Biotron Limited
A.B.N. 60 086 399 144

Level 2, 66 Hunter Street
Sydney NSW 2000
Tel: (61-2) 9300 3344
Fax: (61-2) 9221 6333
E-mail: pnightingale@biotron.com.au
Website: www.biotron.com.au

29 October 2018

Ms Isabella Wong
Adviser, Listings Compliance
ASX Limited
20 Bridge Street
SYDNEY NSW 2000

(6 pages by email)

Dear Ms Wong

I refer to your letter dated 25 October 2018 and provide the following responses:

1. Did BIT set benchmarks to determine the success rate of the Phase 2 Trial?

   Yes.

   [NOTE – ***We define "benchmark" as a clinical trial objective when forming the answers to these questions. In some other situations, not relevant here, benchmark evaluation for HIV-1 antiviral trials generally refers to the use of a standard result as a point of evaluating the performance of a new antiviral agent. BIT225-009 trial was designed to measure the antiviral efficacy and safety of a BIT225. Its mode of action is the inhibition of HIV-1 replication primarily in a subset of HIV-1 infected cells called macrophages. This is a novel target where no benchmark antiviral agent has been investigated previously. This study was an exploratory study with multiple Objectives and end points measured.***
   For the purpose of responding to these questions, we are using the words benchmark and objectives interchangeably.]

2. If the answer to question 1 is "yes", please state (i) the end points to the benchmarks; (ii) whether the end points were reached; (iii) provision of the data to demonstrate these benchmarks were reached; and (iv) an explanation as to why this information was not disclosed in the Announcement.

   The BIT225-009 Phase 2 clinical trial was designed to assess the safety and antiviral activity of three month's dosing of BIT225 in combination with antiretroviral drugs in treatment-naïve HIV-positive subjects. This was a double-blind, placebo-controlled study undertaken at trial sites in Thailand. A total of 27 HIV-infected subjects, who had not previously taken any antiretroviral drugs, took once daily doses of 200 mg BIT225 or placebo for 12 weeks in combination with antiretroviral drugs. At the end of 12 weeks, all continued to take antiretroviral drugs as per standard protocols. A smaller cohort of 9 subjects took once daily doses of 100 mg BIT225 or placebo; this cohort was set up for detailed pharmacokinetic profiling of the BIT225 and its interactions with antiretroviral drugs.

   The BIT225-009 study has previously disclosed the Primary and Secondary Objectives as outline in the announcement to the ASX: "Commencement of BIT225 Phase 2 HIV-1 Clinical Trial" lodged 9.36 am on 13 February 2017.

   As set out in that 13 February 2017 announcement, the aim of this Phase 2 trial was to demonstrate:

   - ***Accelerated reduction of HIV-1 in patients treated with BIT225 in combination with cART, indicating that BIT225 can significantly improve current standard of care anti- HIV-1 treatment; and***

- ***Reduction in HIV-1-induced immune activation, indicating that BIT225 is targeting viral reservoirs not impacted by cART.***

The Objectives and outcomes are set out below. Due to the exploratory design of the trial, BIT had multiple endpoints for each objective and to date some of the data is still being evaluated.

Primary Objectives:

- ***Determine the efficacy of 12 weeks of BIT225 treatment in HIV-1 infected subjects receiving cART: Atripla® [Tenofovir disoproxil fumarate (TDF) / emtricitabine (FTC) / efavirenz (EFV)] by measuring plasma viral load decay and modelling HIV-1 decay.***

This primary objective was designed to investigate a virologic effect. This virologic approach involved measuring plasma viral load decay i.e. blood levels of HIV-1. Two different methods were used to investigate this objective. The first was measurement of cell-free virus in the blood (known as plasma viral load). The second was measurement of cell-associated virus in specific cell populations isolated from the blood.

As disclosed in the announcement of 28 September 2018, no differences were noted in the levels of cell-free virus (plasma viral load) in the blood. This result was expected because of the effectiveness of current ART, which all trial participants were taking. Plasma viral load was rapidly reduced to undetectable levels in all subjects.

The second component of this virological analysis, i.e. measurement of cell-associated virus in specific cell populations, is ongoing. This is a very sensitive method compared to measurement of free virus in the blood and may provide additional virologic information on relative differences in HIV-1 decay in different blood cell populations.

- ***Determine the safety and tolerability of BIT225 QD administered for 12 weeks in HIV-1 infected subjects on cART: Atripla® [Tenofovir disoproxil fumarate (TDF) / emtricitabine (FTC) / efavirenz (EFV)].***

As set out in the 28 September 2018 announcement, preliminary analysis of the safety data has shown that BIT225 was well tolerated at the 200mg once daily dose, with no severe adverse events or withdrawals.

Secondary Objectives:

- ***Determine if 12 weeks of BIT225 treatment in addition to cART: Atripla® [Tenofovir disoproxil fumarate (TDF) / emtricitabine (FTC) / efavirenz (EFV)] will impact levels of sCD163, a primary biomarker of monocyte immune activation.***

Assessment of the immunologic effect was the subject of this Objective.

Results were obtained, as specified in the trial protocol, by analysing the change from baseline data of plasma levels of sCD163 by ELISA assay, comparing the time-course trends in patients treated with ART+BIT225 or ART+Placebo. The data from the BIT225 200mg and placebo cohorts were compared by ANOVA using R statistical software by fitting a generalised model. The estimate indicates a statistically larger overall decrease in sCD163 for the BIT225 treated group compared to placebo cohort.

sCD163 is a primary biomarker specific for monocyte and macrophage immune activation. sCD163 is shed by these cells during activation and is measurable by ELISA assay in blood plasma samples. sCD163 is elevated in subjects with chronic HIV-1 infection and, during ART, plasma levels of sCD163 decrease in parallel with declining HIV-1 RNA. However, even in patients with well-controlled viral loads, the marker remains elevated (~500 ng/ml) compared to healthy normal subjects (>1 ng/ml), reflecting a level of ongoing immune activation. This marker is strongly correlated with macrophage-mediated pathogenesis and is also a better predictor than T-cell activation markers of all-cause morbidity and mortality in HIV-1 patients who are on successful suppressive anti-retroviral therapy. In these patients, immune activation and inflammation are known to persist despite ART viral control. (Knudsen, T.B., et al., Plasma Soluble CD163 Level Independently Predicts All-Cause Mortality in HIV-1-Infected Individuals. J Infect Dis, 2016. 214(8): p. 1198-204.)

sCD163 plasma level is a good indicator of all cause morbidity and mortality in HIV-1 patients with well-controlled viral load. Additional reduction of this marker in patients taking BIT225 demonstrates significant immunological benefit.

To further understand the mechanism of action of BIT225 in patients, beyond its effects on sCD163 plasma concentration, additional immunologic studies were performed on patient samples (as per the trial protocol). This involved flow cytometry of cells isolated from blood samples. Cell populations included total T cells, $CD8^+$ T-cells, activated $CD8^+$ T-cells, $CD4^+$ T-cells, activated $CD4^+$ T-cells. The results showed statistically significant differences in the profiles of two specific T-cell populations during the BIT225 treatment period. These reflect the significant differences in immunological responses in patients receiving 200 mg BIT225 with ART compared to placebo with ART. This was reported in the 28 September 2018 announcement as "…changes to the immune cells that fight disease."

The data, detailed analyses and graphs from the sCD163 and the flow cytometric analyses have not been released to the market, as they remain trade secrets and subject to strict confidentiality (and hence within Listing Rule 3.1A.1) until presented at upcoming scientific conference(s) in the USA in late 2018/2019. Details of the date, time and location of presentation(s) will be released to the market when they are available, and the presentation(s) will be released to the market immediately after being presented.

- ***Evaluate the pharmacokinetics of 100 mg BIT225 QD administered for 12 weeks in combination with cART: Atripla® in subjects infected with HIV-1.***

Results relating to the pharmacokinetics (PK) Objective have not been released as analyses are ongoing, confidential and incomplete. Summary outcomes will be released when these are complete. Details of a drug's PK profile are not generally put into the public domain but are disclosed in regulatory filings under confidentiality provisions.

This has been a complex trial, with associated complex post-trial analyses, in keeping with the unique mode of action of BIT225 against HIV-1 in reservoir cells.

The announcement of 28 September 2018 was primarily to inform the market of key outcomes from the trial. It was not designed to be a full disclosure of all trial data.

3. If the answer to question 1 is "no", please advise why not.

N/A.

4. The Announcement states: *"The data shows that there are significant immunological benefits in patients receiving antiretroviral drugs with 200 mg BIT225 compared to antiretroviral drugs plus placebo.*

Please explain how BIT has measured these significant benefits in patients and provide the supporting material to demonstrate this conclusion.

See Q2 above.

5. The Announcement states: *"In previously reported laboratory-based studies, Biotron has shown that BIT225 attacks HIV-1 growing in macrophage cells, resulting in the production of replication-incompetent virus i.e. non-infectious, dead virus. The data from the current BIT225-009 clinical trial reported here shows that the body's immune system recognises this dead virus, which triggers a range of changes to the immune cells that fight disease."*

Did BIT release the clinical data in a previous ASX announcement in relation to the *"previously reported laboratory-based studies"*? If 'yes', when was the announcement released on MAP? If 'no', please explain why not?

Yes.

Please note that this statement refers to laboratory-based studies (as stated), and not to clinical trial data.

BIT225's targeting of HIV-1 in macrophage cells, based on laboratory-based studies, has been well documented and shared with the market in many forms over several years. This information is included in all Biotron investor presentations and has been shared with the international scientific community through international conference presentations and publication in peer-reviewed scientific journals (list available on the Company website www.biotron.com.au). The targeting of HIV-1 in macrophage cells by Biotron compound BIT009 was first advised in an announcement on 23 May 2002. Subsequent to that finding, the Company designed and developed a follow-on drug, BIT225, that had suitable properties for selection as a lead for clinical trials (8 Sept 2005). Scientific papers on laboratory-based HIV-1 studies were published in 2010 and 2016.

6. The Announcement states: *"In addition to the beneficial immunological effects, there was a significant reduction in the level of the macrophage activation marker sCD163 in the BIT225-treated population by the end of the treatment period."*

   Please provide a description of how this significant reduction was assessed and the supporting material which confirms this significant reduction.

   See Q2 above.

7. The Announcement states: *"The headline results indicate that BIT225 has had a profound effect on a source of virus that persists in the presence of antiretroviral drugs."*

   Please provide an explanation of what is meant by profound effect, and in relation to which source of virus.

   In this instance profound means significant. This is based on the information provided in the responses Q2 above.

   BIT225 works by interfering with the assembly of HIV-1 in macrophage cells (previously disclosed, as discussed in Q2 above). The outcome is the production of replication-deficient ie. non-infectious virus by these reservoir cells. The immunological changes seen in trial subjects receiving ART + BIT225 treatment (described in responses to Q2) are consistent with the body's immune system recognising this replication-incompetent virus as a source of antigen. This immunological response is not seen in trial subjects who did not take BIT225 (i.e. took ART + placebo).

   The goal of many immune stimulation-based interventions such as vaccines has been to boost specific T cell responses and the consequent downstream concert approach of the immune system to eliminate viral products including viral load. The addition of BIT225 was found to induce immunological changes, as measured by flow cytometry (see Q2 above). This is consistent with a release of a new antigen source such as replicative incompetent virus from macrophages. These results demonstrate that BIT225 has a unique mechanism of action compared to marketed ART.

8. The Announcement states: *"When we designed this trial, we set up a range of different outcomes to look at. Some of the markers we set out to measure haven't shown any differences, while others have shown very significant changes – and these changes clearly indicate that BIT225 is having a unique and significant effect in these subjects."*

   Please describe all of the markers BIT set out to measure, which ones have not shown any differences; which ones have shown significant differences; and a description of the unique and significant effect shown by the subjects; and provision of the supporting material that supports these comments.

   See Q2 above.

9. The Announcement states: *"One aspect we set out to measure was whether the addition of BIT225 could improve clearance of HIV-1 from the blood. Current antiretroviral drugs are extremely efficient at rapidly clearing this virus, and the study confirms this. It was not surprising that no additional discernible reductions in blood virus levels were seen with BIT225, but it was important to measure this. But we saw other significant differences that clearly show BIT225 is doing something new and different to these current antiretroviral drugs."*

Please explain what BIT means by "*But we saw other significant differences that clearly show BIT225 is doing something new and different to these current antiretroviral drugs."*

See Q2 above.

10. The Announcement states: *"Analysis of the trial data is ongoing. The Company aims to present detailed data at scientific conferences and to potential commercial partners in late 2018/early 2019."*

(a) When does BIT expect the analysis of the trial data will be complete?

Samples from the trial will be subject to ongoing analyses to further characterise the demonstrated immunological effect of BIT225 in these patients. This is likely to take several months and take the form of post-BIT225-009 lab-based studies as part of the Company's ongoing R&D. However, these analyses are not expected to alter the positive findings from the trial, as reported on 28 September 2018. And as reported on 28 September, the data generated to date is expected to be presented at scientific conferences and to potential partners in late 2018/early 2019. Further results will be reported as part of the Company's standard disclosure policies.

(b) Will BIT be releasing a further announcement to the market when the trial data is complete? If 'yes', when? if 'no', please explain why not.

Yes.

The Company will make further announcements on the ongoing analyses of trial samples in accordance with Listing Rules.

(c) Will the trial data be subject to peer review? If 'yes', when and by who? If not please explain why not.

Yes.

As disclosed in the 28 September 2018 announcement, Biotron expects to present trial data at scientific conferences in late 2018/early 2019. Abstracts are subject to review before acceptance for presentation at scientific conferences. Typically, presentation at such meetings precedes peer-reviewed scientific journal submissions. The Company intends to share the data with the scientific community via publication in peer-reviewed scientific journal(s). The Company cannot set an exact timeline for such publications at this stage.

(d) Will the trial data be subject to regulatory review? If 'yes', when and by who? If not please explain why not.

Yes.

As the trial was conducted at two clinical trial sites in Thailand, the trial results are subject to regulatory review by the Thai FDA. The reporting requirement consists of the submission of an annual report on the development of the clinical trial research to the Thai FDA. This review is primarily focused on safety aspects of the trial.

The data from this trial may be included in future regulatory filing for BIT225 with the TGA, US FDA or other regulatory agencies and will be subject to additional review at that time.

11. Please describe the background and identity of the third party as disclosed in the Progress Announcement, who developed the assay and carried out the tests to demonstrate the potential impact of BIT225 on HIV- 1 virus level.

The cell-associated viral load assay has been developed by scientists at a well-known and well-regarded Sydney-based hospital. Their identity cannot be disclosed due to commercial-in-confidence provisions which necessary to protect the commercial interests of the hospitals and the privacy of the patients in the trial. The Company's directors do not consider the identity to be of any sensitivity to the Company's share price.

12. Please describe the background and identity of the independent HIV immunologist as disclosed in the Progress Announcement.

Professor Robert Murphy, MD from Northwestern University in Chicago, who has been a long-term consultant to the Company, had medical oversight of trial. The Company's directors do not consider the identity HIV immunologist, who was recommended for immunological review of the trial data by Professor Robert Murphy, to be of any sensitivity to the Company's share price

13. As outlined in the Code, please provide a statement regarding the implications of the trial results for the further development and potential sale of the product being tested, and indicate whether a further clinical trial or trials is necessary or planned.

The Phase 2 trial data has indicated that BIT225 has significant and unique effects on immunologic endpoints. This is encouraging and could lead to a role of BIT225 as part of a cure strategy. Further clinical trials will be required, either by the Company or a potential partner, to demonstrate and further characterise a clinical impact on viral eradication. As previously announced, Biotron will be seeking a partner to support future clinical trial evaluations.

14. Please confirm that BIT is complying with the Listing Rules and, in particular, Listing Rule 3.1.

Yes, the Company is complying with the Listing Rules, and in particular, Listing Rule 3.1.

15. Please confirm that BIT's responses to the questions above have been authorised and approved in accordance with its published continuous disclosure policy or otherwise by its board or an officer of BIT with delegated authority from the board to respond to ASX on disclosure matters.

We confirm that the Company's responses to the questions above have been so authorised and approved.

Yours sincerely

Peter J. Nightingale
Company Secretary

pjn9654

25 October 2018

Mr Peter Nightingale
Company Secretary
Biotron Limited
Level 2 66 Hunter Street
Sydney NSW 2000

By email:

Dear Mr Nightingale

Biotron Limited ('BIT'): Aware Query

ASX refers to the following:

A. BIT's announcement entitled *"Significant Immunological Outcomes in BIT225 HIV-1 Clinical Trial"* lodged on the ASX Market Announcements Platform ("MAP") and released at 4:00 PM on 28 September 2018 (the 'Announcement'), disclosing results of the Phase 2 trial of its lead drug BIT225 in HIV-infected patients in combination with current antiretroviral drugs.

B. The increase in the price of BIT's securities after the release of the Announcement from a closing price on 27 September 2018 of $0.02 to a closing price on 28 September 2018 of $0.041, a 105% increase. We also note the significant increase in the volume of BIT's securities traded on 28 September 2018.

C. BIT's announcement entitled *"Update on Progress of BIT225 Phase 2 HIV-1 Clinical Trial"* lodged on MAP and released at 10:02 am on 7 August 2018 (the "Progress Announcement"), disclosing that:

"…work is being done by a third party that has developed the assay and is completely independent from Biotron"

"Data from the key component of the trial have been compiled, and are being reviewed by an independent, internationally renowned HIV immunologist based in Europe"

D. BIT's announcement entitled *"Commencement of BIT225 Phase 2 HIV-1 Clinical Trial"* lodge on MAP and released at 9:36 am on 13 February 2017 (the "Clinical Trial Commencement Announcement"), disclosing that:

"The primary objectives of the study are to:

- *Determine the efficacy of 12 weeks of BIT225 treatment in HIV-1 infected subjects receiving cART: Atripla® by measuring plasma viral load decay and modelling HIV-1 decay.*

- *Determine the safety and tolerability of BIT225 administered once daily for 12 weeks in HIV-1 infected subjects on cART: Atripla®.*

The secondary objectives of this study are to:

- *Determine if 12 weeks of BIT225 treatment in addition to cART: Atripla® will impact levels of sCD163, a primary biomarker of monocyte immune activation.*

- *Evaluate the pharmacokinetics of 100 mg BIT225 administered once daily for 12 weeks in combination with cART:Atripla® in subjects infected with HIV-1.*

The Company is aiming to demonstrate:

- *Accelerated reduction of HIV-1 in patients treated with BIT225 in combination with cART, indicating that BIT225 can significantly improve current standard of care anti-HIV-1 treatment; and*

- *Reduction in HIV-1-induced immune activation, indicating that BIT225 is targeting viral reservoirs not impacted by cART."*

E. The second edition of the *Code of Best Practice for Reporting by Life Science Companies (*the "Code"), which states the following in relation to the reporting of clinical trial results.

"Reporting of results of clinical trials should be made regardless of whether the outcome is positive or negative, and should be clear and unambiguous, specifically addressing the endpoints announced at the commencement of the trial. There should be a clear statement regarding the implications of the trial results for the further development and potential sale of the product being tested. Companies should indicate whether a further clinical trial or trials is necessary or planned.

In meeting these requirements for disclosure, companies need to keep in mind the concerns of regulatory agencies regarding interpretation of results before they have been subjected to regulatory review. For example, companies need to be aware of the need to be consistent with the US Food and Drug Administration (FDA) guidance for media releases.

The Code recognises the importance of peer review in the validation process and acknowledges that in some circumstances disclosure of results before peer review (through publication in a medical journal, presentation at a scientific meeting or otherwise) may be premature."

The Code expects companies reporting results of clinical trials will provide the information as outlined on page 11 of the Code. A copy of the Code can be found at the following link on the ASX website.

https://www.asx.com.au/documents/research/Code_of_Best_Practice_for_Reporting_by_Life_Science_Companies.pdf

F. Listing Rule 3.1, which requires a listed entity to immediately give ASX any information concerning it that a reasonable person would expect to have a material effect on the price or value of the entity's securities.

G. The definition of "aware" in Chapter 19 of the Listing Rules, which states that:

"an entity becomes aware of information if, and as soon as, an officer of the entity (or, in the case of a trust, an officer of the responsible entity) has, or ought reasonably to have, come into possession of the information in the course of the performance of their duties as an officer of that entity" and section 4.4 in Guidance Note 8 Continuous Disclosure: Listing Rules 3.1 – 3.1B "When does an entity become aware of information."

H. Listing Rule 3.1A, which sets out exceptions from the requirement to make immediate disclosure, provided that each of the following are satisfied.

"3.1A Listing rule 3.1 does not apply to particular information while each of the following is satisfied in relation to the information:

3.1A.1 One or more of the following applies:

- *It would be a breach of a law to disclose the information;*
- *The information concerns an incomplete proposal or negotiation;*
- *The information comprises matters of supposition or is insufficiently definite to warrant disclosure;*
- *The information is generated for the internal management purposes of the entity; or*
- *The information is a trade secret; and*

3.1A.2 The information is confidential and ASX has not formed the view that the information has ceased to be confidential; and

3.1A.3 A reasonable person would not expect the information to be disclosed."

I. ASX's policy position on the concept of "confidentiality", which is detailed in section 5.8 of Guidance Note 8 *Continuous Disclosure*: Listing Rules 3.1 – 3.1B. In particular, the Guidance Note states that:

"Whether information has the quality of being confidential is a question of fact, not one of the intention or desire of the listed entity. Accordingly, even though an entity may consider information to be confidential and its disclosure to be a breach of confidence, if it is in fact disclosed by those who know it, then it ceases to be confidential information for the purposes of this rule."

Request for Information

Having regard to the above, ASX asks BIT to respond separately to each of the following questions and requests for information:

1. Did BIT set benchmarks to determine the success rate of the Phase 2 Trial?

2. If the answer to question 2 is "yes", please state (i) the end points to the benchmarks; (ii) whether the end points were reached; (iii) provision of the data to demonstrate these benchmarks were reached; and (iv) an explanation as to why this information was not disclosed in the Announcement.

3. If the answer to question 2 is "no", please advise why not.

4. The Announcement states: *"The data shows that there are significant immunological benefits in patients receiving antiretroviral drugs with 200 mg BIT225 compared to antiretroviral drugs plus placebo."*

Please explain how BIT has measured these significant benefits in patients and provide the supporting material to demonstrate this conclusion.

5. The Announcement states: *"In previously reported laboratory-based studies, Biotron has shown that BIT225 attacks HIV-1 growing in macrophage cells, resulting in the production of replication-incompetent virus i.e. non-infectious, dead virus. The data from the current BIT225-009 clinical trial reported here shows that the body's immune system recognises this dead virus, which triggers a range of changes to the immune cells that fight disease."*

   Did BIT release the clinical data in a previous ASX announcement in relation to the *"previously reported laboratory-based studies"*? If 'yes', when was the announcement released on MAP? If 'no', please explain why not?

6. The Announcement states: *"In addition to the beneficial immunological effects, there was a significant reduction in the level of the macrophage activation marker sCD163 in the BIT225-treated population by the end of the treatment period."*

   Please provide a description of how this significant reduction was assessed and the supporting material which confirms this significant reduction.

7. The Announcement states: *"The headline results indicate that BIT225 has had a profound effect on a source of virus that persists in the presence of antiretroviral drugs."*

   Please provide an explanation of what is meant by profound effect, and in relation to which source of virus.

8. The Announcement states: *"When we designed this trial, we set up a range of different outcomes to look at. Some of the markers we set out to measure haven't shown any differences, while others have shown very significant changes – and these changes clearly indicate that BIT225 is having a unique and significant effect in these subjects."*

   Please describe all of the markers BIT set out to measure, which ones have not shown any differences; which ones have shown significant differences; and a description of the unique and significant effect shown by the subjects; and provision of the supporting material that supports these comments.

9. The Announcement states: *"One aspect we set out to measure was whether the addition of BIT225 could improve clearance of HIV-1 from the blood. Current antiretroviral drugs are extremely efficient at rapidly clearing this virus, and the study confirms this. It was not surprising that no additional discernable reductions in blood virus levels were seen with BIT225, but it was important to measure this. But we saw other significant differences that clearly show BIT225 is doing something new and different to these current antiretroviral drugs."*

   Please explain what BIT means by "*But we saw other significant differences that clearly show BIT225 is doing something new and different to these current antiretroviral drugs."*

10. The Announcement states: *"Analysis of the trial data is ongoing. The Company aims to present detailed data at scientific conferences and to potential commercial partners in late 2018/early 2019."*

    (a) When does BIT expect the analysis of the trial data will be complete?

(b) Will BIT be releasing a further announcement to the market when the trial data is complete? If 'yes', when? if 'no', please explain why not.

(c) Will the trial data be subject to peer review? If 'yes', when and by who? If not please explain why not.

(d) Will the trial data be subject to regulatory review? If 'yes', when and by who? If not please explain why not.

11. Please describe the background and identity of the third party as disclosed in the Progress Announcement, who developed the assay and carried out the tests to demonstrate the potential impact of BIT225 on HIV-1 virus level.

12. Please describe the background and identity of the independent HIV immunologist as disclosed in the Progress Announcement.

13. As outlined in the Code, please provide a statement regarding the implications of the trial results for the further development and potential sale of the product being tested, and indicate whether a further clinical trial or trials is necessary or planned.

14. Please confirm that BIT is complying with the Listing Rules and, in particular, Listing Rule 3.1.

15. Please confirm that BIT's responses to the questions above have been authorised and approved in accordance with its published continuous disclosure policy or otherwise by its board or an officer of BIT with delegated authority from the board to respond to ASX on disclosure matters.

When and where to send your response

This request is made under Listing Rule 18.7. Your response is required as soon as reasonably possible and, in any event, by no later than 4:00 PM AEDT on Monday, 29 October 2018.

If we do not have your response by then, ASX will have no choice but to consider suspending trading in BIT's securities under Listing Rule 17.3. You should note that if the information requested by this letter is information required to be given to ASX under Listing Rule 3.1 and it does not fall within the exceptions mentioned in Listing Rule 3.1A, BIT's obligation is to disclose the information "immediately". This may require the information to be disclosed before the deadline set out in the previous paragraph.

ASX reserves the right to release a copy of this letter and your response on the ASX Market Announcements Platform under Listing Rule 18.7A. Accordingly, your response should be in a form suitable for release to the market. Your response should be sent to me by e-mail at **ListingsComplianceSydney@asx.com.au**. It should not be sent directly to the ASX Market Announcements Office. This is to allow me to review your response to confirm that it is in a form appropriate for release to the market, before it is published on the ASX Market Announcements Platform.

Listing Rules 3.1 and 3.1A

Listing Rule 3.1 requires a listed entity to give ASX immediately any information concerning it that a reasonable person would expect to have a material effect on the price or value of the entity's securities. Exceptions to this

requirement are set out in Listing Rule 3.1A. In responding to this letter, you should have regard to BIT's obligations under Listing Rules 3.1 and 3.1A and also to Guidance Note *8 Continuous Disclosure: Listing Rules 3.1 – 3.1B*. It should be noted that BIT's obligation to disclose information under Listing Rule 3.1 is not confined to, nor is it necessarily satisfied by, answering the questions set out in this letter.

Trading halt

If you are unable to respond to this letter by the time specified above, you should discuss with us whether it is appropriate to request a trading halt in BIT's securities under Listing Rule 17.1. If you wish a trading halt, you must tell us:

- the reasons for the trading halt;
- how long you want the trading halt to last;
- the event you expect to happen that will end the trading halt;
- that you are not aware of any reason why the trading halt should not be granted; and
- any other information necessary to inform the market about the trading halt, or that we ask for.

We require the request for a trading halt to be in writing. The trading halt cannot extend past the commencement of normal trading on the second day after the day on which it is granted.

You can find further information about trading halts in Guidance Note 16 Trading Halts & Voluntary Suspensions.

Suspension

If you are unable to respond to this letter by the time specified above ASX will likely suspend trading in BIT's securities under Listing Rule 17.3.

Enquiries

If you have any queries or concerns about any of the above, please contact me immediately.

Yours sincerely

Isabella Wong

Adviser, Listings Compliance (Sydney)