December 28, 2022

VIA EDGAR

U.S. Securities and Exchange Commission Division of Corporation Finance Office of Life Sciences 100 F Street, N.E. Washington, DC 20549 Attn: Tracie Mariner Kevin Vaughn

> Re: Aptorum Group Ltd Form 20-F for Fiscal Year Ended December 31, 2021 Response Dated December 2, 2022 File No. 001-38764

Ladies and Gentlemen:

Aptorum Group Ltd (the "**Company**", "**APM**," "**we**", "**us**" or "**our**") hereby transmits its response to the letter received from the staff (the "**Staff**") of the Securities and Exchange Commission (the "**Commission**"), dated December 15, 2022 regarding our Form 20-F for fiscal year ended December 31, 2021. For ease of reference, we have repeated the Commission's comments in this response and numbered them accordingly.

Response Dated December 2, 2022

Part I Item 3.D. Risk Factors, page 1

1. We note your response to comment 1, including your statement that the "majority of [y]our operations are in Hong Kong" and you "do not conduct any business in the PRC," and reissue. The legal and operational risks associated with operating in China apply to your operations in Hong Kong. Additionally, please ensure that you address throughout your filing the material legal and regulatory risks associated with your specific operations in Hong Kong.

Response: In response to this comment, as well as comment 5, we added China-related risks associated with our operations in Hong Kong to our Risk Factor section and revised the risk factor "*The recent joint statement by the SEC, proposed rule changes submitted by Nasdaq, and an act passed by the U.S. Senate and the U.S. House of Representatives, all call for additional and more stringent criteria to be applied to emerging market companies. <i>These developments could add uncertainties to our offering, business operations, share price and reputation*" from our response dated December 2, 2022 (the "Prior Response").

We added the following to our Risk Factor section.

Risks Related to Doing Business in Hong Kong

There remain some uncertainties as to whether we will be required to obtain approvals from Chinese authorities to list on the U.S. exchanges and offer or continue to offer securities in the future, and if required, we cannot assure you that we will be able to obtain such approval.

The Regulations on Mergers and Acquisitions of Domestic Companies by Foreign Investors (the "M&A Rules"), adopted by six PRC regulatory agencies in 2006 and amended in 2009, requires an overseas special purpose vehicle formed for listing purposes through acquisitions of PRC domestic companies and controlled by PRC companies or individuals to obtain the approval of the China Securities Regulatory Commission ("CSRC") prior to the listing and trading of such special purpose vehicle's securities on an overseas stock exchange.

We are also aware that recently, the PRC government initiated a series of regulatory actions and statements to regulate business operations in certain areas in mainland China with little advance notice, including cracking down on illegal activities in the securities market, enhancing supervision over mainland-China-based companies listed overseas using variable interest entity structure, adopting new measures to extend the scope of cybersecurity reviews, and expanding the efforts in anti-monopoly enforcement. For example, on July 6, 2021, the General Office of the Communist Party of China Central Committee and the General Office of the State Council jointly issued a document to crack down on illegal activities in the securities market and promote the high-quality development of the capital market, which, among other things, requires the relevant governmental authorities to strengthen cross-border oversight of law-enforcement and judicial cooperation, to enhance supervision over mainland-China-based companies listed overseas, and to establish and improve the system of extraterritorial application of the PRC securities laws.

On December 28, 2021, the Cyberspace Administration of China ("CAC"), and other PRC authorities promulgated the Cybersecurity Review Measures, which took effect on February 15, 2022. In addition, the Cybersecurity Law, which was adopted by the Standing Committee of the National People's Congress on November 7, 2016 and came into force on June 1, 2017, and the Cybersecurity Review Measures, or the "Review Measures", provide that personal information and important data collected and generated by a critical information infrastructure operator in the course of its operations in mainland China must be stored in mainland China, and if a critical information infrastructure operator purchases internet products and services that affect or may affect national security, it should be subject to national security review by the CAC together with competent departments of the State Council. In addition, for critical information infrastructure operators, or the "CIIOs", that purchase network-related products and services, the CIIOs shall declare any network-related product or service that affects or may affect national security review. Due to the lack of further interpretations, the exact scope of what constitutes a "CIIO" remains unclear. Further, the PRC government authorities may have wide discretion in the interpretation and enforcement of these laws. In addition, the Review Measures stipulates that any online platform operators holding more than one million users/users' individual information shall be subject to cybersecurity review before listing abroad. As of the date of the annual report, neither we nor our subsidiaries to undertake a cybersecurity review by the CAC. Further, as of the date of this annual report, neither we nor our subsidiaries to any penalties, fines, suspensions, or investigations from any competent authorities for violation of the regulations or policies that the CAC has issued.

On June 10, 2021, the Standing Committee of the National People's Congress promulgated the Data Security Law, which took effect on September 1, 2021. The Data Security Law requires that data shall not be collected by theft or other illegal means, and it also provides for a data classification and hierarchical protection system. The data classification and hierarchical protection system protects data according to its importance in economic and social development, and the damages it may cause to national security, public interests, or the legitimate rights and interests of individuals and organizations if the data is falsified, damaged, disclosed, illegally obtained or illegally used, which protection system is expected to be built by the state for data security in the near future. On November 14, 2021, CAC published the Regulations on the Data Security Administration Draft, or the "Data Security Regulations Draft", to solicit public opinion and comments. Under the Data Security Regulations Draft, an overseas initial public offering to be conducted by a data processor processing the personal information of more than one million individuals shall apply for a cybersecurity review. Data processor means an individual or organization that independently makes decisions on the purpose and manner of processing in data processing activities, and data processing activities refers to activities such as the collection, retention, use, processing, transmission, provision, disclosure, or deletion of data. Currently we do not expect the Review Measures to have an impact on the business and operations of our Hong Kong subsidiaries, because (i) our Hong Kong subsidiaries are incorporated and operating in Hong Kong without any subsidiary or variety interest entity ("VIE") structure in mainland China, and it is unclear whether the Review Measures shall be applied to a Hong Kong company; (ii) as of the date of this annual report, our Hong Kong subsidiaries have not collected or stored personal information of any individual clients of mainland China; and (iii) as of the date of this annual report, our Hong Kong subsidiaries have not been informed by any PRC governmental authority of any requirement that it file for a cybersecurity review for the offering. Based on laws and regulations currently in effect in the PRC as of the date of this annual report, we believe our Hong Kong subsidiaries are not required to pass the cybersecurity review of the CAC in order to list our Class A Ordinary Shares in the U.S.

In addition, on December 24, 2021, the CSRC issued the Administrative Provisions of the State Council Regarding the Overseas Issuance and Listing of Securities by Domestic Enterprises (the "Draft Administrative Provisions") and the Measures for the Overseas Issuance of Securities and Listing Record-Filings by Domestic Enterprises (Draft for Comments) (the "Draft Filing Measures"), collectively, the Draft Rules Regarding Overseas Listings. The Draft Rules Regarding Overseas Listing aim to lay out the filing regulation arrangement for both direct and indirect overseas listing and clarify the determination criteria for indirect overseas listing in overseas markets. According to the Draft Rules Regarding Overseas Listings, among other things, after making initial applications with overseas stock markets for initial public offerings or listings, all mainland-China-based companies shall file with the CSRC within three working days. The required filing materials with the CSRC include (without limitation): (i) record-filing reports and related undertakings, (ii) compliance certificates, filing or approval documents from the primary regulators of applicants' businesses (if applicable), (iii) security assessment opinions issued by related departments (if applicable), (iv) PRC legal opinions, and (v) prospectus. In addition, overseas offerings and listings may be prohibited for such mainland-China-based companies when any of the following applies: (1) if the intended securities offerings and listings are specifically prohibited by the laws, regulations or provisions of the PRC; (2) if the intended securities offerings and listings may constitute a threat to, or endanger national security as reviewed and determined by competent authorities under the State Council in accordance with laws; (3) if there are material ownership disputes over applicants' equity interests, major assets, core technologies, or the others; (4) if, in the past three years, applicants' domestic enterprises, controlling shareholders or de facto controllers have committed corruption, bribery, embezzlement, misappropriation of property, or other criminal offenses disruptive to the order of the socialist market economy, or are currently under judicial investigation for suspicion of criminal offenses, or are under investigation for suspicion of major violations; (5) if, in the past three years, any directors, supervisors, or senior executives of applicants have been subject to administrative punishments for severe violations, or are currently under judicial investigation for suspicion of criminal offenses, or are under investigation for suspicion of major violations; (6) other circumstances as prescribed by the State Council. The Draft Administrative Provisions further stipulate that a fine between RMB 1 million and RMB 10 million may be imposed if an applicant fails to fulfill the filing requirements with the CSRC or conducts an overseas offering or listing in violation of the Article 7 of Draft Administrative Provisions regarding the prohibited circumstances for overseas offering or listing, and in cases of severe violations, a parallel order to suspend relevant businesses or halt operations for rectification may be issued, and relevant business permits or operational license may be revoked. The Draft Rules Regarding Overseas Listings, if enacted, may subject us to additional compliance requirements in the future, if they are determined to be applicable to Hong Kong companies. If we are determined to be subject to the Draft Rules Regarding Overseas Listings, we cannot assure you that we will be able to receive clearance of such filing requirements in a timely manner, or at all, even though we believe that none of the situations that would clearly prohibit overseas listing and offering applies to us. Based on laws and regulations currently in effect in the PRC as of the date of this annual report, we believe our Hong Kong subsidiaries are not required to obtain regulatory approval from the CSRC in order to list our Class A Ordinary Shares in the U.S.

Since these proposed rules, statements and regulatory actions are new, it is highly uncertain how soon the legislative or administrative regulation making bodies will respond and what existing or new laws or regulations or detailed implementations and interpretations will be modified or promulgated, if any. Any failure of us to fully comply with new regulatory requirements may significantly limit or completely hinder our ability to offer or continue to offer the Class A Ordinary Shares, cause significant disruption to our business operations, severely damage our reputation, materially and adversely affect our financial condition and results of operations, and cause the Class A Ordinary Shares to significantly decline in value or become worthless.

As of the date of this annual report, on the basis that we currently do not have any business operations in mainland China, we believe are not required to obtain approvals from the PRC authorities to operate our business or list on the U.S. exchanges and offer or continue to offer securities; specifically, we are currently not required to obtain any permission or approval from the CSRC, the CAC or any other PRC governmental authority to operate our business or to list our securities on a U.S. securities exchange or issue securities to foreign investors. However, if we and our Hong Kong subsidiaries (i) do not receive or maintain such approval, should the approval be required in the future by the PRC government, (ii) inadvertently conclude that such approval is not required, or (iii) applicable laws, regulations, or interpretations change and we are required to obtain such approval in the future, our operations and financial condition could be materially adversely affected, and our ability to offer or continue to offer securities to investors could be significantly limited or completely hindered and the securities currently being offered may substantially decline in value and become worthless.

Nevertheless, since these statements and regulatory actions are new, it is highly uncertain how soon the legislative or administrative regulation making bodies will respond and what existing or new laws or regulations or detailed implementations and interpretations will be modified or promulgated, if any. It is also highly uncertain what potential impact such modified or new laws and regulations will have on Aptorum Group's daily business operations, our ability to accept foreign investments and the listing of our Class A Ordinary Shares on a U.S. or other foreign exchanges. If there is significant change to current political arrangements between mainland China and Hong Kong, the PRC government intervenes or influences operations of companies operated in Hong Kong like us, or exerts more control through change of laws and regulations over offerings conducted overseas and/or foreign investment in issuers like us, it may result in a material change in our operations and/or the value of the securities we are registering for sale or could significantly limit or completely hinder our ability to offer or continue to offer securities to investors and cause the value of our Class A Ordinary Shares to significantly decline or become worthless.

It may be difficult for overseas shareholders and/or regulators to conduct investigations or collect evidence within China.

Shareholder claims or regulatory investigations that are common in the United States generally are difficult to pursue as a matter of law or practicality in China. For example, in China, there are significant legal and other obstacles to providing information needed for regulatory investigations or litigation initiated outside China. Although the authorities in China may establish a regulatory cooperation mechanism with the securities regulatory authorities of another country or region to implement cross-border supervision and administration, such cooperation with the securities regulatory authorities in the Unities States may not be efficient in the absence of mutual and practical cooperation mechanisms. Furthermore, according to Article 177 of the PRC Securities Law, or Article 177, which became effective in March 2020, no overseas securities regulator is allowed to directly conduct investigation or evidence collection activities within the territory of the PRC. While detailed interpretation of or implementation rules under Article 177 have yet to be promulgated, the inability for an overseas securities regulator to directly conduct investigation or evidence difficulties faced by you in protecting your interests.

Our auditor's audit working papers are located in PRC. In the event that the U.S. regulators carry out investigation on us and there is a need to conduct investigation or collect evidence within the territory of the PRC, the U.S. regulators may not be able to carry out such investigation or evidence collection directly in the PRC under the PRC laws. The U.S. regulators may consider cross-border cooperation with securities regulatory authority of the PRC by way of judicial assistance, diplomatic channels or regulatory cooperation mechanism established with the securities regulatory authority of the PRC.

We revised the risk factor "The recent joint statement by the SEC, proposed rule changes submitted by Nasdaq, and an act passed by the U.S. Senate and the U.S. House of Representatives, all call for additional and more stringent criteria to be applied to emerging market companies. These developments could add uncertainties to our offering, business operations, share price and reputation" as follows:

The recent joint statement by the SEC, proposed rule changes submitted by Nasdaq, and an act passed by the U.S. Senate and the U.S. House of Representatives, all call for additional and more stringent criteria to be applied to emerging market companies. These developments could add uncertainties to our offering, business operations, share price and reputation.

U.S. public companies that have substantially all of their operations in China and Hong Kong have been the subject of intense scrutiny, criticism and negative publicity by investors, financial commentators and regulatory agencies, such as the SEC. Much of the scrutiny, criticism and negative publicity has centered on financial and accounting irregularities and mistakes, a lack of effective internal controls over financial accounting, inadequate corporate governance policies or a lack of adherence thereto and, in many cases, allegations of fraud.

On December 7, 2018, the SEC and the PCAOB issued a joint statement highlighting continued challenges faced by the U.S. regulators in their oversight of financial statement audits of U.S.-listed companies with significant operations in China. On April 21, 2020, SEC Chairman Jay Clayton and PCAOB Chairman William D. Duhnke III, along with other senior SEC staff, released a joint statement highlighting the risks associated with investing in companies based in or have substantial operations in emerging markets including China, including Hong Kong, reiterating past SEC and PCAOB statements on matters including the difficulty associated with inspecting accounting firms and audit work papers in China and Hong Kong and higher risks of fraud in emerging markets and the difficulty of bringing and enforcing SEC, Department of Justice and other U.S. regulatory actions, including in instances of fraud, in emerging markets generally.

On May 20, 2020, the U.S. Senate passed the HFCA Act requiring a foreign company to certify it is not owned or controlled by a foreign government if the PCAOB is unable to audit specified reports because the company uses a foreign auditor not subject to PCAOB inspection. If the PCAOB is unable to inspect the company's auditors for three consecutive years, the issuer's securities are prohibited to trade on a national exchange. On December 2, 2020, the U.S. House of Representatives approved the HFCA Act.

On May 21, 2021, Nasdaq filed three proposals with the SEC to (i) apply minimum offering size requirement for companies primarily operating in a "Restrictive Market", (ii) prohibit Restrictive Market companies from directly listing on Nasdaq Capital Market, and only permit them to list on Nasdaq Global Select or Nasdaq Global Market in connection with a direct listing and (iii) apply additional and more stringent criteria to an applicant or listed company based on the qualifications of the company's auditors.

On March 24, 2021, the SEC announced the adoption of interim final amendments to implement the submission and disclosure requirements of the HFCA Act. In the announcement, the SEC clarifies that before any issuer will have to comply with the interim final amendments, the SEC must implement a process for identifying covered issuers. The announcement also states that the SEC staff is actively assessing how best to implement the other requirements of the HFCA Act, including the identification process and the trading prohibition requirements.

On June 22, 2021, the U.S. Senate passed the Accelerating Holding Foreign Companies Accountable Act, which, if passed by the U.S. House of Representatives and signed into law, would reduce the number of consecutive non-inspection years required for triggering the prohibitions under the HFCA Act from three years to two.

On September 22, 2021, the PCAOB adopted a final rule implementing the HFCA Act, which provides a framework for the PCAOB to use when determining, as contemplated under the HFCA Act, whether the board of directors of a company is unable to inspect or investigate completely registered public accounting firms located in a foreign jurisdiction because of a position taken by one or more authorities in that jurisdiction.

On December 2, 2021, the SEC adopted amendments to finalize rules implementing the submission and disclosure requirements in the HFCA Act.



On December 16, 2021, the PCAOB issued a report on its determinations that it is unable to inspect or investigate completely PCAOB-registered public accounting firms headquartered in mainland China and in Hong Kong because of positions taken by PRC and Hong Kong authorities in those jurisdictions.

The lack of access to the PCAOB inspection in China prevents the PCAOB from fully evaluating audits and quality control procedures of the auditors based in China. As a result, investors may be deprived of the benefits of such PCAOB inspections. The inability of the PCAOB to conduct inspections of auditors in China makes it more difficult to evaluate the effectiveness of these accounting firm's audit procedures or quality control procedures as compared to auditors outside of China that are subject to the PCAOB inspections, which could cause investors and potential investors in our Class A Ordinary Shares to lose confidence in our audit procedures and reported financial information and the quality of our financial statements.

Our auditor, Marcum Asia CPAs LLP, as the auditor of companies that are traded publicly in the U.S. and firms registered with the PCAOB, are subject to laws in the U.S., pursuant to which the PCAOB conducts regular inspections to assess their compliance with the applicable professional standards. Marcum Asia CPAs LLP is headquartered in Manhattan, New York, and have been inspected by the PCAOB on a regular basis, with the last inspections in 2020, and Marcum Asia CPAs LLP is not subject to the determinations announced by the PCAOB on December 16, 2021.

However, the recent developments would add uncertainties to our ability to offer or continue to offer securities and we cannot assure you whether the national securities exchange we apply to for listing or regulatory authorities would apply additional and more stringent criteria to us after considering the effectiveness of our auditor's audit procedures and quality control procedures, adequacy of personnel and training, or sufficiency of resources, geographic reach, or experience as it relates to our audit. In addition, the HFCA Act, which requires that the PCAOB be permitted to inspect an issuer's public accounting firm within three years, may result in the delisting of our Company or prohibition of trading in our Class A Ordinary Shares in the future if the PCAOB is unable to inspect our accounting firm at such future time. The Accelerating Holding Foreign Companies Accountable Act, if passed by the U.S. House of Representatives and signed into law, would reduce the period of time for foreign companies to comply with PCAOB audits to two consecutive years instead of three, thus reducing the time period for triggering the prohibition on trading.

On August 26, 2022, the China Securities Regulatory Commission, the MOF, and the PCAOB signed the Protocol governing inspections and investigations of audit firms based in mainland China and Hong Kong, taking the first step toward opening access for the PCAOB to inspect and investigate registered public accounting firms headquartered in mainland China and Hong Kong. Pursuant to the fact sheet with respect to the Protocol disclosed by the SEC, the PCAOB shall have independent discretion to select any issuer audits for inspection or investigation and has the unfettered ability to transfer information to the SEC. On December 15, 2022, the PCAOB Board determined that the PCAOB was able to secure complete access to inspect and investigate registered public accounting firms headquartered in mainland China and Hong Kong and voted to vacate its previous determinations to the contrary. However, should PRC authorities obstruct or otherwise fail to facilitate the PCAOB's access in the future, the PCAOB Board will consider the need to issue a new determination.

As a result of this scrutiny, criticism and negative publicity, the publicly traded stock of many U.S. listed Chinese and Hong Kong companies sharply decreased in value and, in some cases, has become virtually worthless. Many of these companies are now subject to shareholder lawsuits and SEC enforcement actions and are conducting internal and external investigations into the allegations. It is not clear what effect this sector-wide scrutiny, criticism and negative publicity will have on us, our ability to offer or continue to offer securities, business and our share price. If we become the subject of any unfavorable allegations, whether such allegations are proven to be true or untrue, we will have to expend significant resources to investigate such allegations and/or defend our company. This situation will be costly and time consuming and distract our management from developing our growth. If such allegations are not proven to be groundless, we and our business operations will be severely affected and you could sustain a significant decline in the value of our share.

2. We note your response to comment 2, including your statement that "the VIEs are located and incorporated outside of China; China does not have any control over the VIEs," and reissue. Please clarify whether or not your VIEs conduct operations in Hong Kong or otherwise advise. To the extent your VIEs conduct operations in Hong Kong please revise your risk factor accordingly.

Response: We respectfully advise the Staff that as of the date of this report, in accordance with the U.S. GAAP, we determined we have three VIEs, Libra Sciences Limited ("**Libra**"), Mios Pharmaceuticals Limited ("**Mios**") and Scipio Life Sciences Limited ("**Scipio**"). In addition, according to the provisions of Accounting Standards Codification ("**ASC**") 810, Consolidation, we consolidate the financial statements of Mios and Scipio, of which we are the primary beneficiary, but not that of Libra, as we are not deemed as a primary beneficiary of it.

Libra, Mios and Scipio were our subsidiaries. However, on December 30, 2021, we lost the majority voting rights in them, only holding 48.33%, 48.39% and 48.36% economic interest in Libra, Mios and Scipio, respectively. However, we still hold a majority of each of these three companies' outstanding Class A ordinary shares, therefore, we absorb and/or receive portions of these entities' expected losses or residual returns. In addition, none of these three entities have sufficient equity to sustain their own activities, and they have two classes of ordinary shares which have different rights, benefits and obligations. We determined that all these three companies are VIEs for accounting purpose. On December 31, 2021, Libra, Mios and Scipio further issued Class A ordinary shares to their shareholder, Aptorum Therapeutics Limited, in exchange of certain projects licenses. Aptorum Therapeutics Limited is a wholly owned subsidiary of us, upon these share issuances, we held 97.27% economic interest and 31.51% voting power in Libra, 97.93% economic interest and 35.06% voting power in Scipio, respectively.

We have considered each of three VIEs' memorandum and article of association and their respective board of directors (the sole director of each of Mios and Scipio is an executive director of ours), and determined that we have the power to manage and make decisions that affect Mios and Scipio's research and development activities, which activities most significantly impact Mios and Scipio's economic performance. However, we do not have such power over Libra's research and development activities, which activities most significantly impact Libra's economic performance. Accordingly, we determined that we are the primary beneficiary of Mios and Scipio, but not the primary beneficiary of Libra. Therefore, we have three VIEs, and two of them, Mios and Scipio, are consolidated VIEs.

All three VIEs are incorporated under the laws of Cayman Islands and conduct operations in Hong Kong. We agree that we may be subject to legal and operational risks associated with doing business in China as they apply to the VIEs' operations in Hong Kong. Therefore, in addition to including the risk factors as set forth in our response to comment #1, we updated the following risk factors as per your comment:

Our business, financial condition and results of operations, and/or the value of our Class A Ordinary Shares or our ability to offer or continue to offer securities to investors may be materially and adversely affected to the extent the laws and regulations of the PRC become applicable to a company such as us.

We currently do not have or intend to have any subsidiary or any contractual arrangement to establish a variable interest entity structure with any entity in mainland China, and all of our operating entities are in jurisdictions outside of China. However, as our principal place of business is in Hong Kong, a special administrative region of China, there is no guarantee that if certain existing or future laws of the PRC become applicable to a company such as us, it will not have a material adverse impact on our business, financial condition and results of operations and/or our ability to offer or continue to offer securities to investors, any of which may cause the value of such securities to significantly decline or be worthless.

Except for the Basic Law, the national laws of the PRC do not apply in Hong Kong unless they are listed in Annex III of the Basic Law and applied locally by promulgation or local legislation. National laws that may be listed in Annex III are currently limited under the Basic Law to those which fall within the scope of defense and foreign affairs as well as other matters outside the limits of the autonomy of Hong Kong. National laws and regulations relating to data protection, cybersecurity and anti-monopoly have not been listed in Annex III and so do not apply directly to Hong Kong.

The laws and regulations in the PRC are evolving, and their enactment timetable, interpretation and implementation involve significant uncertainties. To the extent any PRC laws and regulations become applicable to us, we may be subject to the risks and uncertainties associated with the legal system in the PRC, including with respect to the enforcement of laws and the possibility of changes of rules and regulations with little or no advance notice. We currently do not have plan to expand our operation or acquire any operation in the mainland China. However, we may also become subject to the laws and regulations of the PRC to the extent we commence business and customer facing operations in mainland China as a result of any future acquisition, expansion or organic growth.

The PRC government exerts substantial influence and discretion over the manner in which companies incorporated under the laws of PRC must conduct their business activities. We have business operations in Hong Kong but not in in mainland China. However, if we were to become subject to such direct influence or discretion, it may result in a material change in our operations and/or the value of our Class A Ordinary Shares, which would materially affect the interest of the investors.

The PRC legal system is evolving rapidly and the PRC laws, regulations, and rules may change quickly with little advance notice. In particular, because these laws, rules and regulations are relatively new, and because of the limited number of published decisions and the non-precedential nature of these decisions, the interpretation of these laws, rules and regulations may contain inconsistences, the enforcement of which involves uncertainties. The PRC government has exercised and continues to exercise substantial control over many sectors of the PRC economy through regulation and/or state ownership. Government actions have had, and may continue to have, a significant effect on economic conditions in the PRC and businesses which are subject to such government actions.

We have business operations in Hong Kong but not in mainland China, and we have direct ownership of our operating entities, none of which are located in mainland China. Our principal executive offices are located in Europe, but our principal place of business is in Hong Kong, a special administrative region of China. The PRC government currently does not exert direct influence and discretion over the manner in which we conduct our business activities outside of mainland China, however, there is no guarantee that we will not be subject to such direct influence or discretion in the future due to changes in laws or other unforeseeable reasons or as a result of our future expansion or acquisition of operations in mainland China. See "- Our business, financial condition and results of operations, and/or the value of our Class A Ordinary Shares or our ability to offer or continue to offer securities to investors may be materially and adversely affected to the extent the laws and regulations of the PRC become applicable to a company such as us."

We currently do not have plans to expand our operation or acquire any operation in the mainland China. However, if we were to become subject to the direct intervention or influence of the PRC government at any time due to changes in laws or other unforeseeable reasons or as a result of our future development, expansion or acquisition of operations in the PRC, it may require a material change in our operations and/or result in increased costs necessary to comply with existing and newly adopted laws and regulations or penalties for any failure to comply. In addition, the market prices of our Class A Ordinary Shares could be adversely affected as a result of anticipated negative impacts of any such government actions, as well as negative investor sentiment towards Hong Kong-based companies subject to direct PRC government oversight and regulation, regardless of our actual operating performance. There can be no assurance that the Chinese government would not intervene in or influence our operations at any time.

We were not required to obtain permission from the PRC government to list on a U.S. securities exchange, however there is no guarantee that this will continue to be the case in the future in relation to the continued listing of our securities on a securities exchange outside of the PRC, or even when such permission is obtained, it will not be subsequently denied or rescinded. Any actions by the PRC government to exert more oversight and control over offerings (including of businesses whose primary operations are in Hong Kong) that are conducted overseas and/or foreign investments in Hong Kong-based issuers could significantly limit or completely hinder our ability to offer or continue to offer securities to investors and cause the value of our securities, including our Class A Ordinary Shares, to significantly decline or be worthless.

The enactment of Law of the PRC on Safeguarding National Security in the Hong Kong Special Administrative Region (the "Hong Kong National Security Law") could impact our Hong Kong holding subsidiary.

On June 30, 2020, the Standing Committee of the PRC National People's Congress adopted the Hong Kong National Security Law. This law defines the duties and government bodies of the Hong Kong National Security Law for safeguarding national security and four categories of offences - secession, subversion, terrorist activities, and collusion with a foreign country or external elements to endanger national security - and their corresponding penalties. On July 14, 2020, the former U.S. President Donald Trump signed the Hong Kong Autonomy Act, or HKAA, into law, authorizing the U.S. administration to impose blocking sanctions against individuals and entities who are determined to have materially contributed to the erosion of Hong Kong's autonomy. On August 7, 2020 the U.S. government imposed HKAA-authorized sanctions on eleven individuals, including former HKSAR chief executive Carrie Lam. On October 14, 2020, the U.S. State Department submitted to relevant committees of Congress the report required under HKAA, identifying persons materially contributing to "the failure of the Government of China to meet its obligations under the Joint Declaration or the Basic Law." The HKAA further authorizes secondary sanctions, including the imposition of blocking sanctions, against foreign financial institutions that knowingly conduct a significant transaction with foreign persons sanctioned under this authority. The imposition of sanctions may directly affect the foreign financial institutions as well as any third parties or customers dealing with any foreign financial institution that is targeted. It is difficult to predict the full impact of the Hong Kong National Security Law and HKAA on Hong Kong and companies located in Hong Kong. If our Hong Kong subsidiaries are determined to be in violation of the Hong Kong National Security Law or the HKAA by competent authorities, our business operations, financial position and results of operations could be materially and adversely affected.

The Hong Kong legal system embodies uncertainties which could limit the availability of legal protections.

As one of the conditions for the handover of the sovereignty of Hong Kong to China, China accepted conditions such as Hong Kong's Basic Law. The Basic Law ensured Hong Kong will retain its own currency (Hong Kong Dollar), legal system, parliamentary system and people's rights and freedom for fifty years from 1997. This agreement has given Hong Kong the freedom to function with a high degree of autonomy. The Special Administrative Region of Hong Kong is responsible for its own domestic affairs including, but not limited to, the judiciary and courts of last resort, immigration and customs, public finance, currencies and extradition. Hong Kong continues using the English common law system.

However, if the PRC attempts to alter its agreement to allow Hong Kong to function autonomously, this could potentially impact Hong Kong's common law legal system and may in turn bring about uncertainty in, for example, the enforcement of our contractual rights. This could, in turn, materially and adversely affect our business and operations. Additionally, intellectual property rights and confidentiality protections in Hong Kong may not be as effective as in the United States or other countries. Accordingly, we cannot predict the effect of future developments in the Hong Kong legal system, including the promulgation of new laws, changes to existing laws or the interpretation or enforcement thereof, or the preemption of local regulations by national laws. These uncertainties could limit the legal protections available to us, including our ability to enforce our agreements with our customers.

Risks Related to Our Corporate Structure

We may not be able to consolidate the financial results of some of our affiliated companies or such consolidation could materially adversely affect our operating results and financial condition.

The Company currently consolidates two VIEs in which the Group has a variable interest and is determined to be the primary beneficiary under the U.S. GAPP. This determination is based on whether the Group has a variable interest (or combination of variable interests) that provides the Company with (a) the power to direct the activities that most significantly impact the VIEs' economic performance and (b) the obligation to absorb losses or right to receive benefits that could be potentially significant to the VIE. The Group continually reassesses whether it is the primary beneficiary of a VIE throughout the entire period the Group is involved with the VIE. According to those standards, we determined that we have the power to manage and make decisions that affect Mios and Scipio's research and development activities, which activities most significantly impact Mios and Scipio's economic performance. However, we do not have such power over Libra's research and development activities, which activities most significantly impact Libra's economic performance. Accordingly, we determined that we are the primary beneficiary of Mios and Scipio, but not the primary beneficiary of Libra. As a result, Mios and Scipio's financial results are consolidated in our consolidated financial statements. In the event that in the future the VIEs no longer meet the definition of a VIE, or we are deemed not to be the primary beneficiary of the VIE for accounting purpose, we would not be able to consolidate line by line that VIE's financial results in our consolidated financial statements. Also, if in the future an affiliate company becomes a VIE and we become the primary beneficiary of it for accounting purposes, we would be required to consolidate that entity's financial results in our consolidated financial statements. If such entity's financial results were negative, this could have a corresponding negative impact on our operating results.

Item 4. Information on the Company

A. History and Development of the Company, page 45

3. We note your response to comment 6 and reissue. At the onset of Item 4, please disclose prominently that you are not a Chinese operating company but a Cayman Islands holding company with operations conducted by your subsidiaries and through contractual arrangements with variable interest entities (VIEs) based in Hong Kong and that this structure involves unique risks to investors. If true, disclose that these contracts have not been tested in court. In addition, please clarify here where the VIEs are operating or otherwise advise and explain whether the VIE structure is used to provide investors with exposure to foreign investment in China-based companies where Chinese law prohibits direct foreign investment in the operating companies, and disclose that investors may never hold equity interests in the Chinese operating company or otherwise advise. Your disclosure should acknowledge that Chinese regulatory authorities could disallow this VIE structure, which would likely result in a material change in your operations and/or a material change in the value of your securities, including that it could cause the value of your securities to significantly decline or become worthless. We note in your response that you included a cross-reference but do not see a cross reference in the proposed amended disclosure. Please revise or otherwise advise.

Response: We respectfully inform the Staff that the only contractual arrangement that we have involving Mios' and Scipio's controlling voting interests are the two concerted action agreements ("**Concerted Action Agreements**"), each by and between Peace Range Limited, a shareholder of the two consolidated VIEs, and Aptorum Therapeutics Limited on December 30, 2021. There is no such arrangement between us or any of our subsidiaries and Libra.

Nevertheless, since the VIEs do have operations in Hong Kong, we agree that they may be subject to legal and operational risks associated with operating in China, and added the relevant disclosure in accordance with comments #1 and #5.



We will add the following disclosure to the outset of Item 4, but in light of the information presented above, we respectfully do not believe any other requested disclosure is necessary:

"Aptorum is not a Chinese operating company. Aptorum is a Cayman Islands holding company with operations conducted through our subsidiaries and the variable interest entities (VIEs). We have determined that we three VIEs, namely, Libra, Mios and Scipio according to the U.S. GAAP. In accordance with ASC 810, we concluded that we are the primary beneficiary of two VIEs, Mios and Scipio, therefore, are able to consolidate their financial statements into ours. Mios and Scipio are incorporated under the laws of the Cayman Islands and conduct operations in Hong Kong. Our corporate structure is based on the equity ownership and control we have over our subsidiaries and the consolidated VIEs. Our corporate structure was not set up to be used to provide investors with exposure to foreign investment in China-based companies where Chinese law prohibits direct foreign investment in the operating companies. Foreign investment can be made directly into the VIEs, however, your investments into Aptorum are made into the Cayman Islands holding company, not any of our VIEs, and you may never own any equity into the VIEs or any other subsidiary.

Aptorum Therapeutics Limited, a Cayman Islands company with limited liability, entered into two concerted action agreements ("Concerted Action Agreements"), with Peace Range Limited, a shareholder of the two consolidated VIEs, on December 30, 2021.

Pursuant to the two Concerted Action Agreements, Peace Ranger Limited and Aptorum Therapeutics Limited agreed to act in concert and give the same expression of intentions in regard with (1) exercising voting rights at shareholders' meetings; (2) making proposals to shareholder's meetings; (3) nominating candidates of directors and supervisors; (4) making material decisions for the consolidated VIEs (save for the administrative and managerial duty of work being managed by the board of directors and executives of the consolidated VIEs); (5) exercising the rights as shareholders of the consolidated VIEs in accordance with their articles of association and other relevant agreements or documents between the consolidated VIEs and other relevant agreements or documents between the consolidated VIEs and other relevant agreements or documents between the consolidated VIEs and other relevant agreements or documents between the consolidated VIEs and other relevant agreements or documents between the consolidated VIEs and other relevant agreements or documents between the consolidated VIEs and other relevant agreements or documents between the consolidated VIEs and other relevant agreements or documents between the consolidated VIEs and other related parties; and (7) exercising other rights granted to shareholders of the consolidated VIEs under laws, administrative regulations, other normative documents, and the articles of association of the consolidated VIEs. The Concerted Action Agreements are governed by and interpreted in accordance with the laws of Hong Kong. The copies of the Concerted Action Agreements were filed as exhibits 4.47 and 4.48 to the Form 20-F filed on April 29, 2022. The Concerted Action Agreements are governed by the laws of Hong Kong. The Hong Kong courts will enforce unless the agreements with substantially the same nature have been tested in the courts in Hong Kong. The Hong Kong courts will enforce unless the agreements are unenforceable for other reason(s) such as the agreements are, among others

The cross reference was to the "Risks Related to doing business in Hong Kong" and "Risks Related to Our Corporate Structure" that we shall now include in the filing.

4. We note your response to prior comment 7. Please tell us and revise your future filings to identify the jurisdiction in which Libra Sciences Limited is incorporated or chartered.

Response: As per your comment we will add the following disclosure to our future filings: Libra Sciences Limited is incorporated under the laws of the Cayman Islands.

B. Business Overview, page 48

5. We note your response to comment 8 and reissue as we do not agree that proposed disclosure in your risk factor section is sufficient. The legal and operational risks associated with operating in China apply to your operations in Hong Kong. Please revise your Business Overview section to provide prominent, upfront, disclosure about the legal and operational risks associated with being based in or having the majority of the company's operations in China. Your disclosure should make clear whether these risks could result in a material change in your operations and/or the value of your securities or could significantly limit or completely hinder your ability to offer or continue to offer securities to investors and cause the value of such securities to significantly decline or be worthless. Your disclosure should address how recent statements and regulatory actions by China's government, such as those related to the use of variable interest entities and data security or anti-monopoly concerns, have or may impact the company's ability to conduct its business, accept foreign investments, or list on a U.S. or other foreign exchange.

Response: In response to the Staff's comment, please find the following revised disclosure for your review:

"Aptorum is not a Chinese operating company. Aptorum is a Cayman Islands holding company with operations conducted through our subsidiaries and the variable interest entities (VIEs). We have determined that we three VIEs, namely, Libra, Mios and Scipio according to the U.S. GAAP. All three of the VIEs are incorporated in Cayman Islands and operate in Hong Kong. In accordance with ASC 810, we concluded that we are the primary beneficiary of two VIEs, Mios and Scipio, therefore, are able to consolidate their financial statements into ours. Our corporate structure is based on the equity ownership and control we have over our subsidiaries and the consolidated VIEs. Our corporate structure was not set up to be used to provide investors with exposure to foreign investment in China-based companies where Chinese law prohibits direct foreign investment in the operating companies. Foreign investment can be made directly into Mios and Scipio; however, your investments into Aptorum are made into the Cayman Islands holding company, not any of the consolidated VIEs, and you may never own any equity into the VIEs or any other subsidiary.

Since the consolidated VIEs operate in Hong Kong, they face various legal and operational risks and uncertainties associated with doing business in Hong Kong. Our current corporate structure does not contain any variable interest entity in mainland China and we do not have intention establishing any VIEs in mainland China in the future. However, if in the future there is any significant change to the current political arrangements between mainland China and Hong Kong and mainland China's expanded authority in Hong Kong result in the PRC regulatory authorities disallowing our current corporate structure, or if in the future our structure were to contain a VIE and the mainland PRC regulatory authorities expand to Hong Kong and disallow our corporate structure, it would likely result in a material adverse change in the VIE's operations, and the value of our securities may decline significantly in value or become worthless.

Although currently we do not have any business operations or VIE in mainland China and we believe that the laws and regulations of the PRC applicable in China do not currently have any material impact on our business, financial condition or results of operations, we face risks and uncertainties associated with the complex and evolving PRC laws and regulations and as to whether and how the recent PRC government statements and regulatory developments, such as those relating to VIE, data and cyberspace security, and anti-monopoly concerns, would be applicable to a company such as Mios and Scipio given their substantial operations in Hong Kong and the Chinese government's significant oversight authority over the conduct of business in Hong Kong.

In light of China's recent expansion of authority in Hong Kong, we are subject to the risks of uncertainty about any future actions of the PRC government or authorities in Hong Kong. The Chinese government may intervene or influence our current and future operations in Hong Kong at any time, or may exert more control over offerings conducted overseas and/or foreign investment in issuers likes ourselves. We believe that, on the basis that we currently do not have any business operations in mainland China, we currently are not required to obtain approvals from Chinese authorities to operate our business or list on the U.S. exchanges and offer securities; specifically, none of Mios or Scipio is currently required to obtain any permission or approval from the China Securities Regulatory Commission ("CSRC"), Cyberspace Administration of China ("CAC") or any other PRC governmental authority to operate its business or for us to continue to list our securities on a U.S. securities exchange or issue securities to foreign investors. However, there is no assurance that there will not be any changes in the economic, political and legal environment in Hong Kong in the future. Should the PRC government choose to affect operations of any company with any level of operations in Hong Kong, or should certain PRC laws and regulations or these statements or regulatory actions become applicable to the VIEs in the future. Such governmental actions: (i) could significantly limit or completely hinder our ability to continue our operations; (ii) could significantly limit or chinacy of regulatory Shares to investors; and (iii) may cause the value of our Class A Ordinary Shares to significantly decline or be worthless.

We are also aware that recently, the PRC government initiated a series of regulatory actions and statements to regulate business operations in certain areas in mainland China with little advance notice, including cracking down on illegal activities in the securities market, enhancing supervision over mainland Chinese companies listed overseas using variable interest entity structure, adopting new measures to extend the scope of cybersecurity reviews, and expanding the efforts in anti-monopoly enforcement. Nevertheless, since these statements and regulatory actions are new, it is highly uncertain how soon the legislative or administrative regulation making bodies will respond and what existing or new laws or regulations or detailed implementations and interpretations will be modified or promulgated, if any. It is also highly uncertain what the potential impact such modified or new laws and regulations will have on the VIEs' daily business operation, and the continued listing of our Class A Ordinary Shares on a U.S. or other foreign exchanges. If any or all of the foregoing were to occur, it may significantly limit or completely hinder our ability to complete this offering or cause the value of our Class A Ordinary Shares to significantly decline or become worthless. See "Risk Factors - Risks Related to Our Corporate Structure" and "Risk Factors - Risks Relating to Doing Business in Hong Kong".

In addition, our Class A Ordinary Shares may be prohibited from trading on a national exchange or over-the-counter under the Holding Foreign Companies Accountable Act (the "HFCA Act") if the Public Company Accounting Oversight Board (United States) (the "PCAOB") is unable to inspect our auditors for three consecutive years beginning in 2021. Our auditor, Marcum Asia CPAs LLP, have been inspected by the PCAOB on a regular basis, with the last inspections in 2020, and Marcum Asia is not subject to the determinations announced by the PCAOB on December 16, 2021. If trading in our Class A Ordinary Shares is prohibited under the HFCA Act in the future because the PCAOB determines that it cannot inspect or fully investigate our auditor at such future time, Nasdaq may determine to delist our Class A Ordinary Shares and trading in our Class A Ordinary Shares could be prohibited. On June 22, 2021, the U.S. Senate passed the Accelerating Holding Foreign Companies Accountable Act, which, if passed by the U.S. House of Representatives and signed into law, would reduce the period of time for foreign companies to comply with the PCAOB audits to two consecutive years instead of three, thus reducing the time period for triggering the prohibition on trading. While our auditor is based in the U.S. and is registered with the PCAOB and subject to PCAOB inspection, in the event it is later determined that the PCAOB is unable to inspect or investigate completely our auditor because of a position taken by an authority in a foreign jurisdiction, then such lack of inspection could cause trading in our Ordinary Shares to be prohibited under the HFCA Act, and ultimately result in a determination by a securities exchange to delist our Ordinary Shares. On August 26, 2022, the PCAOB signed a Statement of Protocol (the "SOP") Agreement with the CSRC and China's Ministry of Finance. The SOP Agreement, together with two protocol agreements (collectively, "SOP Agreements"), governing inspections and investigations of audit firms based in mainland China and Hong Kong, taking the first step toward opening access for the PCAOB to inspect and investigate registered public accounting firms headquartered in mainland China and Hong Kong. Pursuant to the fact sheet with respect to the Protocol disclosed by the U.S. Securities and Exchange Commission (the "SEC"), the PCAOB shall have independent discretion to select any issuer audits for inspection or investigation and has the unfettered ability to transfer information to the SEC. On December 15, 2022, the PCAOB Board determined that the PCAOB was able to secure complete access to inspect and investigate registered public accounting firms headquartered in mainland China and Hong Kong and voted to vacate its previous determinations to the contrary. However, should PRC authorities obstruct or otherwise fail to facilitate the PCAOB's access in the future, the PCAOB Board will consider the need to issue a new determination."

6. We note your revised disclosure in Annex I states Aptorum Innovations Holding Limited owns 75% of Aptorum Innovations Holding Pte. Ltd., Accelerate Technologies Pte. Ltd. holds 15%, and the inventors of RPIDD technologies in A*STAR hold the remaining 15%. Please revise or otherwise advise. Also, revise the chart to use dashes instead of solid lines for the arrows indicating your contractual arrangements with the VIEs.

Response: In response to the Staff's comment, we revised the chart attached hereto as Annex I.

7. We note your response to comments 11 and 12 and reissue in part. We note you state in your response letter "our VIEs." Refrain from using terms such as "we" or "our" when describing activities or functions of a VIE. Do not use language that suggests control of the VIEs. In addition, please revise your definitions of Mios and Scipio to clarify that you are the primary beneficiary of the VIE for accounting purposes.

Response: In response to the Staff's comment, we revised the definitions of Mios and Scipio as follows.

- "Mios" refers to Mios Pharmaceuticals Limited, a VIE in which we hold 97.93% economic interest and 36.17% voting power. Aptorum is regarded as the primary beneficiary of Mios for accounting purposes.
- ii. "Scipio" refers to Scipio Life Sciences Limited, a VIE in which we hold 97.93% economic interest and 35.06% voting power. Aptorum is regarded as the primary beneficiary of Scipio for accounting purposes.

Pursuant to your comment, we also revised related language that was previously provided in response to comment 10 of the Prior Response as follows (revisions in italic font):

Currently, we conduct the majority of our operations through the following subsidiaries: Aptorum Therapeutics Limited, Acticule Life Sciences Limited, Nativus Life Sciences Limited, Aptorum Medical Limited and Aptorum Innovations Holding Pte. Limited. All investments into our company are into the parent company, Aptorum Group Limited; you may never hold direct equity interests in our subsidiaries or *the* VIEs.

In accordance with the provisions of Accounting Standards Codification ("ASC") 810, Consolidation, we consolidate any variable interest entity ("VIE") of which we are *regarded as* the primary beneficiary *for accounting purposes*. The typical condition for a controlling financial interest ownership is holding a majority of the voting interests of an entity; however, a controlling financial interest may also exist in entities, such as VIEs, through arrangements that do not involve controlling voting interests. On December 30, 2021, Libra Sciences Limited ("Libra", formerly known as Aptorum Pharmaceutical Development Limited), Mios and Scipio, issued Class A and Class B ordinary shares to various parties; for each such entity, each Class A ordinary share is entitled to 1 vote and 1 share of economic benefit of the respective company, while each Class B ordinary share is entitled to 10 votes and 0.001 share of economic benefit of the respective company. Following such share issuances, the Group lost its majority voting rights in each of these three companies and only holds 48.33%, 48.39% and 48.36% economic interest in Libra, Mios and Scipio, respectively. However, the Group still holds a majority of each of these three company's outstanding Class A ordinary shares and therefore will absorb/receive portions of these entities' expected losses or residual returns. In addition, none of these three companies have sufficient equity to sustain its own activities, and they have two classes of ordinary shares which have different rights, benefits and obligations. We determined that all these three companies are VIEs. On December 31, 2021, Libra, Mios and Scipio further issued Class A ordinary shares to the Group in exchange of certain projects licenses. Upon these share issuances, the Group was holding 97.27% economic interest and 31.51% voting power in Libra, 97.93% economic interest and 36.17% voting power in Mios, and 97.93% economic interest and 35.06% voting power in Scipio, respectively.

We have considered each of these entity's Memorandum and Article of Association and their respective board of directors (the sole director of each of Mios and Scipio is an executive director of the Group), and determined that we have the power to manage and make decisions that affect Mios and Scipio's research and development activities, which activities most significantly impact Mios and Scipio's economic performance. However, we do not have such power over Libra's research and development activities, which activities, which activities most significantly impact Libra's economic performance. Accordingly, we determined that we are *regarded as* the primary beneficiary of Mios and Scipio *for accounting purposes*, but not the primary beneficiary of Libra.

8. We note your response to comment 13 including your disclosure in your response that you "are not required to obtain any permissions or approvals from Chinese Authorities" and reissue. Please revise your 20-F to state affirmatively whether you have received all requisite permissions or approvals in China, including Hong Kong, and whether any permissions or approvals have been denied. Please also describe the consequences to you and your investors if you, your subsidiaries, or the VIEs: (i) do not receive or maintain such permissions or approvals, (ii) inadvertently conclude that such permissions or approvals are not required, or (iii) applicable laws, regulations, or interpretations change and you are required to obtain such permissions or approvals in the future. Place the revised disclosure in your Business Overview section.

Response: Please note that we did not receive and are not being denied any permissions or approval for VIEs because they do not require such permission or approval in Hong Kong. In response to the Staff's comment, we added the following disclosure to Business Overview-Regulations-PRC Regulation.

Permission Required from the PRC Authorities

As of the date of this annual report, on the basis that we currently do not have any business operations in mainland China, we are not required to obtain approvals from the PRC authorities to operate our business or list on the U.S. exchanges and offer or continue to offer securities; specifically, we are currently not required to obtain any permission or approval from the CSRC, the CAC or any other PRC governmental authority to operate our business or to list our securities on a U.S. securities exchange or issue securities to foreign investors. The laws and regulations of mainland China do not currently have any material impact on our business, financial condition or results of operations and we are currently not subject to the PRC government's direct influence or discretion over the manner in which we conduct our business activities outside of the mainland China.

Nevertheless, we are aware that recently, the PRC government initiated a series of regulatory actions and statements to regulate business operations in certain areas in mainland China with little advance notice, including cracking down on illegal activities in the securities market, enhancing supervision over mainland Chinese companies listed overseas using a VIE structure, adopting new measures to extend the scope of cybersecurity reviews, and expanding the efforts in anti-monopoly enforcement. Since these statements and regulatory actions are new, it is highly uncertain how soon the legislative or administrative regulation making bodies will respond and what existing or new laws or regulations or detailed implementations and interpretations will be modified or promulgated, if any. It is also highly uncertain what potential impact such modified or new laws and regulations will have on Aptorum Group's daily business operations, its ability to accept foreign investments and the listing of our Class A Ordinary Shares on a U.S. or other foreign exchange. If there is significant change to current political arrangements between mainland China and Hong Kong, the PRC government intervenes or influences operations of companies operated in Hong Kong like us, or exerts more control through change of laws and regulations over offerings conducted overseas and/or foreign investment in issuers like us, it may result in a material change in our operations and/or the value of the securities we are registering for sale or could significantly limit or completely hinder our ability to offer or continue to offer securities to investors and cause the value of our Class A Ordinary Shares to significantly decline or become worthless.

We shall include a cross-reference to our detailed discussion of risks facing the company and direct your attention to our response to Comment 1 regarding the additional risk factors that we included.

9. We note your response to comment 14 and reissue. Please update your disclosure in your 20-F consistent with your response that the "VIEs do not hold cash" and that "[n]o transfers, dividends, or distributions have been made to any investor to date." In addition, please provide a clear description of how cash is transferred through your organization. State whether or not you have established cash management policies relating to the transfer of funds through your organization and describe them, as applicable. Disclose your intentions to distribute earnings or settle amounts owed under the VIE agreements. Quantify any cash flows and transfers of other assets by type that have occurred between the holding company, its subsidiaries, and the consolidated VIEs, and direction of transfer. In addition, your response does not appear to address any restrictions and limitations the PRC or Hong Kong may impose on your funds or assets located inside Hong Kong. Please amend your disclosure to describe any restrictions on foreign exchange and your ability to transfer cash between entities, across borders, and to U.S. investors. Describe any restrictions and limitations on your ability to distribute earnings from the company, including your subsidiaries and/or the consolidated VIEs, to the parent company and U.S. investors as well as the ability to settle amounts owed under the VIE agreements.

Response: We respectfully advise the Staff that, the Concerted Action Agreements are the only contractual arrangements that we have which involves the controlling voting interests of the consolidated VIEs. The Concerted Action Agreements do not govern the distribution of the VIEs' earnings or income. The consolidated VIEs do not owe any amount to Aptorum Therapeutics Limited based on the Concerted Action Agreements.

In response to the Staff's comment, please find the revised disclosure below:

"Our management is directly supervising cash management. Our finance department is responsible for establishing the cash management policies and procedures among our departments and the operating entities. Majority of the cash are managed by a few of the subsidiaries of Aptorum Group. Each department or operating entity initiates a cash request by putting forward a payment requisition form, which explains the specific amount and timing of cash requested, and submitting it to designated management members of our Company, based on the amount and the nature of payment. The designated management member examines and approves the cash transfer based on the sources of cash and the priorities of the needs, and submit it to the cashier specialists of our finance department for a second review. Other than the above, we currently do not have other cash management policies or procedures that dictate how funds are transferred.

We are permitted under the laws of Cayman Islands to provide funding to our subsidiaries and the consolidated VIEs through loans or capital contributions without restrictions on the amount of the funds. Under the Cayman Islands law, the VIEs are permitted to pay a dividend on its shares out of either profit or share premium amount, provided that in no circumstances may a dividend be paid if this would result in the consolidated VIEs being unable to pay its debts due in the ordinary course of business.

As of the date of this annual report, none of our subsidiaries or the consolidated VIEs have made any dividends or distributions to our Company and our Company has not made any dividends or distributions to our shareholders. We intend to keep any future earnings to finance the expansion of our business, and we do not anticipate that any cash dividends will be paid in the foreseeable future. Subject to the passive foreign investment company ("PFIC") rules, the gross amount of distributions we make to investors with respect to our Class A Ordinary Shares (including the amount of any taxes withheld therefrom) will be taxable as a dividend, to the extent that the distribution is paid out of our current or accumulated earnings and profits, as determined under U.S. federal income tax principles.

On December 31, 2021, Mios and Scipio has issued Class A ordinary shares to Aptorum Therapeutics Limited, in exchange of Aptorum Therapeutics Limited's granting of license of certain patents to each of them. Other than this, there has been no transfer of cash or other assets occurred between us, our subsidiaries, and the consolidated VIEs.

We thank the Staff for its review of the foregoing. If you have further comments, we ask that you forward them by electronic mail to our counsel, Louis Taubman, Esq. at ltaubman@htflawyers.com or by telephone at (212) 530-2208.

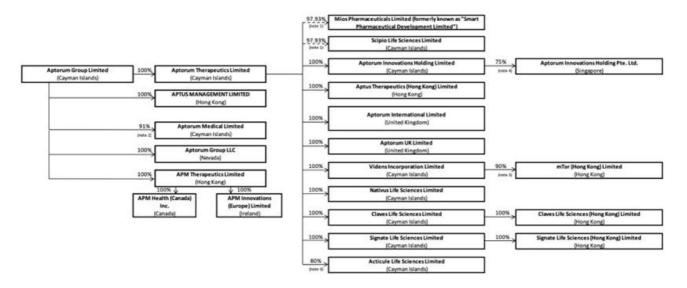
Very truly yours,

/s/ Darren Lui

Darren Lui Chief Executive Officer

cc: Louis Taubman, Esq. Hunter Taubman Fischer & Li LLC

Annex I



Note 1: Both Mios Pharmaceuticals Limited ("Mios") and Scipio Life Sciences Limited ("Scipio") issued Class A and Class B ordinary shares to various parties; for each such entity, each Class A ordinary share is entitled to 1 vote and 1 share of economic interest of the respective company, while each Class B ordinary share is entitled to 10 votes and 0.001 share of economic interest of the respective company.

As of the date of this annual report, we hold 97.93% economic interest and 36.17% voting power in Mios, and 97.93% economic interest and 35.06% voting power in Scipio. An independent third party shareholder, Peace Range Limited, holds 0.15% economic interest and 63.61% voting power in Mios, and 0.15% economic interest and 64.72% voting power in Scipio. The remaining shareholders hold 1.92% economic interest and 0.22% voting power in Scipio respectively. Our ownership interest in these entities is through direct equity ownership and not through any contractual arrangements.

Note 2: Dr. Clark Cheng, an Executive Director of Aptorum Group, holds the remaining 9% shareholding of Aptorum Medical Limited.

Note 3: Angen Funds Limited, a company designated by an investor of ALS series projects, holds the remaining 20% shareholding of Acticule Life Sciences Limited.

Note 4: Accelerate Technologies Pte. Ltd., the commercialization arm of the Singapore Agency for Science, Technology and Research ("A*STAR"), hold 15% shareholding of Aptorum Innovations Holding Pte. Ltd.. The inventors of RPIDD technologies in A*STAR hold the remaining 10% of shareholding of Aptorum Innovations Holding Pte. Ltd.

Note 5: An investor of project VLS-2 holds the remaining 10% shareholding of mTor (Hong Kong) Limited.