

Aptorum Group Ltd
17 Hanover Square
London W1S 1BN, United Kingdom

December 2, 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
Filed April 29, 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 November 22, 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.

Form 20-F for the Fiscal Year Ended December 31, 2021

Part I

Item 3.D. Risk Factors, page 1

1. In your summary of risk factors, disclose the risks that your corporate structure and being based in or having the majority of the company’s operations in China poses to investors. In particular, describe the significant regulatory, liquidity, and enforcement risks. For example, specifically discuss risks arising from the legal system in China, including risks and uncertainties regarding the enforcement of laws and that rules and regulations in China can change quickly with little advance notice; and the risk that the Chinese government may intervene or influence your operations at any time, or may exert more control over offerings conducted overseas and/or foreign investment in China-based issuers, which could result in a material change in your operations and/or the value of the securities you are registering for sale. Acknowledge any risks that any actions by the Chinese government to exert more oversight and control over offerings that are conducted overseas and/or foreign investment in China-based issuers could significantly limit or completely hinder your ability to offer or continue to offer securities to investors and cause the value of your securities to significantly decline or be worthless.

Response: Please note that although we are the exclusive licensee to certain PRC patents directed to our drug candidates, and we intend to file application for certain products in the PRC, the majority of our operations are in Hong Kong. Please also note that none of our subsidiaries are incorporated in China and that our VIE’s are incorporated in the Cayman Islands. Please also be reminded that the 20-F has a risk factor, “*Although we do not currently conduct any business in the PRC, we may in the future; in doing so we would be exposed to various risks related to doing business in the PRC*” to alert investors to potential issues with PRC regulation.

In response to your comment, we added the following to our Summary Risk Factors section; please also see our response to Comment 2 below:

Risks Related to Doing Business in the PRC

We currently do not conduct any business in the PRC. If in the future, we commence business or operation in the PRC, we may face risks and uncertainties relating to doing business in the PRC in general, including, but not limited to, the following:

- Our Class A Ordinary Shares may be delisted under the HFCA Act if the PCAOB is unable to inspect our auditors. The delisting of our Class A Ordinary Shares, or the threat of their being delisted, may materially and adversely affect the value of your investment. Furthermore, on June 22, 2021, the U.S. Senate passed the AHFCA Act, which, if enacted, would amend the HFCA Act and require the SEC to prohibit an issuer's securities from trading on any U.S. stock exchanges if its auditor is not subject to PCAOB inspections for two consecutive years instead of three, which would reduce the time before our securities may be prohibited from trading or be delisted.
 - Even though our auditor is based in New York, New York and under full inspection by the PCAOB and that it is not currently subject to the determinations announced by the PCAOB on December 16, 2021, if any PRC law relating to the access of the PCAOB to auditor files were to apply to a company such as Marcum Asia CPAs LLP or its auditor, the PCAOB may be unable to fully inspect our auditor, which may result in our securities being delisted or prohibited from being traded "over-the-counter" pursuant to the HFCA Act and materially and adversely affect the value and/or liquidity of your investment.
 - The uncertainties with respect to the Chinese legal system, including uncertainties regarding the enforcement of laws, and sudden or unexpected changes in laws and regulations in China with little advance notice could adversely affect us and limit the legal protections available to you and us.
2. **Revise your risk factors to acknowledge that if the PRC government determines that the contractual arrangements constituting part of the VIE structure do not comply with PRC regulations, or if these regulations change or are interpreted differently in the future, your securities may decline in value or become worthless if the determinations, changes, or interpretations result in your inability to assert contractual control over the assets of your PRC subsidiaries or the VIEs that conduct all or substantially all of your operations.**

Response: In response to your comment, we did add the risk factors regarding the potential impact of PRC regulations that are included in response to Comment 3 below. However, we respectfully submit that no further risk factors are necessary since the VIEs are located and incorporated outside of China; China does not have any control over the VIEs.

3. Given the Chinese government’s significant oversight and discretion over the conduct of your business, please revise to highlight separately the risk that the Chinese government may intervene or influence your operations at any time, which could result in a material change in your operations and/or the value of your securities. Also, given recent statements by the Chinese government indicating an intent to exert more oversight and control over offerings that are conducted overseas and/or foreign investment in China- based issuers, acknowledge the risk that any such action could significantly limit or completely hinder your ability to offer or continue to offer securities to investors and cause the value of your securities to significantly decline or be worthless.

Response: In response to this Comment, as well as Comment 5 and 8, we added the following to our Risk Factor section. Please note the risk factor “*If the U.S. Public Company Accounting Oversight Board, or the PCAOB, is unable to inspect our auditors as required under the Holding Foreign Companies Accountable Act, the SEC will prohibit the trading of our Class A Ordinary Shares. A trading prohibition for our Class A Ordinary Shares, or the threat of a trading prohibition, may materially and adversely affect the value of your investment. Additionally, the inability of the PCAOB to conduct inspections of our auditors would deprive our investors of the benefits of such inspections*” that is included in the 20-F.

Risks Related to Doing Business in Hong Kong

Our company currently does not have any operations in mainland China. Accordingly, the laws and regulations of the PRC do not currently have any material impact on our business, financial condition and results of operations. However, if certain PRC laws and regulations were to become applicable to a company such as us in the future, the application of such laws and regulations may have a material adverse impact on our business, financial condition and results of operations and our ability to offer or continue to offer securities to investors, any of which may cause the value of our Class A Ordinary Shares, to significantly decline or become worthless. See the following risk factors of “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” and “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 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 your Class Ordinary Shares, which would materially affect the interests of investors.”

Political risks associated with conducting business in Hong Kong.

Most of our operations are based in Hong Kong. Accordingly, our business operations and financial conditions will be affected by the political and legal developments in Hong Kong. During the period covered by the financial information incorporated by reference into and included in this Report, we maintain substantially most of our operations in Hong Kong. Any adverse economic, social and/or political conditions, material social unrest, strike, riot, civil disturbance or disobedience, as well as significant natural disasters, may affect the market may adversely affect the business operations of our operations. Hong Kong is a special administrative region of the PRC and the basic policies of the PRC regarding Hong Kong are reflected in the Basic Law (the “Hong Kong Basic Law” or the “Basic Law”), namely, Hong Kong’s constitutional document, which provides Hong Kong with a high degree of autonomy and executive, legislative and independent judicial powers, including that of final adjudication under the principle of “one country, two systems”. 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. Since our operation is based in Hong Kong, any change of such political arrangements may pose immediate threat to the stability of the economy in Hong Kong, thereby directly and adversely affecting our results of operations and financial positions.

Under the Basic Law of the Hong Kong Special Administrative Region of the People's Republic of China, Hong Kong is exclusively in charge of its internal affairs and external relations, while the government of the PRC is responsible for its foreign affairs and defense. As a separate customs territory, Hong Kong maintains and develops relations with foreign states and regions. Based on certain recent development including the Law of the People's Republic of China on Safeguarding National Security in the Hong Kong Special Administrative Region issued by the Standing Committee of the PRC National People's Congress in June 2020, the U.S. State Department has indicated that the United States no longer considers Hong Kong to have significant autonomy from China and Former President Trump signed an executive order and Hong Kong Autonomy Act ("HKAA") to remove Hong Kong's preferential trade status and to authorize 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. The United States may impose the same tariffs and other trade restrictions on exports from Hong Kong that it places on goods from mainland China. These and other recent actions may represent an escalation in political and trade tensions involving the U.S., China and Hong Kong, which could potentially harm our business.

Given the relatively small geographical size of Hong Kong, any of such incidents may have a widespread effect on our business operations, which could in turn adversely and materially affect our business, results of operations and financial condition. It is difficult to predict the full impact of the HKAA on Hong Kong and companies with operations in Hong Kong like us. Furthermore, legislative or administrative actions in respect of China-U.S. relations could cause investor uncertainty for affected issuers, including us, and the market price of our Ordinary Shares could be adversely affected.

If we become directly subject to the recent scrutiny, criticism and negative publicity involving U.S.-listed Chinese companies, we may have to expend significant resources to investigate and resolve the matter which could harm our business operations, stock price and reputation and could result in a loss of your investment in our stock, especially if such matter cannot be addressed and resolved favorably.

Recently, U.S. public companies that have substantially all of their operations in China, including 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 around 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. As a result of the scrutiny, criticism and negative publicity, the publicly traded stock of many U.S. listed Chinese companies has 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 our company, our business and our stock 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 growing our company.

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.

As a result of these 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 offering, 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.

Nasdaq may apply additional and more stringent criteria for our continued listing because our insiders hold a large portion of our listed securities.

Nasdaq Listing Rule 5101 provides Nasdaq with broad discretionary authority over the initial and continued listing of securities in Nasdaq and Nasdaq may use such discretion to deny initial listing, apply additional or more stringent criteria for the initial or continued listing of particular securities, or suspend or delist particular securities based on any event, condition, or circumstance that exists or occurs that makes initial or continued listing of the securities on Nasdaq inadvisable or unwarranted in the opinion of Nasdaq, even though the securities meet all enumerated criteria for initial or continued listing on Nasdaq. In addition, Nasdaq has used its discretion to deny initial or continued listing or to apply additional and more stringent criteria in the instances, including but not limited to: (i) where the company engaged an auditor that has not been subject to an inspection by PCAOB, an auditor that PCAOB cannot inspect, or an auditor that has not demonstrated sufficient resources, geographic reach, or experience to adequately perform the company's audit; (ii) where the company planned a small public offering, which would result in insiders holding a large portion of the company's listed securities; and (iii) where the company did not demonstrate sufficient nexus to the U.S. capital market, including having no U.S. shareholders, operations, or members of the board of directors or management. The insiders of our Company hold a large portion of the company's listed securities. Therefore, we may be subject to the additional and more stringent criteria of Nasdaq for our continued listing, which might result in deficiency letters or inquiries that will take management's time away from focusing on our operations.

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 we have direct ownership of our operating entities, all of which 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 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 inconsistencies, 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 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 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 VIEs in which the Group has a variable interest and is determined to be the primary beneficiary. 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 VIE's 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.

The economic substance legislation of the Cayman Islands may adversely impact us or our operations.

The Company is subject to Cayman Islands economic substance legislation (“ESA”) requiring that where the Company carries on a relevant activity (as defined in the ESA) it must maintain economic substance within the Cayman Islands, including adequate premises and employees within the Cayman Islands. As an entity subject to the ESA, the Company is required to assess its operations to determine the required compliance (if any) with the ESA, to file an annual notification with the Cayman Islands Registrar of Companies disclosing whether the Company is carrying out any relevant activities within the meaning of the ESA and an annual return with the Department of International Tax Co-Operation. Where applicable, the Company must establish that its operations satisfy the economic substance requirements of the ESA. The Company is required to monitor its operations to ensure it remains in compliance with all requirements under the ESA. Failure to satisfy these requirements may subject the Company to penalties under the ESA.

EU AML High-Risk Third Countries List

On March 13, 2022, the European Commission (“EC”) updated its list of ‘high-risk third countries’ (“EU AML List”) identified as having strategic deficiencies in their anti-money laundering/counter-terrorist financing regimes to add nine countries, including the Cayman Islands. The EC has noted it is committed to there being a greater alignment between the EU AML List and the FATF listing process. The addition of the Cayman Islands to the EU AML List is a direct result of the inclusion of the Cayman Islands on the FATF grey list in February 2021. It is unclear how long this designation will remain in place and what ramifications, if any, the designation will have for the Company.

The Financial Action Task Force has increased monitoring of the Cayman Islands.

In February 2021, the Cayman Islands was added to the Financial Action Task Force (“FATF”) list of jurisdictions whose anti-money laundering practices are under increased monitoring, commonly referred to as the “FATF grey list.” When the FATF places a jurisdiction under increased monitoring, it means the country has committed to resolve swiftly the identified strategic deficiencies within agreed timeframes and is subject to increased monitoring during that timeframe. In its October 2021 and October 2022 plenary, the FATF recognized the progress made by the Cayman Islands to improve its anti-money laundering and counter-terrorist financing regime. Despite this recognition, it is still unclear how long this designation will remain in place and what ramifications, if any, the designation will have for the Company.

- 4. In light of recent events indicating greater oversight by the Cyberspace Administration of China (CAC) over data security, particularly for companies seeking to list on a foreign exchange, please revise your disclosure to explain how this oversight impacts your business and your securities and to what extent you believe that you are compliant with the regulations or policies that have been issued by the CAC to date.**

Response: Please see our response to comment 3 above.

- 5. Please update your disclosure in the risk factor regarding the Holding Foreign Companies Accountable Act on page 37 to reflect that the Commission adopted rules to implement the HFCAA and that, pursuant to the HFCAA, the PCAOB has issued its report notifying the Commission of its determination that it is unable to inspect or investigate completely accounting firms headquartered in mainland China or Hong Kong.**

Response: Please see our response to Comment 3.

Item 4. Information on the Company

A. History and Development of the Company, page 45

6. 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 China and that this structure involves unique risks to investors. If true, disclose that these contracts have not been tested in court. 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. Your disclosure should acknowledge that Chinese regulatory authorities could disallow this 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. Provide a cross-reference to your detailed discussion of risks facing the company as a result of this structure.

Response: Although our operations are not conducted through contractual arrangements with VIES based in China, in response to your comment, we added the following disclosure at the onset of Item 4:

Aptorum was incorporated under the laws of the Cayman Islands on September 13, 2010. Our current business consists of “therapeutics” and “non-therapeutics” segments, all of which we operate through our subsidiaries (See the ownership chart on page [47] of our 20-F).

We refer to our therapeutics segment as Aptorum Therapeutics Group, which 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 whose subsidiaries (who we sometimes refer to herein as project companies) are based in the United Kingdom, Singapore and Hong Kong.

We refer to our non-therapeutics segment as Aptorum Non-Therapeutics Group. The Non-Therapeutics Group consists of: (i) diagnostics projects including a novel molecular-based rapid pathogen identification and detection diagnostics (“RPIDD”) technology, (ii) natural supplements including NativusWell[®], and (iii) AML Clinic. RPIDD technology is currently under co-development with A*STAR. The sale of natural supplements is operated through Nativus Life Sciences Limited (“Nativus”), a subsidiary of Aptorum Therapeutics Limited incorporated in the Cayman Islands. The Group’s outpatient clinic is operated through our subsidiary, Aptorum Medical Limited, which is a Hong Kong-based company incorporated in the Cayman Islands with an office in Central, Hong Kong.

On September 25, 2020, Aptorum, via its subsidiaries, enters into a series of transactions with Accelerate Technologies Pte. Ltd.’s (“Accelerate Technologies”), the commercialization arm of the Singapore Agency for Science, Technology and Research (“A*STAR”), in relation to the research and development of novel molecular-based rapid pathogen identification and detection diagnostics (“RPIDD”) technology through its subsidiaries. Specifically, Aptorum Innovations Holding Pte. Limited, one of the Company’s subsidiaries, entered into an Exclusive Licence Agreement with Accelerate Technologies to co-develop the RPIDD technology. The term of the Exclusive Licence Agreement is described in Exhibit 4.62 on Form 20-F filed with the SEC on April 19, 2021. Furthermore, Accelerate Technologies, the inventors of the RPIDD technologies in A*STAR (“Founding Scientists”), Aptorum Innovations Holding Pte. Limited, and Aptorum Innovations Holding Limited (“AIHL”), a wholly owned subsidiary of the Company, entered into a Share Subscription & Shareholders Agreement on the same day to subscribe ordinary shares of Aptorum Innovations Holding Pte. Limited. The shares are subscribed and issued in two tranches, the first tranche has taken place at closing of the Share Subscription & Shareholders Agreement, while the second tranche will take place after the certain first milestone is met. The total number of shares subscribed by the shareholders under the Share Subscription & Shareholders Agreement is around 2.7 million. After the two tranches of subscription, Aptorum, Accelerate Technologies and the Founding Scientists are expected to control 71.23%, 14.25% and 9.53% of the share of Aptorum Innovations Holding Pte. Limited respectively, with 4.99% of the shares reserved for its employee share plan.

Finally, we included a cross-reference to our detailed discussion of risks facing the company as a result of this structure and direct your attention to our response to Comment 3 regarding the additional risk factors that we included.

7. We note that the consolidated VIEs constitute a material part of your consolidated financial statements. Please provide in tabular form condensed consolidating schedule - depicting the financial position, cash flows and results of operations for the parent, the consolidated variable interest entities, and any eliminating adjustments separately - as of the same dates and for the same periods for which audited consolidated financial statements are required. Highlight the financial statement information related to the variable interest entity and parent, so an investor may evaluate the nature of assets held by, and the operations of, entities apart from the variable interest entity, which includes the cash held and transferred among entities. As part of your revisions, disclose the jurisdiction in which Libra Sciences Limited is incorporated or chartered.

Response: Please note that we do not view the VIEs that we consolidate to be a material part of our consolidated financial statements. We respectfully direct your attention to Note 14 of the financial statements, wherein we disclose the aggregate carrying value of the VIE's assets and liabilities. As noted therein, such amounts are not material, which is part of the reason we do not deem these VIEs to be material to our Group for the year ended 2021. If the VIEs become material parts of our business in the future, we will disclose the separate financial position, cash flow and results of operation for parents and VIEs. Therefore, we respectfully do not believe we need to add the requested disclosure.

B. Business Overview, page 48

8. Provide prominent 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: We direct your attention to our response to comment 3 above. We respectfully submit that the disclosure we are now including in our risk factor section is sufficient to satisfy this comment.

9. Please disclose whether your auditor is subject to the determinations announced by the PCAOB on December 16, 2021 and whether and how the Holding Foreign Companies Accountable Act and related regulations will affect your company.

Response: We respectfully direct your attention to the risk factor included in our 20-F: *"If the U.S. Public Company Accounting Oversight Board, or the PCAOB, is unable to inspect our auditors as required under the Holding Foreign Companies Accountable Act, the SEC will prohibit the trading of our Class A Ordinary Shares. A trading prohibition for our Class A Ordinary Shares, or the threat of a trading prohibition, may materially and adversely affect the value of your investment. Additionally, the inability of the PCAOB to conduct inspections of our auditors would deprive our investors of the benefits of such inspections."* Please see below extract.

“Our current independent accounting firm, Marcum Asia CPAs LLP (f/k/a Marcum Bernstein & Pinchuk LLP) (“Marcum”), whose audit report is included in this annual report on Form 20-F, is headquartered in Manhattan, New York, and was not included in the list of PCAOB Identified Firms in the PCAOB December Release. Our ability to retain an auditor subject to PCAOB inspection and investigation, including but not limited to inspection of the audit working papers related to us, may depend on the relevant positions of U.S. and Chinese regulators. Marcum’s audit working papers related to us are located in China. With respect to audits of companies with operations in China, such as the Company, there are uncertainties about the ability of our auditor to fully cooperate with a request by the PCAOB for audit working papers in China without the approval of Chinese authorities. If in the future Marcum is included in the list of PCAOB Identified Firms and we are unable to retain a PCAOB-registered auditor subject to PCAOB inspection and investigation, a trading prohibition for our Class A Ordinary Shares could be issued shortly after our filing of the second consecutive annual report on Form 20-F for which we have retained a PCAOB Identified Firm.”

10. Please revise your diagram of the company’s corporate structure, identifying the person or entity that owns the equity in each depicted entity, including voting and economic rights. Describe all contracts and arrangements through which you claim to exercise control that results in consolidation of the VIEs’ operations and financial results into your financial statements. Identify clearly the entity in which investors are purchasing their interest and the entities in which the company’s operations are conducted. Describe the relevant contractual agreements between the entities and how this type of corporate structure may affect investors and the value of their investment, including how and why the contractual arrangements may be less effective than direct ownership and that the company may incur substantial costs to enforce the terms of the arrangements. Disclose the uncertainties regarding the status of the rights of the Cayman Islands holding company with respect to its contractual arrangements with the VIEs, its founders and owners, and the challenges the company may face enforcing these contractual agreements due to legal uncertainties and jurisdictional limits.

Response: We respectfully direct your attention to the chart on page [] of our 20-F, which shows that we own 100% of all but six of our subsidiaries (the “Chart”); the Chart explains the Group’s ownership interest in Mios and Scipio. Pursuant to your comment, we updated the chart to disclose the person or entity that owns the other equities over which we do not maintain 100% control; the revised chart is attached hereto as Annex I. We direct your attention to Note 3 and 14 of our financial statements and advise that we added the following disclosure under the Chart:

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 VIEs.

In accordance with the provisions of Accounting Standards Codification (“ASC”) 810, Consolidation, we consolidate any variable interest entity (“VIE”) of which we are the primary beneficiary. 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, three of the Group’s subsidiaries, Libra Sciences Limited (“Libra”, formerly known as Aptorum Pharmaceutical Development Limited), 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 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 subsidiaries’ 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 variable interest entities (“VIE”). 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 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.

We also direct your attention to the risk factor "*Since we are a Cayman Islands exempted company, the rights of our shareholders may be more limited than those of shareholders of a company organized in the United States*" in the 20-F.

11. Clearly disclose how you will refer to the holding company, subsidiaries, and VIEs when providing the disclosure throughout the document so that it is clear to investors which entity the disclosure is referencing and which subsidiaries or entities are conducting the business operations. Refrain from using terms such as "we" or "our" when describing activities or functions of a VIE. For example, disclose, if true, that your subsidiaries and/or the VIE conduct operations in China, that the VIE is consolidated for accounting purposes but is not an entity in which you possess majority voting power, and that the holding company does not conduct operations.

Response: In response to your comment, we updated language in the definitions section and in other appropriate places throughout the Form to state,

- i. "Company," "we" and "us" refer to Aptorum Group Limited, a Cayman Islands exempted company with limited liability whose principal place of business is in Hong Kong.
- ii. "Aptorum Group" and "Group" refer to Aptorum Group Limited, all of its subsidiaries, and VIEs to which we are a primary beneficiary.
- iii. "VIE" refers to a variable interest entity.
- iv. "Mios" refers to Mios Pharmaceuticals Limited, a VIE in which we hold 97.93% economic interest and 36.17% voting power. We are the primary beneficiary of Mios.
- v. "Scipio" refers to Scipio Life Sciences Limited, a VIE in which we hold 97.93% economic interest and 35.06% voting power. We are the primary beneficiary of Scipio.
- vi. "Libra" refers to Libra Sciences Limited, a VIE in which we hold 97.27% economic interest and 31.51% voting power. We are not the primary beneficiary of Libra.

12. Please revise your disclosure here to state that you are the primary beneficiary of the VIEs for accounting purposes. Please also disclose, if true, that the VIE agreements have not been tested in a court of law.

Response: Due to the immateriality of our VIEs and the disclosure in Note 14, we respectfully do not believe it is necessary to include the requested disclosure in the Business Overview section. Since we do not rely on those entities for the majority of our operations, we think it may be misleading to include them in that section.

13. Disclose each permission or approval that you, your subsidiaries, or the VIEs are required to obtain from Chinese authorities to operate your business and to offer securities to foreign investors. State whether you, your subsidiaries, or VIEs are covered by permissions requirements from the China Securities Regulatory Commission (CSRC), Cyberspace Administration of China (CAC) or any other governmental agency that is required to approve the VIE's operations, and state affirmatively whether you have received all requisite permissions or approvals 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.

Response: At this time, we are not required to obtain any permissions or approvals from Chinese Authorities. However, we added the disclosure noted in response to Comment 3 above and direct your attention to same.

14. Provide a clear description of how cash is transferred through your organization. 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. Quantify any dividends or distributions that a subsidiary or consolidated VIE have made to the holding company and which entity made such transfer, and their tax consequences. Similarly quantify dividends or distributions made to U.S. investors, the source, and their tax consequences. Your disclosure should make clear if no transfers, dividends, or distributions have been made to date. 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: Currently, VIEs do not hold cash. Aptorum Group helps VIEs to settle the payment in accordance to the administrative management service agreement signed on January 6, 2022. The VIEs do not have intention to distribute earnings. If an investment is made into a VIE, part of those funds will be used to settle the outstanding balance owed to Aptorum Group. No transfers, dividends, or distributions have been made to any investor to date.

[Operating and Financial Review and Prospects](#)

[Results of Operations](#)

[Results of Operations for the Years ended December 31, 2021 and 2020](#)

[Research and development expenses, page 92](#)

15. We note you disclose research and development expenses by type of expense. Please expand your disclosure in future filings to provide the costs incurred during each period presented for each of your key research and development programs. If you do not track your research and development costs by program, please disclose that fact, and explain why you do not maintain and evaluate research and development costs by program. Provide proposed disclosure with your response.

Response: Pursuant to your comment, we will insert the below table in our MD&A section.

	2021	2020
	US\$	US\$
R&D expenses by projects		
ALS-4	5,430,177	6,673,591
SACT-1	3,702,955	2,333,137
NLS-2	934,869	688,151
Other projects	801,641	1,892,044
Total	10,869,642	11,586,923

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.

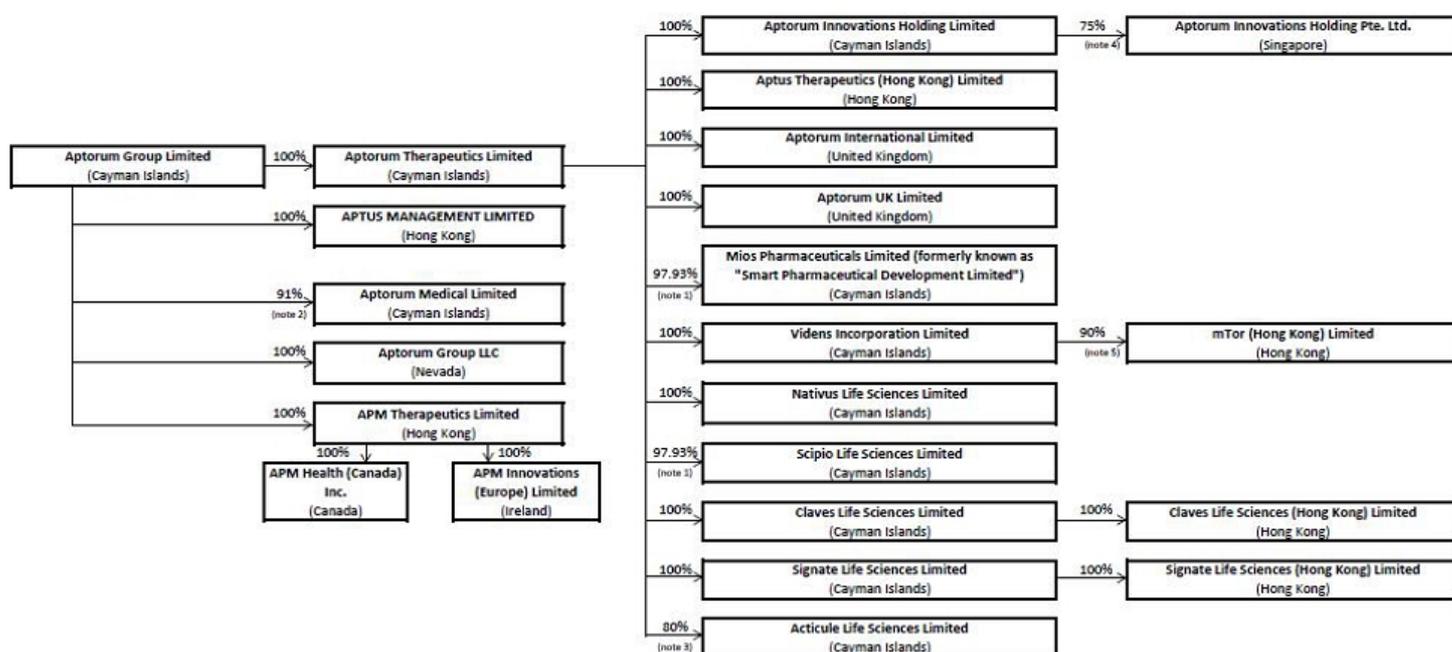
Very truly yours,

/s/ Darren Lui

Darren Lui

Chief Executive Officer

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



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 Mios, and 1.92% economic interest and 0.22% voting power in Scipio respectively.”

Note 2: Dr. Clark Cheng, an Executive Director of Aptom Group, holds the remaining 9% shareholding of Aptom 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 Aptom Innovations Holding Pte. Ltd.. The inventors of RPIDD technologies in A*STAR hold the remaining 15% of shareholding of Aptom Innovations Holding Pte. Ltd.

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