

October 5, 2018

**VIA EDGAR**

Keira Nakada  
U.S. Securities and Exchange Commission  
Division of Corporation Finance  
Office of Consumer Products  
100 F Street, N.E.  
Mail Stop 4631  
Washington, DC 20549

**Re: Aptorum Group Limited  
Registration Statement on Form F-1  
September 5, 2018  
File No. 333-227198**

Dear Ms. Nakada:

Aptorum Group Limited (the “**Company**,” “**Aptorum**,” “**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 September 20, 2018 regarding our Registration Statement on Form F-1 (the “**Registration Statement**”) previously submitted on September 5, 2018. For ease of reference, we have repeated the Commission’s comments in this response and numbered them accordingly. An amended F-1 submitted publicly accompanying this Response Letter is referred to as Form F-1.

Please note that new language we are including in Form F-1 pursuant to your comments, is indicated in this letter in **bold, italicized** font; any deletions from the initial Registration Statement are indicated in this letter as ~~strike through~~ font.

**Registration Statement on Form F-1 filed September 5, 2018**

**Cover page**

1. We note your response to comment 1, which we reissue in part. You continue to reference a minimum and maximum dollar amount of offered securities. Please amend your prospectus cover page to state the volume of securities being offered on a minimum and maximum offering basis. Refer to Item 501(b)(2) of Regulation S-K.

**Response:** In response to the Staff’s comment, we updated the information on the prospectus cover page to state the volume of securities being offered on a minimum and maximum offering basis.

2. Please expand your revisions in response to prior comment 3 to disclose what the selling shareholders’ fixed price will be. If it will be the same as the primary offering price, please revise to so state.

**Response:** In response to the Staff’s comment, we disclosed that the selling shareholders’ fixed price is equal to the Offering Price until the Class A Ordinary Shares are listed on NASDAQ and thereafter, the Selling Shareholders will be able to sell their Class A Ordinary Shares at prevailing market prices or privately negotiated prices.

## Prospectus Summary

### Aptorum's Lead Projects

#### ALS-1: Small molecule intended for the treatment of viral infections caused by Influenza virus A, page 3

3. We note your response to comment 10 and your revised disclosure stating your belief that “it is unlikely that ALS-1 will experience the resistance developed by the viruses against the existing anti-viral therapy.” As you have not yet conducted any clinical studies, it is premature for you imply that ALS-1 will be effective. Please remove this statement. Similarly, please remove the disclosure on page 4 stating your belief that ALS-4 is “less likely to be susceptible to antibiotic resistance.”

**Response:** Pursuant to the Staff’s comment, we removed the noted language.

#### NLS-1: A Derivative of Epigallocatechin-3-Gallate (“Pro-EGCG”) for the treatment of Endometriosis, page 5

4. We note your response to comment 11, which we reissue in part. Please remove your conclusion that studies of EGCG for the treatment of endometriosis have produced “encouraging results.” Additionally, please move the discussion of p-values observed to the Business section and expand your disclosure to explain how p-values are used to measure statistical significance and how they relate to the U.S. Food and Drug Administration’s evidentiary standards of efficacy. Additionally, please revise your discussion of preclinical studies of NLS-1 stating that it “prevents the progression of fibrosis” and “reduced lesion size significantly better than EGCG and other hormone-based therapy” to remove these conclusions regarding the efficacy of NLS-1. We will not object to a discussion of objective data points in the Business section.

**Response:** In response to the Staff’s comment, we removed and revised the noted language. With regards to p-values, we added the following section to the Business section of the amendment:

P. 82

#### ***“Statistical Significance***

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

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

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

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

**Capitalization, page 54**

5. We reissue our prior comment 18 since it does not appear that you have revised your capitalization table.

**Response:** In response to the Staff’s comment, we revised our capitalization table to include a column reflecting our capitalization on a pro forma basis to give effect to the issuance of 22,437,754 Class A Ordinary Shares issuable upon conversion of the Class B Ordinary Shares.

The revised capitalization section is provided below for your convenience.

“The following table presents our capitalization as of June 30, 2018:

- on an actual basis (**column 1**);
- on a pro forma basis, to give effect to the issuance of **22,437,754** Class A Ordinary Shares issuable upon conversion of the Class B Ordinary Shares; (See “Transactions with Related Persons”) (**column 2**); and
- on a pro forma as-adjusted basis, to give effect and the issuance of **1,290,323** Class A Ordinary Shares in this Offering and the issuance of **234,648** Class A Ordinary Shares<sup>1</sup> as a result of the automatic conversion of the Notes issued in the Series A Note Offering, each at an assumed price to the public of **\$15.5** per share, the midpoint of the price range set forth on the cover page of this prospectus after deducting underwriting discounts and commissions and estimated offering expenses, and the issuance of **125,681** Class A Ordinary Shares as a result of the automatic partial conversion of the Bond (**columns 3 and 4**).

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<sup>1</sup> Pursuant to the terms of the Note, no fractional shares or securities shall be issued upon conversion of the Note; in lieu thereof, the Company shall pay an amount equal to the product obtained by multiplying the applicable Conversion Price in such conversion, by the fraction of a share or such other security not issued pursuant to the previous sentence. Accordingly, full conversion of the Notes would result in the issuance of an aggregate of 234,648 Class A Ordinary Shares and \$100.64, based on a conversion price of \$6.82 per share.

This table should be read in conjunction with “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our financial statements, consolidated financial statements and related notes included elsewhere in this prospectus.

	<b>June 30, 2018</b>			
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>
			<b>As adjusted (Minimum offering amount)</b>	<b>As adjusted (Maximum offering amount)</b>
	<b>Actual</b>	<b>Pro Forma</b>	<b>US\$</b>	<b>US\$</b>
<b>Equity</b>				
Class A Ordinary Shares	5,426,381	27,864,135	28,869,625	30,159,948
Class B Ordinary Shares	22,437,754	-	-	-
Additional paid-in capital <sup>(1)</sup>	5,346,129	5,346,129	16,440,941	33,150,618
Accumulated other comprehensive loss	(545,642)	(545,642)	(545,642)	(545,642)
Accumulated deficit	(8,035,834)	(8,035,834)	(8,035,834)	(8,035,834)
Non-controlling interests	(113,341)	(113,341)	(113,341)	(113,341)
<b>Total equity</b>	<b>24,515,447</b>	<b>24,515,447</b>	<b>36,615,749</b>	<b>54,615,749</b>
<b>Total capitalization</b>	<b>24,515,447</b>	<b>24,515,447</b>	<b>36,615,749</b>	<b>54,615,749</b>

- (1) Pro forma additional paid-in capital reflects the net proceeds we expect to receive, after deducting underwriting fee, underwriters expense allowance and other expenses. We expect to receive net proceeds of (a) approximately **\$9,000,000** if minimum offering is raised or (b) approximately **\$27,000,000** if maximum offering is raised).

The information above is illustrative only and our capitalization following the completion of this Offering and the Series A Note Offering will be adjusted based on the actual initial public offering price and other terms of this Offering determined at pricing.

A \$1.00 increase (decrease) in the assumed initial public offering price of **\$15.5** per Class A Ordinary Share, the midpoint of the estimated price range shown on the cover page of this prospectus, would increase (decrease) the amount of cash and cash equivalents, additional paid-in capital, total (deficit) equity and total capitalization on a pro forma as adjusted basis by approximately **\$1.16 million**, assuming the number of Class A Ordinary Shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase (decrease) of **100,000** Class A Ordinary Shares offered by us would increase (decrease) cash and cash equivalents, total (deficit) equity and total capitalization on a pro forma as adjusted basis by approximately **\$1.40** million, assuming the assumed initial public offering price remains the same, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

## Business

### Lead Projects

#### ALS-1: Small molecule intended for the treatment of viral infections caused by Influenza virus A, page 70

6. We note your response to comment 22. Please expand your disclosure to briefly explain EC50. Additionally, please remove your conclusion that the “animal study results strongly suggest that ALS-1 protected mice against hypervirulent influenza A H5N1 virus in vivo.” Please also expand your disclosure on page 72 to briefly explain IC50.

**Response:** We revised the disclosure in the Amendment as per the Staff’s comment. In addition to removing the noted language, we included the following regarding IC<sub>50</sub> on the pages noted; reference to EC<sub>50</sub> was a typo and reference to same has been revised to IC<sub>50</sub>.

Page 73:

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

Page 75:

“In a recent publication by the inventor, Prof. Richard Kao, in mBio (8(5): e01224, 2017), ALS-4 demonstrates potent activity against Staphylococcus aureus pigment formation in vitro, as indicated in Figure 2A, with an IC<sub>50</sub> ~~equal to 300 nM (Figure 2B)~~. (**IC<sub>50</sub> is defined as the concentration of a drug which inhibits half of the maximal response of a biochemical process. In this case, inhibition of the formation of the golden pigment is the response**) equal to 300 nM (Figure 2B). In addition, ALS-4 exhibits low cytotoxicity in MDCK, Vero, A549, Huh-7, or 293T cells, with 50% toxic concentrations higher than 500  $\mu\text{M}$ .”

#### Patent License, page 71

7. We note your response to comment 24, which we reissue in part as it does not appear that you have disclosed the aggregate regulatory development and aggregate sales milestones payable under the license agreement. Please revise here and make similar revisions concerning the license agreement related to each of ALS-4 discussed on page 74 and NLS-1 discussed on page 79.

**Response:** In response to the Staff’s comment, we disclosed the aggregate regulatory development and aggregate sales milestones payable under the license agreements. Examples of this disclosure are as follows:

We updated the Contingent Payment Obligations section within MD&A (P. 65):

“Contingent Payment Obligations:

We have entered into agreements with unrelated parties for purchasing office and laboratory equipment. As of June 30, 2018, we had non-cancellable purchase commitments of \$358,099.

The Company has additional contingency payment obligations under each of the license agreements, such as milestone payments, royalties, research and development funding, if certain condition or milestone is met.

*Milestone payments are to be made upon achievements of certain conditions, such as Investigational New Drugs (“IND”) filing or U.S. Food and Drug Administration (“FDA”) approval, first commercial sale of the licensed products, or other achievements. The aggregate amount of the milestone payments that the Company are required to pay up to different achievements of conditions and milestones for all the license agreements signed as of June 30, 2018 are below:*

	<u>Amount</u>
<i>Drug molecules: up to the conditions and milestones of</i>	
<i>Preclinical to IND filing</i>	\$ 372,564
<i>From entering phase 1 to before first commercial sale</i>	24,216,410
<i>First commercial sale</i>	15,656,410
<i>Net sales amount more than certain threshold in a year</i>	75,769,231
<i>Subtotal</i>	<u>116,014,615</u>
<i>Surgical robotics and medical devices: up to the conditions and milestones of</i>	-
<i>Before FDA approval</i>	300,000
<i>FDA approval obtained</i>	200,000
<i>Subtotal</i>	<u>500,000</u>
<i>Total</i>	<u>\$116,514,615</u>

For the period January 1, 2018 through June 30, 2018 and period March 1, 2017 through December 31, 2017, the Company did not owe any milestone payments, royalties or research and development funding. As of June 30, 2018, no milestone payments had been triggered under any of the existing license agreements.”

Additionally, we revised disclosure regarding the milestone payments included in the respective Patent License section for each of the three Lead Projects in the Business section as follows:

ALS-1 (P. 74)

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

ALS-4 (P. 77)

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

NLS-1 (P. 81)

~~“We paid an upfront fee upon entering into the license agreement and are obligated to pay certain milestone payments as the product achieves specified regulatory, clinical and commercial/sale milestone, as applicable, as set forth in the license agreement.”~~

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

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

Notes to Consolidated Financial Statements (Successor Basis)

14. Summary of Significant Accounting Policies

Intangible Assets, page F-37

8. Refer to your response to comment 36. We believe that the aggregate amount of the milestone obligations and the description of the events that would trigger these milestones are significant terms of an agreement that should be disclosed. Please revise your disclosures accordingly.

**Response:** We reviewed the Staff's comment and believe we updated the disclosure in the Amendment accordingly. We respectfully direct the Staff's attention to our response to Comment 7 above and also note that we made similar disclosure in Note 30 to the Consolidated Financial Statements (Successor Basis) for the period March 1, 2017 through December 31, 2017 and in Note 18 to the Condensed Consolidated Financial Statements for the interim period ended June 30, 2018. We believe that these revisions respond to the concerns raised in this Comment 8.

We thank the Staff for your review of the foregoing. If you have further comments, we ask that you forward them by electronic mail to our counsel, Louis Taubman at [ltaubman@htflawyers.com](mailto:ltaubman@htflawyers.com) or by telephone at (917) 512-0827.

Very truly yours,

/s/ Ian Huen

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Ian Huen

CEO

cc: Louis Taubman  
Hunter Taubman Fischer & Li LLC