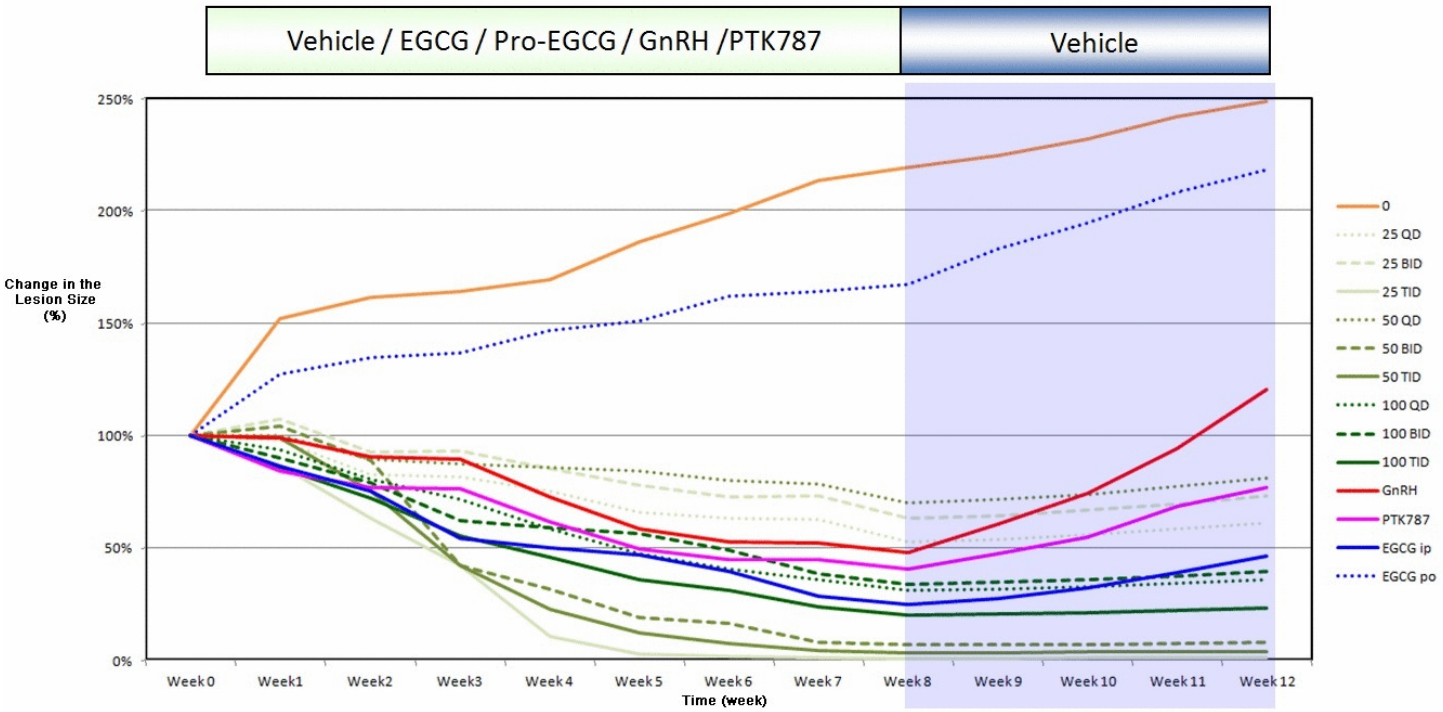


Figure 8
Comparison of the efficacy of different treatment in an experimental endometriosis model

The current approved treatment for endometriosis is hormonal therapy, which can cause severe undesirable side effects. At present, there are only a few non-hormonal therapeutics with different mechanisms than NLS-1 that are under preclinical or clinical development, such as:

1) BAY 1128688, which is a non-hormonal approach developed by Bayer HealthCare for endometriosis and which entered Phase 2 study in Spain in 2017 (https://adisinsight.springer.com/drugs/800041929); and,

2) Small molecules co-developed by Bayer and Evotec that have entered Phase 1 studies (Source: https://www.businesswire.com/news/home/20180417006820/en/Evotec-Bayer-Advance-Endometriosis-Programme-Phase-Clinical).

NLS-1 is under active development for the treatment of endometriosis. It is currently at the Lead Optimization stage to optimize its drug-like properties.

Patent License

On July 3, 2017, the Company's subsidiary, Aptorum Therapeutics Limited, entered into an exclusive license agreement with PolyU Technology and Consultancy Limited, The Royal Institution for the Advancement of Learning/McGill University, Wayne State University, H. Lee Moffitt Cancer Center and Research Institute Inc. and CUHK (all representing the licensors) for NLS-1.

We paid an upfront fee upon entering into the license agreement. We are required to pay less than 10% of the net sales of the licensed products sold by us or our affiliates as royalties, as well as a percentage of sublicense royalties that do not exceed 30% from what we receive from our sublicensees, if any. In addition, we agreed to pay the licensor aggregate regulatory and development milestones of up to HK$41.9 million (approximately US$5.37 million) for the first drug product subject to the following achievements: submission of investigational new drug application; commencement of phase 1, 2 and 3 clinical trials; submission of new drug application; and grant of first, second and third regulatory approval among the FDA, EMA and NMPA. We also agreed to pay the licensor aggregate sales milestones of up to HK$80 million (approximately US$10.26 million) subject to the following achievements: first commercial sale; and annual net sales exceeding US$100 million in one jurisdiction.

Further, for each of the second and third drug products, we agreed to pay aggregate regulatory development milestones of up to HK$9 million (approximately US$1.15 million) and aggregate sales milestone of up to HK$40 million (approximately US$5.13 million) subject to achievement of similar milestones for the first drug product. We have also agreed to pay certain one-time payments for non-drug product upon the commercialization and market launch of such non-drug product. In addition, following the filing of the IND, the Company has to pay an immaterial annual fee to the licensors.

Pursuant to the license agreement, Aptorum Therapeutics Limited became the exclusive licensee of 6 U.S. patents, 1 European Patent, 1 PRC patent, 1 Indian patent and 1 Japanese patent, as well as 1 pending US patent application, 1 pending PRC patent application and 1 pending Hong Kong patent application. Two technologies are claimed in the patents: "Epigallocatechin Gallate Derivatives for Inhibiting Proteasome," which is jointly owned by PolyU Technology and Consultancy Limited, The Royal Institution for the Advancement of Learning/McGill University, Wayne State University and H. Lee Moffitt Cancer Center and Research Institute Inc. and "Pro-EGCG for Use in the Treatment of Endometriosis," which is jointly owned by PolyU Technology and Consultancy Limited and CUHK. The licensors have nominated PolyU Technology and Consultancy Limited to represent them and take the lead in negotiating and managing the license.

Aptorum Therapeutics Limited has the right to grant sublicenses under the license agreement with prior consent from the licensors, and such approval shall not be unreasonably withheld. In the event that Aptorum Therapeutics Limited develops any improvements or new development, such licensee inventions are to be jointly owned by the licensors and Aptorum Therapeutics Limited, so that both owners will have the right to use any such inventions for any purpose. In such a case, the Company expects to negotiate a separate agreement with the licensors governing the terms on which the licensors may use such inventions.

In addition, Aptorum Therapeutics Limited also committed to providing HK$3 million (US$384,615) of research funding before July 3, 2020 to sponsor research carried out by the three principal individual inventors upon their request with respect to further R&D on the licensed technologies. The research funding shall be in the form of matching funds provided by the Innovation Technology Fund ("ITF"). The ITF is administered by the Innovation and Technology Commission of the Government of Hong Kong and encompasses a scheme where the Hong Kong government offers matching grant for joint researches to foster collaboration between private companies and public research institutions. If an ITF application is approved, the Hong Kong government will provide a grant that matches the contribution by the private company in the research projects. Since the ITF funding is merit-based and there is no guarantee that an ITF application will be granted, Aptorum Therapeutics' obligation to contribute to the research fund under the agreement will be contingent on the successful application of ITF scheme granting HK$3 million fund that matches our proposed contribution. In the event that an ITF application related to NLS-1 is not successful, the parties have agreed to negotiate for and agree to enter into new funding terms to support the ongoing research. As of today, the inventors have not filed such ITF application.

During the term of the license agreement and for two years thereafter, Aptorum Therapeutics Limited undertakes not to develop or commercialize any product that directly competes with any marketed product that is covered by the licensed technology.

The exclusive license agreement shall be in effect until the later of (1) the expiry of the term of the last to expire licensed patent set forth in the agreement, (2) final disposition of the last of the pending patent application set forth in the agreement, and (3) ten years following the first commercial sale of the product. Please refer to the patent expiration dates under "Item 4. Information on the Company – B. Business Overview – Intellectual Property" for information regarding (1) and (2). Either party may terminate the agreement upon a material breach by or insolvency of the other party. Further, the Licensors may terminate the agreement if the licensee commits any act or omission that could tarnish the reputation of any licensors.

Statistical Significance

The term statistical significance is to define the probability that a measured difference between two groups (e.g. two treatment groups, treatment versus control groups) is the result of a real difference in the tested variations and not the result of chance. It means that the result of a test does not appear randomly or by chance, but because of a specific change that is tested, so it can be attributed to a specific cause.

The confidence level indicates to what percentage the test results will not commit a type 1 error, the false positive. A false positive occurs when a change in the result is due to randomness (or other noise) and not the change in variations. At a 95% confidence level ($p = 0.05$), there is a 5% chance that the test results are due to a type 1 error. 95% has become the standard and usually be the minimum confidence level for the tests. To make the test more stringent, a 99% confidence level ($p = 0.01$) is also commonly employed, which means that there is a 1% chance that the test results are due to a type 1 error.

In other words, a p value represents the confidence level. For example, if the p-value for a test is < 0.05, it means that there is less than 5% chance the difference between two groups is due to random error or by chance. If the p-value is < 0.01, it means that there is less than 1% chance the difference between two groups is due to random error or by chance.

We employed statistical testing to compare different treatment groups in animal studies simply for proof of concept and to aid internal decision making for further development. We do not intend to use this standard for any regulatory submission. The US FDA or other regulatory agencies may not necessarily employ the same statistical standard to assess the efficacy in clinical trials, the results of which would be submitted for regulatory approval. Although a p-value of 0.05 has become the standard, the US FDA or other regulatory agencies may also individualize their efficacy standard for different clinical programs based on the indications, the purpose of a clinical trial, among others.

FDA Application Status

As of the date of this annual report, we have not submitted any applications for investigational new drugs ("IND") to the US Food and Drug Administration ("FDA"). By 2020 or 2021, we expect to be in a position to submit at least one application for one of our drug candidates to commence trials in humans (INDs to the FDA or an equivalent application to the regulatory authorities in another jurisdiction such as the China's National Medical Products Administration (the "NMPA") or the European Medicines Agency ("EMA")). However, there can be no assurance we will be able to make any such application by such time. Should we be delayed in making such filing or should such filing not be approved, our business will be adversely affected.

Other Projects under Development

The following provides additional detail regarding Other Projects under Development. Prior filings we have made with the SEC disclose that we were developing the drug candidate VLS-3. We have discontinued the development of such candidate because the expected result could not be generated, so we decided to focus our capital and efforts on our other candidates.

VLS-1: Curcumin-conjugated superparamagnetic iron oxide nanoparticles ("Curcumin-MNP") for MRI ("magnetic resonance imaging") imaging of amyloid beta plaques in Alzheimer's disease ("AD")

VLS-1 is an MRI contrast agent, which the Company believes may enable superior imaging for identifying amyloid beta plaques in Alzheimer's disease. VLS-1 differs from other existing contrast agents for amyloid imaging, such as Amyvid (Eli Lilly), Vizamyl (GE Healthcare) and Neuraceq (Piramal Healthcare), in the following respects: 1) utilization of a natural compound, curcumin, with a known high amyloid beta binding affinity and proven safety; 2) a nanoparticle-based system to enhance delivery efficiency to the brain; and 3) the combination of curcumin with iron oxide, known to be an effective MRI contrast agent. VLS-1 is currently at the Lead Discovery stage.

VLS-2: mTOR-independent transcription factor EB activator ("MITA") as autophagy activator for treatment of neurodegenerative diseases

Autophagy is an endogenous cellular mechanism for clearing multiple pathological protein aggregates including tau, the presence of which is believed to account for neurodegeneration in AD and other neurodegenerative diseases. mTOR is part of a biological pathway that is a central regulator of mammalian metabolism and physiology. Inhibition of mTOR activity is associated with various side effects, such as immunosuppression. Many other molecules that activate autophagy also inhibit mTOR activity. VLS-2 is a small drug molecule that appears to activate autophagy without inhibiting mTOR function. VLS-2 is currently at the Lead Discovery stage.

VLS-4: Other contrast agents for MRI diagnostics

In addition to VLS-1, the Company is actively developing a new class of MRI contrast agents for diagnosis of neurodegenerative diseases. The design of these agents takes into consideration the physicochemical properties that need to be optimized for best imaging performance, and the novel agents are currently undergoing rigorous evaluation. VLS-4 is currently at the Lead Discovery stage.

ALS-2: Small molecule for the treatment of bacterial infections caused by Staphylococcus aureus including MRSA

ALS-2 is a next generation small molecule targeting bacterial virulence for the treatment of bacterial infections caused by Staphylococcus aureus including MRSA. In a recent paper published by the inventor, Professor Richard Kao from The University of Hong Kong (also the Founder and Principal Investigator of Acticule), in PNAS (115(310: 8003, 2018), ALS-2 suppresses the expression of multiple virulence factors in Staphylococcus aureus simultaneously. In a lethal infection mouse model, compared with the vehicle group, ALS-2 protected against Staphylococcus aureus for all the mice in the group, with significant differences between the treatment and control groups [P = 0.0057, by log-rank (Mantel-Cox) test].

ALS-2 is currently at the Lead Optimization stage to optimize its drug-like properties.

ALS-3: Small molecule acting synergistically with certain existing antibiotics

ALS-3 is a novel small molecule that is at present under investigation to combine with certain classes of existing antibiotics to overcome drug resistance. We are exploring ALS-3 for the treatment of bacterial infections including MRSA. ALS-3 is currently at the Lead Optimization stage to optimize its drug-like properties.

NLS-2: An extract from Chinese Yam for relief of menopausal symptoms

NLS-2 is an extract isolated from Chinese Yam, Dioscorea opposita Thunb. In development for the treatment of menopausal syndrome, we expect NLS-2 is to be formulated into an oral dosage form or nasal spray for administration. Each therapy cycle is expected to last for 3 months. Menopausal syndrome refers to the symptoms experienced by women during menopause, such as hot flashes, mood disorders, night sweats, depression, nervous tension and insomnia that are related to estrogen deficiency. Our research suggests that NLS-2 stimulates estradiol biosynthesis in rat ovarian granulosa cells; induces estradiol and progesterone secretion in aged rats by upregulating expressions of follicle-stimulating hormone receptor and ovarian aromatase; counteracts the progression of osteoporosis and augments bone mineral density; and improves cognitive functioning by upregulating protein expressions of brain-derived neurotrophic factor and TrkB receptors in the prefrontal cortex. Furthermore, NLS-2 does not appear to stimulate the proliferation of breast cancer and ovarian cancer cells, which suggests that it could be a more efficacious and safer alternative to hormone replacement therapy (Sci Rep. 2015 5:10179). NLS-2 is currently at the Lead Discovery stage. We are also evaluating whether the yam extract is suited for production as dietary supplement.

NLS-3: Extract from garlic for the treatment of and protection against retinal ischemia/reperfusion injury

NLS-3 is based on S-Allyl L-Cysteine (“SAC”), an active organosulfur compound in aged garlic extract which has been reported to possess antioxidative activity. In macrophages and endothelium, it has been shown that SAC possesses potent antioxidative effects involving the scavenging of superoxide radicals, hydroxyl radicals and hydrogen peroxide. Central/branch retinal artery/vein occlusion, glaucoma and, possibly, age related macular degeneration (“AMD”) are conditions associated with retinal ischemia. All these diseases may lead to severe complications or after-effects. Furthermore, after retinal ischemia/reperfusion (“I/R”), large amounts of reactive oxygen species (“ROS”) are produced, which attack nearby cells and cause tissue damage. Therefore, management of retinal ischemia is vital and NLS-3 is being developed for the treatment of and protection against ischemia/reperfusion injury. NLS-3 is currently at the Lead Discovery stage.

SPLS-1: A quinoline derivate for liver cancer treatment

SPLS-1, a novel quinoline derivative from Ephedra pachyclada, is at present under active investigation for the treatment of liver cancer. It is currently at the Lead Discovery stage.

SLS-1: Robotic Catheter Platform for Intra-operative MRI-guided Cardiac Catheterization

SLS-1 is our robotic catheter platform for MRI-guided cardiovascular intervention for the treatment of arrhythmia. The platform consists of a magnetic resonance imaging-guided ("MRI-guided") robotic electrophysiology ("EP") catheter system, an MR-based positional tracking unit, and a navigation interface. This platform has the potential to offer a major step toward achievement of several clinical goals: (i) enhancing catheter manipulation and lesion ablation, which we believe will decrease the chance of arrhythmia recurrence; (ii) improving the safety of catheter navigation, thereby decreasing the rates of undesired or inadvertent tissue damage; and (iii) enhancing catheter control, thus facilitating shorter learning curves for surgeons and better treatment in more complex patient cases. Should such goals be demonstrated, patient outcomes should be improved, compensating for the cost of using MRI and reducing the overall expenditure.

To date, a product prototype has been developed. Lab-based experiments have been conducted to verify the performance of the robot towards an image-guided pulmonary vein isolation ("PVI") task. The MR-based tracking unit has also been developed and validated in MRI scanners. The next step is to test the robotic catheterization using a dynamic heart phantom simulated with the pulsatile liquid flow. Preclinical trials can then be conducted with all the components ready. Radiofrequency ablation will be conducted in a live porcine model, prepared with arrhythmia. If all the results are positive, we will approach the US FDA or other regulatory agencies to apply for conducting clinical trials on the equipment.

SLS-1 is currently in Lab-based Phantom Trial and it will follow the regulatory pathway for approval as indicated in the table in Page 43.

Aptorum Medical Limited - AML Clinic

Incorporated in August 2017, Aptorum Medical Limited is a Hong Kong-based company incorporated in Cayman Islands focused on delivering premium healthcare and clinic services. AML can draw on the expertise of many of the region's most experienced medical practitioners, and is committed to providing a comprehensive cross-functional facility for healthcare professionals to practice evidence-based medicine and offer high-quality medical services to their patients. We also intend that AML will offer to conduct clinical trials of both the Company's and third parties' new drug and device products.

Effective as of March 2018, we leased office space in Central, Hong Kong, the commercial and financial heart of Hong Kong, as the home to AML Clinic. We operate the AML Clinic under the name of Talem Medical. AML Clinic commenced operation in June 2018.

The recently renovated medical center is staffed by our group of medical professionals and offers state-of-the-art facilities. Initially we expect to focus our expertise on treatment of chronic diseases resulting from modern sedentary lifestyles and an aging population.

Competition

Our industry is highly competitive and subject to rapid and significant change. While we believe that our development and commercialization experience, scientific knowledge and industry relationships provide us with competitive advantages, we face competition from pharmaceutical and biotechnology companies, including specialty pharmaceutical companies, and generic drug companies, academic institutions, government agencies and research institutions.

There are a number of large pharmaceutical and biotechnology companies that currently market and sell drugs or are pursuing the development of drugs and devices for the diagnosis and treatment of diseases for which we are developing products or technology. Moreover, a number of additional drugs are currently in clinical trials and may become competitors if and when they receive regulatory approval.

Many of our competitors have longer operating histories, better name recognition, stronger management capabilities, better supplier relationships, a larger technical staff and sales force and greater financial, technical or marketing resources than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Our commercial opportunity could be reduced or eliminated if our competitors develop or market products or other novel therapies that are more effective, safer or less costly than our current drug candidates, or any future drug candidates we may develop, or obtain regulatory approval for their products more rapidly than we may obtain approval for our current drug candidates or any such future drug candidates. Our success will be based in part on our ability to identify, develop and manage a portfolio of drug and device candidates that are safer and more effective than competing products.

Inflation

Inflation affects us by generally increasing our cost of labor and research and development costs, the way it does to all labor and research costs. However, we do not anticipate that inflation will materially affect our business in the foreseeable future.

Seasonality

We believe our operation and sales do not experience seasonality.

Employees

As of the date of this annual report, we have 41 employees, including 39 full-time employees and 2 part-time employees. Of these, 13 are engaged in full-time research and development and laboratory operations, 20 are engaged in general and administrative functions, 6 are full-time employees engaged in the clinic operation and 2 part-time employees are engaged in sponsored research and development, laboratory operations and legal clerical support. As of the date of this annual report, 40 of our employees are located in Hong Kong and 1 of our employees is located in the UK. In addition, we have engaged and may continue to engage 24 independent contracted consultants and advisors to assist us with our operations. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We have never experienced any employment related work stoppages, and we consider our relations with our employees to be good.

Intellectual Property

The technologies underlying our various research and development projects are the subject of various patents and patent applications claiming, in certain instances, composition of matter and, in other instances, methods of use. Prosecution, maintenance and enforcement of these patents, as well as those on any future protectable technologies we may acquire, are and will continue to be an important part of our strategy to develop and commercialize novel medicines and medical devices, as described in more detail below. Through entering into license agreements with their owners, we have obtained exclusive rights to these patents, applications and related know-how in the U.S. and certain other countries to develop, manufacture and commercialize the products using or incorporating the protected inventions that are described in this annual report and that are expected to contribute significant value to our business. The technologies protected by these patents may also for the basis for the development of other products.

In addition to licensed intellectual property, our in-house science team has been actively developing our own proprietary intellectual property. No patent applications have yet been filed in the Company's own name for the Lead Projects. We have, however, filed 2 U.S. provisional patent applications for two proprietary projects, including the U.S. Provisional Application No. 62/729,998 directed to a metal-based probes for in-vivo non-invasive detection of amyloid plaques (VLS-4), which was filed on September 11, 2018, allowing us to secure an earlier filing date for the underlying invention; the other U.S. provisional patent application was for VLS-3, which as discussed elsewhere in this annual report, we have discontinued developing and therefore allowed the provisional application to expire. We have also filed a number of provisional applications to establish earlier filing dates for certain of our other ongoing researches, the specifics of which are currently proprietary and confidential.

The U.S. patent system permits the filing of provisional and non-provisional patent applications (i.e., a regular patent application). A non-provisional patent application is examined by the USPTO, and can mature into a patent once the USPTO determines that the claimed invention meets the standards for patentability. On the other hand, a provisional patent application is not examined for patentability, and automatically expires 12 months after its filing date. As a result, a provisional patent application cannot mature into a patent.

Provisional applications are often used, among other things, to establish an earlier filing date for a subsequent non-provisional patent application. The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained.

The effective filing date of a non-provisional patent application is used by the USPTO to determine what information is prior art when it considers the patentability of a claimed invention. If certain requirements are satisfied, a non-provisional patent application can claim the benefit of the filing date of an earlier filed provisional patent application. As a result, the filing date accorded by the provisional patent application may supersede information that otherwise could preclude the patentability of an invention.

A provisional patent application is not eligible to become an issued patent unless, among other things, we file a non-provisional patent application within 12 months of the filing date of the provisional patent application. If we do not timely file a non-provisional patent application claiming priority to said provisional application, we may lose our priority date with respect to our provisional patent applications. Further, if any (self or by others) publication of the invention is made after such priority date, and if we do not file a non-provisional application claiming priority to said provisional application, our invention may become unpatentable.

Moreover, we cannot predict whether such future patent applications will result in the issuance of patents that effectively protect any of our product candidates or will effectively prevent others from commercializing competitive products.

We do not expect to incur material expenses in the prosecution of the provisional applications or other licensed patent applications. We expect to fund the patent costs from our cash and restricted cash.

The value of our drug and device products will depend significantly on our ability to obtain and maintain patent and other proprietary protection for those products, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of other parties.

As of the date of this report, in addition to the 2 provisional patent applications discussed above, we are the exclusive licensee of 12 U.S. patents and 6 pending U.S. non-provisional applications, as well as corresponding patents and patent applications internationally. In addition, we are the exclusive licensee of 3 international patent applications under the Patent Cooperation Treaty (the "PCT") which we have filed and/or plan to file nationally in member states of the EPO, PRC and other jurisdictions before the expiration of the time limits for entry of national stage application. The following table sets forth a list related to our Lead Projects of our patent rights under the exclusive licenses as of the date of this annual report:

Project Company / Project name	License Agreement	Licensor(s)	Licensee	Licensed / IP Rights	Patent Expiration Dates
Acticule / ALS-1	Exclusive Patent License Agreement, dated October 18, 2017 First Amendment to Exclusive License Agreement, dated June 7, 2018	Versitech Limited	Acticule Life Sciences Limited	Exclusive licensee: 1 U.S. patent (US9212177), 1 European Patent (EP2462138B1), 1 PRC patent (CN102596946B), 1 German patent (DE60 2010 019 171.0)	The licensed IP rights include granted patents in the U.S., Switzerland, Germany, Great Britain and PRC. The U.S. patent will expire in 2031; the European Patent in 2030; the PRC patent in 2030 and the German patent in 2030.
Acticule / ALS-4	Exclusive Patent License Agreement, dated October 18, 2017 First Amendment to Exclusive License Agreement, dated June 7, 2018 Exclusive Patent License Agreement dated January 11, 2019	Versitech Limited	Acticule Life Sciences Limited	Exclusive licensee: 2 pending U.S. applications (16/041,836 and US 16/041,838), and 2 pending PCT applications (PCT/IB2018/055458, PCT/IB2018/055459)[2]	The licensed IP rights include pending patent applications in the U.S. and under the PCT. Any patent based on the application, if granted, will have a 20-year patent term from 2018.
Nativus / NLS-1	1) Exclusive License Agreement, dated July 3, 2017 2) Addendum to License Agreement, dated February 9, 2018	1) PolyU Technology and Consultancy Company Limited 2) McGill University 3) Wayne State University 4) H. Lee Moffitt Cancer Center and Research Institute Inc. 5) The Chinese University of Hong Kong	Aptorum Therapeutics Limited	Exclusive licensee: 6 U.S. patents (US9713603, US7544816, US8193377, US8710248, US9169230, US10188629), 1 European Patent (EP1778663), 1 PRC patent (CN101072764B), 1 Indian patent (IN263365) and 1 Japanese patent (JP5265915), as well as 1 pending U.S. application (US16/259,620), 1 pending PRC application (CN104703596A), and 1 pending Hong Kong application (HK15111955.3)	The licensed IP rights include granted patents in the U.S., Germany, Great Britain, France, Italy, Spain, PRC, India and Japan, as well as pending patent applications in the U.S., PRC and Hong Kong. We cannot predict whether such future patent applications will result in the issuance of patents that effectively protect the candidate. The U.S., European and PRC patents covering the compound will expire in 2025; the indication U.S. patent will not expire until 2033.

[2] We intend to file national stage applications in at least PRC and before the EPO prior to the 30-month entry deadline of the PCT application falling on January 2021.

Because of the extensive time required for clinical development and regulatory review of a drug we may develop, it is possible that, before any of our drug and device candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of any such patent. If appropriate, the Company may seek to extend the period during which it has exclusive rights to a product by pursuing patent term extensions and marketing exclusivity periods that are available from the regulatory authorities of certain countries (including the United States) and the EPO.

Even though the Company has certain patent rights, the ability to obtain and maintain protection of biotechnology and pharmaceutical products and processes such as those we intend to develop and commercialize involves complex legal and factual questions. No consistent policy regarding the breadth of claims allowed in such patents has emerged to date in the U.S. The scope of patent protection outside the United States is even more uncertain. Changes in the patent laws or in interpretations of patent laws in the United States and other countries have diminished (and may further diminish) our ability to protect our inventions and enforce our IP rights and, more generally, could affect the value of IP.

While we have already secured rights to a number of issued patents directed to our drug candidates, we cannot predict the breadth of claims that may issue from the pending patent applications and provisional patents that we have licensed or that we have filed. Substantial scientific and commercial research has been conducted for many years in the areas in which we have focused our development efforts, which has resulted in other parties having a number of issued patents, provisional patents and pending patent applications relating to such areas. The patent examiner in any particular jurisdiction may take the view that prior issued patents and prior publications render our patent claims "obvious" and therefore unpatentable or require us to reduce the scope of the claims for which we are seeking patent protection.

In addition, patent applications in the United States and elsewhere generally are not available to the public until at least 18 months from the priority date, and the publication of discoveries in the scientific or patent literature frequently occurs substantially later than the date on which the underlying discoveries were made. Therefore, patent applications relating to drugs and devices similar to our drug and device candidates may have already been filed, which (if they result in issued patents) could restrict or prohibit our ability to commercialize our drug and device candidates.

The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other IP rights. Our ability to prevent competition for our drug and device candidates and technologies will depend on our success in obtaining patents containing substantial and enforceable claims for those candidates and enforcing those claims once granted. With respect to any applications which have not yet resulted in issued patents, there can be no assurance that meaningful claims will be obtained. Even issued patents may be challenged or invalidated. If others have prepared and filed patent applications in the United States that also claim technology to which we have filed patent applications or otherwise wish to challenge our patents, we may have to participate in interferences, post-grant reviews, inter parties reviews, derivation or other proceedings in the USPTO and other patent offices to determine issues such as priority of claimed invention or validity of such patent applications as well as our own patent applications and issued patents. Patents may also be circumvented, and our competitors may be able to independently develop and commercialize similar drugs or mimic our technology, business model or strategy without infringing our patents. The rights granted under any issued patents may not provide us with proprietary protection or competitive advantages against competitors with similar technology.

We may rely, in some limited circumstances, on unpatented trade secrets and know-how to protect aspects of our technology. However, it is challenging to monitor and prevent the disclosure of trade secrets. We seek to protect our proprietary trade secrets and know-how, in part, by entering into confidentiality agreements with consultants, scientific advisors and contractors and invention assignment agreements with our employees. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, giving our competitors knowledge of our trade secrets and know-how, and we may not have adequate remedies for any such breach, in which case our business could be adversely affected. Our trade secrets will not prevent our competitors from independently discovering or developing the same know-how. Although our agreements with our consultants, contractors or collaborators require them to provide us only original work product and prohibit them from incorporating or using IP owned by others in their work for us, if they breach these obligations, disputes may arise as to the rights in any know-how or inventions that arise from their work.

Our commercial success will also depend in part on not infringing the proprietary rights of other parties. Although we seek to review the patent landscape relevant to our technologies on an ongoing basis, we may become aware of a new patent which has been issued to others with claims covering or related to aspects of one of our drug or device candidate. The issuance of such a patent could require us to alter our development plans for that candidate, redesign the candidate, obtain a license from the patent holder or cease development. Our inability to obtain a license to proprietary rights that we may require to develop or commercialize any of our drug and device candidates would have a material adverse impact on us.

Trademarks

As of the date of this annual report, we have a total of 21 trademark registrations covering the trade names and logos of Aptorum and our subsidiaries, including but not limited to "APTORUM THERAPEUTICS," "VIDENS LIFE SCIENCES," "ACTICULE LIFE SCIENCES," "TALEM," "Talem in Chinese characters," in jurisdictions Hong Kong, EU and the United Kingdom. Furthermore, we are in the process of applying for registration of trademarks in jurisdictions including the U.S. and PRC.

We also own certain unregistered trademark rights or have submitted applications for trademarks for our and our subsidiaries' trade names and logos.

All other trade names, trademarks and service marks of other companies appearing in this annual report are the property of their respective holders. Solely for convenience, the trademarks and trade names in annual report are referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies' trademarks and trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

Legal Proceedings

From time to time, we are subject to legal proceedings, investigations and claims incidental to the conduct of our business. We are not currently a party to any legal proceeding or investigation which, in the opinion of our management, is likely to have a material adverse effect on our business, financial condition or results of operations.

Regulations

Government authorities in the United States at the federal, state and local level and in other countries extensively regulate, among other things, the research and clinical development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing, pricing, export and import of drug and device products ("Regulated Products"), such as those we are developing. Generally, before a new Regulated Product can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized to address the requirements of and in the format specific to each regulatory authority, submitted for review and approved by the regulatory authority. This process is very lengthy and expensive, and success is uncertain.

Regulated Products are also subject to other federal, state and local statutes and regulations in the United States and other countries, as applicable. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable regulatory requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the regulatory authority's refusal to approve pending applications, withdrawal of an approval, clinical holds, untitled or warning letters, voluntary product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution, injunctions, disbarment, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Any such administrative or judicial enforcement action could have a material adverse effect on us.

As the Company's principal place of business is in Hong Kong, and because AML Clinic is located there, the Company is subject to various Hong Kong laws and regulation covering its business activities there, described in further detail below. Also, the Company anticipates that, if it obtains marketing approval for any of its drug and device candidates, it intends to focus its marketing and sales efforts primarily in three regions: the United States, Europe and PRC. The regulatory framework for each of these regions is described below.

U.S. Drug Development Process

The process of obtaining regulatory approvals and maintaining compliance with appropriate federal, state and local statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process, or after approval, may subject an applicant to administrative or judicial sanctions or lead to voluntary product recalls. Administrative or judicial sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of non-clinical laboratory tests, preclinical studies according to cGLP and manufacturing of clinical supplies according to cGMP;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent IRB, at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials according to cGCP, to establish the safety and efficacy of the proposed product for its intended use;
- preparation and submission to the FDA of an NDA, for a drug;

- satisfactory completion of an FDA advisory committee review, if applicable;

- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with cGMP; and

- payment of user fees and the FDA review and approval of the NDA.

Devices are subject to different forms of testing and approval, but (except for certain laboratory-developed diagnostic tests) still require satisfaction of various FDA requirements in order to be brought to market. As of the date of this annual report, the device candidate currently under development is SLS-1. We do not currently have a commercialization timeline for SLS-1 and cannot assure you that SLS-1 will ever be ready for commercialization.

The testing and approval process requires substantial time, effort and financial resources and we cannot be certain that any approvals for our drug candidates, or any future drug candidates we may develop, will be granted on a timely basis, if at all.

Once a drug candidate is identified for development, it enters the non-clinical testing stage. Non-clinical tests include laboratory evaluations of product chemistry, toxicity, formulation and stability, as well as preclinical studies. An IND sponsor must submit the results of the non-clinical tests, together with manufacturing information, analytical data and any available clinical data or literature, to the FDA as part of the IND prior to commencing any testing in humans. An IND sponsor must also include a protocol detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated if the initial clinical trial lends itself to an efficacy evaluation. Some non-clinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions related to a proposed clinical trial and places the trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns or non-compliance, and may be imposed on all products within a certain class of products. The FDA also can impose partial clinical holds, for example, prohibiting the initiation of clinical trials for certain duration or for certain doses.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with cGCP regulations. These regulations include the requirement that all research subjects provide informed consent in writing before their participation in any clinical trial. Further, an IRB representing each institution participating in a clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. An IRB is responsible for protecting the rights of clinical trial subjects and considers, among other things, whether the risks to individuals participating in the clinical trial are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the information regarding the clinical trial and the consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. Each new clinical protocol and any amendments to the protocol must be submitted to the FDA for review, and to the IRBs for approval. Protocol detail, among other things, includes the objectives of the clinical trial, testing procedures, sublease selection and exclusion criteria, and the parameters to be used to monitor subject safety.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- **Phase 1.** Phase 1 includes the initial introduction of an investigational new drug into humans. These studies are closely monitored and may be conducted in patients, but are usually conducted in healthy volunteer subjects. These studies are designed to determine the metabolic and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. During Phase 1, sufficient information about the drug's pharmacokinetics and pharmacological effects should be obtained to permit the design of well-controlled, scientifically valid, Phase 2 studies. Phase 1 studies also evaluate drug metabolism, structure-activity relationships, and the mechanism of action in humans. These studies also determine which investigational drugs are used as research tools to explore biological phenomena or disease processes. The total number of subjects included in Phase 1 studies varies with the drug, but is generally in the range of twenty to eighty.

- **Phase 2.** Phase 2 includes the early controlled clinical studies conducted to obtain some preliminary data on the effectiveness of the drug for a particular indication or indications in patients with the disease or condition. This phase of testing also helps determine the common short-term side effects and risks associated with the drug. Phase 2 studies are typically well-controlled, closely monitored, and conducted in a relatively small number of patients, usually involving several hundred people.

- **Phase 3.** Phase 3 studies are expanded controlled and uncontrolled trials. They are performed after preliminary evidence suggesting effectiveness of the drug has been obtained in Phase 2, and are intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug. Phase 3 studies are designed to provide an adequate basis for extrapolating the results to the general population and transmitting that information in the physician labeling. Phase 3 studies usually include several hundred to several thousand people.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and safety reports must be submitted to the FDA and clinical investigators within 15 calendar days for serious and unexpected suspected adverse events, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator's brochure, or any findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug candidate. Additionally, a sponsor must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction no later than 7 calendar days after the sponsor's receipt of the information. There is no assurance that Phase 1, Phase 2 and Phase 3 testing can be completed successfully within any specified period, or at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product has been associated with unexpected serious harm to subjects.

Concurrent with clinical trials, companies usually complete additional preclinical studies and must also develop additional information about the chemistry and physical characteristics of the product and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product drug and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product drug does not undergo unacceptable deterioration over its shelf life.

The results of product development, non-clinical studies and clinical trials, together with other detailed information regarding the manufacturing process, analytical tests conducted on the product, proposed labeling and other relevant information, are submitted to the FDA as part of an NDA requesting approval to market the new drug. The FDA reviews all NDAs submitted within 60 days of submission to ensure that they are sufficiently complete for substantive review before it accepts them for filing. If the submission is accepted for filing, the FDA begins an in-depth substantive review.

The approval process is lengthy and difficult and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information. Even if such data and information are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive, and the FDA may interpret data differently than we interpret the same data. The FDA will issue a complete response letter if the agency decides not to approve the NDA in its present form. The complete response letter usually describes all of the specific deficiencies that the FDA identified in the NDA that must be satisfactorily addressed before it can be approved. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application or request an opportunity for a hearing.

If after such review a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. Any products for which we receive the FDA approval would be subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with the FDA promotion and advertising requirements. In addition, the FDA may require post-approval studies, including Phase 4 clinical trials, to further assess a product's safety and effectiveness after NDA approval and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA also may conclude that an NDA may only be approved with a Risk Evaluation and Mitigation Strategy designed to mitigate risks through, for example, a medication guide, physician communication plan, or other elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools.

Post-Approval Requirements

Any products for which we receive the FDA approval are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with the FDA promotion and advertising requirements. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. Further, manufacturers must continue to comply with cGMP requirements, which are extensive and require considerable time, resources and ongoing investment to ensure compliance. In addition, changes to the manufacturing process generally require prior the FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further the FDA review and approval.

The FDA may withdraw a product approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product's marketing or even complete withdrawal of the product from the market. Further, the failure to maintain compliance with regulatory requirements may result in administrative or judicial actions, such as fines, untitled or warning letters, holds on clinical trials, product seizures, product detention or refusal to permit the import or export of products, refusal to approve pending applications or supplements, restrictions on marketing or manufacturing, injunctions or consent decrees, or civil or criminal penalties, or may lead to voluntary product recalls.

Patent Term Restoration and Marketing Exclusivity

Because drug approval can take an extended period of time, there may be limited remaining life for the patents covering the approved drug, meaning that the company has limited time to use the patents to protect the sponsor's exclusive rights to make, use and sell that drug. In such a case, U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date.

In addition, the FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application ("ANDA") or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval.

In the future, if appropriate, we intend to apply for restorations of patent term and/or marketing exclusivity for some of our products; however, there can be no assurance that any such extension or exclusivity will be granted to us.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of the FDA-regulated products, including drugs are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Pharmaceutical Coverage, Pricing and Reimbursement

Much of the revenue generated by new Regulated Products depends on the willingness of third-party payors to reimburse the price of the product. Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. In the United States, sales of any products for which we may receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list, or formulary, which is not required to include all of the FDA-approved products for a particular indication. Moreover, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost- effectiveness of medical products and services, in addition to their safety and efficacy. To obtain coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of any products, in addition to the costs required to obtain regulatory approvals. Our product candidates may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit.

The U.S. government and state legislatures have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future. Unfavorable coverage or reimbursement policies regarding any of the Company's products would have a material adverse impact on the value of that product.

Other Healthcare Laws and Compliance Requirements

If we obtain regulatory approval of our products, we may be subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business.

Patient Protection and the Affordable Care Act

The Affordable Care Act, enacted in March 2010, includes measures that have or will significantly change the way health care is financed in the United States by both governmental and private insurers. Among the provisions of the Affordable Care Act of greatest importance to the pharmaceutical industry are the following:

- The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. The Affordable Care Act increased pharmaceutical manufacturers' rebate liability on most branded prescription drugs from 15.1% of the average manufacturer price to 23.1% of the average manufacturer price, added a new rebate calculation for line extensions of solid oral dosage forms of branded products, and modified the statutory definition of average manufacturer price. The Affordable Care Act also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization and expanding the population potentially eligible for Medicaid drug benefits.

- In order for a pharmaceutical product to receive federal reimbursement under the Medicare Part B and Medicaid programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The Affordable Care Act expanded the types of entities eligible to receive discounted 340B pricing.

- The Affordable Care Act imposed a requirement on manufacturers of branded drugs to provide a 50% discount off the negotiated price of branded drugs dispensed to Medicare Part D patients in the coverage gap (i.e., the "donut hole").

- The Affordable Care Act imposed an annual, non-deductible fee on any entity that manufactures or imports certain branded prescription drugs, apportioned among these entities according to their market share in certain government healthcare programs, although this fee does not apply to sales of certain products approved exclusively for orphan indications.

In addition to these provisions, the Affordable Care Act established a number of bodies whose work may have a future impact on the market for certain pharmaceutical products. These include the Patient-Centered Outcomes Research Institute, established to oversee, identify priorities in, and conduct comparative clinical effectiveness research, the Independent Payment Advisory Board, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program, and the Center for Medicare and Medicaid Innovation within the Centers for Medicare and Medicaid Services, to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

These and other laws may result in additional reductions in healthcare funding, which could have a material adverse effect on customers for our product candidates, if we gain approval for any of them. Although we cannot predict the full effect on our business of the implementation of existing legislation or the enactment of additional legislation pursuant to healthcare and other legislative reform, we believe that legislation or regulations that would reduce reimbursement for, or restrict coverage of, our products could adversely affect how much or under what circumstances healthcare providers will use our product candidates if we gain approval for any of them.

U.S. Medical Device Regulatory Approval Process

Medical Devices are subject to different forms of testing and approval, and require satisfaction of various FDA requirements including the Food, Drug and Cosmetic Act (FDCA) in order to be brought to market.

The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and premarket approval. The type of marketing authorization is generally linked to the classification of the device. The FDA classifies medical devices into one of three classes — Class I, Class II or Class III — based on the degree of risk the FDA determines to be associated with a device and the level of regulatory control deemed necessary to ensure the device's safety and effectiveness. Devices requiring fewer controls because they are deemed to pose lower risk are placed in Class I or II. Class I devices are deemed to pose the least risk and are subject only to general controls applicable to all devices, such as requirements for device labeling, premarket notification, and adherence to the FDA's Good Manufacturing Practices. Class II devices are intermediate risk devices that are subject to general controls and may also be subject to special controls such as performance standards, product-specific guidance documents, special labeling requirements, patient registries, or post-market surveillance. Class III devices are those for which insufficient information exists to assure safety and effectiveness solely through general controls or if the device is a life-sustaining, life-supporting or a device of substantial importance in preventing impairment of human health, or which presents a potential, unreasonable risk of illness or injury and special controls are not adequate to assure safety and effectiveness.

Most Class I devices and some Class II devices are exempted by regulation from the 510(k) clearance requirement and can be marketed without prior authorization from the FDA. Most Class II devices (and certain Class I devices that are not exempt) are eligible for marketing through the 510(k) clearance pathway. By contrast, devices placed in Class III generally require premarket approval or 510(k) de novo clearance prior to commercial marketing. The premarket approval process is more stringent, time-consuming, and expensive than the 510(k) clearance process. However, the 510(k) clearance process has also become increasingly stringent and expensive.

510(k) Clearance Pathway. When a 510(k) clearance is required, a premarket notification must be submitted to the FDA demonstrating that a proposed device is "substantially equivalent" to a previously cleared and legally marketed 510(k) device or a device that was in commercial distribution before May 28, 1976 for which the FDA has not yet called for the submission of a premarket approval application, which is commonly known as the "predicate device." A device is substantially equivalent if, with respect to the predicate device, it has the same intended use and has either (i) the same technological characteristics or (ii) different technological characteristics and the information submitted demonstrates that the device is as safe and effective as a legally marked device and does not raise different questions of safety or effectiveness. By law, the FDA is required to clear or deny a 510(k) premarket notification within 90 days of submission of the application. As a practical matter, clearance often takes significantly longer. The FDA may require further information, including clinical data, to make a determination regarding substantial equivalence. If the FDA determines that the device, or its intended use, is not substantially equivalent to a previously-cleared device or use, the FDA will issue a not substantially equivalent decision. This means the device cannot be cleared through the 510k process and will require marketing authorization through the premarket approval pathway.

Premarket Approval Pathway. A premarket approval application must be submitted to the FDA if the device cannot be cleared through the 510(k) process. The premarket approval application process is much more demanding than the 510(k) premarket notification process and requires the payment of significant user fees. A premarket approval application must be supported by valid scientific evidence, which typically requires extensive data, including but not limited to technical, preclinical, clinical trials, manufacturing and labeling to demonstrate to the FDA's satisfaction reasonable evidence of safety and effectiveness of the device. The FDA has 45 days from its receipt of a premarket approval application to determine whether the application will be accepted for filing based on the FDA's threshold determination that it is sufficiently complete to permit substantive review. After the FDA determines that the application is sufficiently complete to permit a substantive review, the FDA will accept the application and begin its in-depth review. The FDA has 180 days to review an "accepted" premarket approval application, although this process typically takes significantly longer and may require several years to complete. During this review period, the FDA may request additional information or clarification of the information already provided. Also, an advisory panel of experts from outside the FDA may be convened to review and evaluate the application and provide recommendations to the FDA as to the approvability of the device. In addition, the FDA will conduct a preapproval inspection of the manufacturing facility to ensure compliance with quality system regulations. The FDA may delay, limit or deny approval of a premarket approval application for many reasons, including:

- failure of the applicant to demonstrate that there is reasonable assurance that the medical device is safe or effective under the conditions of use prescribed, recommended or suggested in the proposed labeling;

- insufficient data from the preclinical studies and clinical trials;

- the manufacturing processes, methods, controls or facilities used for the manufacture, processing, packing or installation of the device do not meet applicable requirements. If the FDA evaluations of both the premarket approval application and the manufacturing facilities are favorable, the FDA will either issue an approval order or an approvable letter, which usually contains a number of conditions that must be met in order to secure final approval of the premarket approval application. If the FDA's evaluation of the premarket approval application or manufacturing facilities is not favorable, the FDA will deny approval of the premarket approval application or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the premarket approval application. The FDA may also determine that additional clinical trials are necessary, in which case the premarket approval application may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the premarket approval application. Once granted, a premarket approval application may be withdrawn by the FDA if compliance with post approval requirements, conditions of approval or other regulatory standards is not maintained or problems are identified following initial marketing.

Clinical Trials. Clinical trials are almost always required to support premarket approval and are sometimes required for 510(k) clearance. In the United States, these trials generally require submission of an application for an Investigational Device Exemption, or IDE, to the FDA. The IDE application must be supported by appropriate data, such as animal and laboratory testing results, showing it is safe to test the device in humans and that the testing protocol is scientifically sound. The FDA must approve the IDE in advance of trials for a specific number of patients unless the product is deemed a non-significant risk device eligible for more abbreviated IDE requirements or the clinical investigation is exempt from the IDE regulations. Clinical trials for significant risk devices may not begin until the IDE application is approved by the FDA and the appropriate institutional review boards, or IRBs, at the clinical trial sites. The applicant, the FDA or the IRB at each site at which a clinical trial is being performed may suspend a clinical trial at any time for various reasons, including a belief that the risks to study subjects outweigh the benefits. Even if a trial is completed, the results of clinical testing may not demonstrate the safety and efficacy of the device, may be equivocal or may otherwise not be sufficient to obtain approval or clearance of the product.

Both the 510(k) and premarket approval processes can be expensive and lengthy and require the payment of significant fees, unless an exemption applies. The FDA's 510(k) clearance process usually takes from approximately three to 12 months, but may take longer. The process of obtaining a premarket approval is much more costly and uncertain than the 510(k) clearance process and generally takes from approximately one to five years, or longer, from the time the application is submitted to the FDA until an approval is obtained. The process of obtaining regulatory clearances or approvals to market a medical device can be costly and time consuming, and the applicant may not be able to obtain these clearances or approvals on a timely basis, if at all.

As of the date of this annual report, our sole device candidate currently under development is SLS-1, which is a cardiovascular robotic surgical catheter conventionally classified as a cardiovascular steerable catheter. We do not currently have a commercialization timeline for SLS-1 and cannot assure you that SLS-1 will ever be ready for commercialization. If we are ready to seek regulatory approval for the SLS-1 device in the U.S., we expect that the FDA will classify it as a Class II non-exempted device requiring premarket clearance under Section 510(k) of the FDCA. If our device cannot clear through the 510(k) process, we will need to obtain marketing authorization through the premarket approval pathway, which will be more costly, lengthy and uncertain.

European Union Regulation

Regulation in the European Union

The process governing approval of medicinal products in the EU generally follows the same lines as in the United States. It entails satisfactory completion of pharmaceutical development, non-clinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the medicinal product for each proposed indication. It also requires the submission to relevant competent authorities for clinical trials authorization and to the European Medicines Authority, or EMA, for a marketing authorization application, or MAA, and granting of a marketing authorization by these authorities before the product can be marketed and sold in the EU.

Clinical Trial Approval

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on cGCP, a system for the approval of clinical trials in the EU (the equivalent of the IND process in the United States) has been implemented through national legislation of the EU member states. Under this system, an applicant must obtain approval from the competent national authority of an EU member state in which the clinical trial is to be conducted or in multiple EU member states if the clinical trial is to be conducted in a number of EU member states. Furthermore, the applicant may only start a clinical trial at a specific study site after the independent ethics committee has issued a favorable opinion. The clinical trial application, or CTA, must be accompanied by an investigational medicinal product dossier with supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and corresponding national laws of the EU member states and further detailed in applicable guidance documents.

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. It is expected that the new Clinical Trials Regulation will apply in 2019. It will overhaul the current system of approvals for clinical trials in the EU. Specifically, the new regulation, which will be directly applicable in all EU member states, aims at simplifying and streamlining the approval of clinical trials in the EU. For instance, the new Clinical Trials Regulation provides for a streamlined application procedure using a single entry point and strictly defined deadlines for the assessment of clinical trial applications.

Marketing Authorization

To obtain a marketing authorization for a product under the EU regulatory system (the equivalent of the NDA process in the United States), an applicant must submit an MAA, either under a centralized procedure administered by the EMA or one of the procedures administered by competent authorities in EU member states (decentralized procedure, national procedure, or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the EU. Regulation (EC) No. 1901/2006 provides that prior to obtaining a marketing authorization in the EU, an applicant must demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, class waiver, or a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU member states. Pursuant to Regulation (EC) No. 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established by the EMA is responsible for conducting the assessment of a product to define its risk/benefit profile. Under the centralized procedure, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation may be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation.

If the CHMP accepts such a request, the time limit of 210 days will be reduced to 150 days, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that it is no longer appropriate to conduct an accelerated assessment.

Periods of Authorization and Renewals

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk benefit balance by the EMA or by the competent authority of the authorizing Member State. To that end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any authorization that is not followed by the placement of the drug on the EU market (in the case of the centralized procedure) or on the market of the authorizing Member State within three years after authorization ceases to be valid.

Regulatory Requirements after Marketing Authorization

Following approval, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of the medicinal product. These include compliance with the EU's stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. In addition, the manufacturing of authorized products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the EMA's cGMP requirements and comparable requirements of other regulatory bodies in the EU, which mandate the methods, facilities and controls used in manufacturing, processing and packing of drugs to assure their safety and identity. Finally, the marketing and promotion of authorized products, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the EU under Directive 2001/83EC, as amended.

Orphan Drug Designation and Exclusivity

Regulation (EC) No. 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that the marketing of the drug in the EU would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention, or treatment of the condition in question that has been authorized in the EU or, if such method exists, the drug has to be of significant benefit compared to products available for the condition.

An orphan drug designation provides a number of benefits, including fee reductions, regulatory assistance and the possibility to apply for a centralized EU marketing authorization. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. During this market exclusivity period, neither the EMA nor the European Commission or the EU member states can accept an application or grant a marketing authorization for a "similar medicinal product." A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The market exclusivity period for the authorized therapeutic indication may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation because, for example, the product is sufficiently profitable not to justify market exclusivity.

As in the United States, there is a separate regulatory framework for approval of medical devices. If the Company determines to commercialize SLS-1 or another medical device, it will become subject to all of the requirements for approval required by those regulations.

PRC Regulation

In order to protect our potential market in the PRC, we have obtained an exclusive license of certain PRC patents directed to certain of the drug candidates that we are developing and are currently seeking approval of additional patent and other IP filings in the PRC. We do not otherwise conduct business in the PRC. Seeking IP approval in the PRC subjects us to some of the rules and practices of the PRC government. Since the Company intends eventually to market its products in the PRC, at least some of our drug candidates may become subject to regulatory approval and marketing authorization in the PRC.

Hong Kong Regulation

The operations of AML Clinic in Hong Kong are subject to certain general laws and regulations in relation to clinic medical professionals, trade description and safety of consumer goods, medical advertisement and importation, exportation, dealing in and sale of pharmaceutical products and drugs.

Medical Clinics Ordinance

The Medical Clinics Ordinance provides for the registration, control and inspection of medical clinics. It requires a medical clinic to be registered, with name and address and other prescribed particulars. "Medical clinic" means any premises used or intended to be used for the medical diagnosis or treatment of persons suffering from, or believed to be suffering from, any disease, injury or disability of mind or body, with specific exceptions, including private consulting rooms used exclusively by registered medical practitioners in the course of their practice on their own account and not bearing any title or description which includes the word "clinic" or "polyclinic" in the English language.

The application of registration may be refused if:

(i) the income derived or to be derived from the establishment or operation of the clinic is not, or will not be, applied solely towards the promotion of the objects of the clinic; or

(ii) any portion of such income, except payment of remuneration to employed registered medical practitioners, nurses and menial servants, will be paid by way of dividend, bonus or otherwise howsoever by way of profit to the applicant himself, or to any persons properly so employed, or to any other persons howsoever.

We do not believe that the Medical Clinic Ordinance is applicable to the business of our Company and its subsidiaries, having considered, among others, the following:

(iii) the legislative intent behind the Medical Clinics Ordinance was to provide for registration of non-profit making clinics;

(iv) the Food and Health Bureau of Hong Kong published a consultation document, "Regulation of Private Healthcare Facilities" in 2014 which specifically states that the Medical Clinics Ordinance and the Code of Practice For Clinics Registered Under The Medical Clinics Ordinance (Chapter 343 of the Laws of Hong Kong) set out the regulatory framework for non-profit-making medical clinics and that other private healthcare facilities, such as ambulatory medical centers and clinics operated by medical groups or individual medical practitioners, are not subject to direct statutory control beyond the regulation of an individual's professional practice; and

(v) our business is one which makes and intends to continue making profit as a listed entity. The payment of bonuses to some of our Hong Kong Doctors is clearly a reflection of the profit-making nature of our business.

Hence, we do not believe that AML Clinic is required to be registered under the Medical Clinics Ordinance.

Waste Disposal Ordinance

The Waste Disposal Ordinance (Chapter 354 of the Laws of Hong Kong) ("WDO") and the Waste Disposal (Clinical Waste) (General) Regulation (Chapter 354O of the Laws of Hong Kong) (the "WDR") provide for, among others, the control and regulation of the production, storage, collection and disposal of clinical waste.

Under the WDO, clinical waste means waste consisting of any substance, matter or thing generated in connection with:

- a dental, medical, nursing or veterinary practice;
- any other practice, or establishment (howsoever described), that provides medical care and services for the sick, injured, infirm or those who require medical treatment;
- dental, medical, nursing, veterinary, pathological or pharmaceutical research; or
- a dental, medical, veterinary or pathological laboratory practice,

and which consists wholly or partly of any of the materials specified in one or more of the groups listed below:

- used or contaminated sharps;
- laboratory waste;
- human and animal tissues;
- infectious materials;
- dressings; and
- such other wastes as specified by the Director of the Environmental Protection Department ("EPD") of Hong Kong.

Given the medical services provided by AML Clinic and the research works in our R&D Center may produce used or contaminated sharps such as syringes and needles as well as dressings, we are subject to WDO, WDR and the Code of Practice.

Rest of the World Regulation

For other countries in the world, the requirements governing the conduct of clinical trials, medical product licensing, pricing and reimbursement vary from country to country. In all cases if clinical trials are required, they must be conducted in accordance with cGCP requirements and the applicable regulatory requirements and the ethical principles having their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

C. Our Structure

See "Item 4. Information on the Company – A. History and Development of the Company."

Item 19. EXHIBITS

EXHIBIT INDEX

Exhibit No.	Description
1.1	Second Amended and Restated Articles of Association *
2.1	Registrant's Specimen Certificate for Ordinary Shares*
2.2	Form of Underwriter's Warrant+++
4.1	Form of Underwriting Agreement+++
4.2	Appointment Letter between the Company and Ian Huen (Founder, Chief Executive Officer & Executive Director), dated September 25, 2017 *
4.3	Employment Letter between the Company and Sabrina Khan (Chief Financial Officer), dated September 1, 2017 *
4.4	Addendum to Employment Letter between Company and Sabrina Khan (Chief Financial Officer) dated April 24, 2018 *
4.5	Appointment Letter between the Company and Darren Lui (Chief Business Officer, President & Director), dated September 25, 2017 *
4.6	Employment Letter between the Company and Clark Cheng (Chief Medical Officer & Director), dated August 31, 2017 *
4.7	Addendum to Appointment Letter between the Company and Clark Cheng (Chief Medical Officer & Director), dated September 25, 2017 *
4.8	Second Addendum to Appointment Letter between the Company and Clark Cheng (Chief Medical Officer & Director), dated October 30, 2017 *
4.9	Third Addendum to Appointment Letter between the Company and Clark Cheng (Chief Medical Officer & Director), dated January 2, 2018*
4.10	Appointment letter between the Company and Keith Chan (former Chief scientific officer) (Terminated March 13, 2019)*

4.11	Appointment Letter between the Company and Charles Bathurst (Independent Non-Executive Director), dated September 24, 2017 *
4.12	Appointment Letter between the Company and Mirko Scherer (Independent Non-Executive Director), dated September 24, 2017 *
4.13	Employment Agreement between the Company and Justin Wu (Independent Non-Executive Director), dated September 18, 2017 *
4.14	Employment Agreement between the Company and Douglas Arner (Independent Non-Executive Director), dated February 13, 2018 *
4.15	Management Agreement between the Company and Guardian Capital Management Limited, dated March 1, 2017 *
4.16	Consulting Agreement between the Company and GloboAsia, LLC (includes provisions for the appointment of Keith Chan as Chief Scientific Officer) dated August 18, 2017 * (Terminated March 13, 2019)
4.17	Management Agreement between the Company and APTUS CAPITAL LIMITED, dated October 26, 2010 *
4.18	First Addendum to the Management Agreement between the Company and APTUS CAPITAL LIMITED, dated February 10, 2012 *
4.19	Second Addendum to the Management Agreement between the Company and APTUS CAPITAL LIMITED, December 9, 2016 *
4.20	Subscription Agreement between the Company and Peace Range Limited, dated April 6, 2018 *
4.21	Share Charge Agreement between the Company, Jurchen Investment Corporation and Peace Range Limited, dated April 25, 2018 * (Terminated March 12, 2019)
4.22	Deed of Guarantee of Jurchen Investment Corporation, acknowledged by Peace Range Limited, dated April 25, 2018 *
4.23	Charge Account Agreement between the Company and Peace Range Limited, dated April 25, 2018 *
4.24	Bond Certificate between the Company and Peace Range Limited, dated April 25, 2018 *
4.25	Escrow Agreement between the Company and Peace Range Limited, dated April 25, 2018* (Terminated February 22, 2019)
4.26	2017 Share Option Plan *
4.27	Form of Securities Purchase Agreement for the Series A Convertible Promissory Notes, dated May 15, 2018 *
4.28	Lock-up Agreement for Series A Convertible Promissory Notes, dated May 15, 2018 *
4.29	Service Agreement Between Covar Pharmaceuticals Incorporated and Videns Incorporation Limited*
4.30	Appointment Letter and Addendum to Service Agreement with Covar Pharmaceuticals Incorporated and Dr. Kwok Chow dated December 15, 2017*
4.31	Appointment Letter and Addendum to Service Agreement with Covar Pharmaceuticals Incorporated and Mr. Austin Feedman dated December 26, 2017*
4.32	Consulting Agreement between the Company and GloboAsia, LLC (includes provisions for the appointment of Keith Chan as member of the Scientific Advisory Board) dated March 13, 2019+
4.33	Exclusive License agreement for NLS-1 dated July 3, 2017#*
4.34	Addendum to License Agreement for NLS-1 dated February 9, 2018*
4.35	Exclusive License agreement for NLS-1 dated July 3, 2017#*
4.36	Addendum to License Agreement for NLS-1 dated February 9, 2018*
4.37	Exclusive License agreement for NLS-1 dated July 3, 2017#*
4.38	Addendum to License Agreement for NLS-1 dated February 9, 2018*
4.39	Exclusive Patent License Agreement for ALS-4 dated January 11, 2019****
4.40	Employment Agreement with Dr. Lee dated March 13, 2019++
4.41	Employment Agreement with Dr. Ng, dated March 13, 2019++
8.1	List of Subsidiaries*
12.1	Certification of Chief Executive Officer Pursuant to Rule 13a-14(a)/15d-14(a)**
12.2	Certification of Chief Financial Officer Pursuant to Rule 13a-14(a)/15d-14(a)**
13.1	Certification of Chief Executive Officer and Chief Financial Officer Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002***
99.1	Code of Business Ethics *
101.INS	XBRL Instance Document+
101.SCH	XBRL Taxonomy Extension Schema Document+
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document+
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document+
101.LAB	XBRL Taxonomy Extension Label Linkbase Document+
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document+

\# Portions of the exhibit have been omitted pursuant to a request for confidential treatment under Rule 24b-2 of the Securities Exchange Act of 1934, as amended, and the agreement with the omitted portions has been separately filed with the Securities and Exchange Commission.

**** Incorporated by reference to our Annual Report filed on Form 20-F on April 15, 2019. Portions of the exhibit have been omitted in reliance on the confidential treatment provisions available pursuant to revised paragraph 4(a) of Instructions as to Exhibits of Form 20-F.

*** Furnished with this amendment to the annual report on Form 20-F.

** Filed with this amendment to the annual report on Form 20-F.

* Incorporated by reference to our Registration Statement Filed on Form F-1 on September 5, 2018.

+++ Incorporated by reference to our Registration Statement Filed on Form F-1 on November 15, 2018.

++ Incorporated by reference to our Current Report on Form 6-K filed on April 1, 2019.

\+ Incorporated by reference to our Annual Report filed on Form 20-F on April 15, 2019.

SIGNATURES

The registrant hereby certifies that it meets all of the requirements for filing on Form 20-F/A and that it has duly caused and authorized the undersigned to sign this Amendment No. 1 to the annual report on its behalf.

Aptorum Group Limited

Date: April 22, 2019

By: /s/ Ian Huen
Ian Huen
Chief Executive Officer,
Chairman of the Board of Directors
(Principal Executive Officer)

/s/ Sabrina Khan
Sabrina Khan
Chief Financial Officer
Principal Accounting and Financial Officer

Exhibit 12.1

Certification
Pursuant to Rule 13a-14(a) of the Exchange Act

I, Ian Huen, certify that:

1. I have reviewed this annual report on Form 20-F, as amended by Amendment No. 1 thereto, of Aptorum Group Limited;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;

4. The company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the company and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting; and

5. The company's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of the company's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Date: April 22, 2019

By: /s/ Ian Huen
Name: Ian Huen
Title: Chief Executive Officer
(Principal Executive Officer)

Exhibit 12.2

Certification
Pursuant to Rule 13a-14(a) of the Exchange Act

I, Sabrina Khan, certify that:

1. I have reviewed this annual report on Form 20-F, as amended by Amendment No. 1 thereto, of Aptorum Group Limited;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;

4. The company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the company and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting; and

5. The company's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of the company's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Date: April 22, 2019

By: /s/ Sabrina Khan
Name: Sabrina Khan
Title: Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 13.1

Certification
Pursuant to 18 U.S.C. Section 1350

Pursuant to U.S.C. Section 1350 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, United States Code), each of the undersigned officers of Aptorum Group Limited (the "Company"), does hereby certify, to such officer's knowledge, that the Amendment No. 1 to Annual Report on Form 20-F for the year ended December 31, 2018 of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 and information contained in the Form 20-F, as amended fairly presents, in all material respects, the financial condition and results of operations of the Company.

Aptorum Group Limited

April 22, 2019

By: /s/ Ian Huen
Name: Ian Huen
Title: Chief Executive Officer
(Principal Executive Officer)

April 22, 2019

By: /s/ Sabrina Khan
Name: Sabrina Khan
Title: Chief Financial Officer
(Principal Financial and Accounting Officer)