



19 February 2024

Ms Lisa Bahn  
Senior Adviser, ASX Listings Compliance (Sydney)  
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Exchange Centre  
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By email: [ListingsComplianceSydney@asx.com.au](mailto:ListingsComplianceSydney@asx.com.au)

Dear Lisa

## **AWARE QUERY**

We refer to the Aware Query from the ASX dated 16 February 2024 and respond as follows:

**1. Please outline:**

**1.1 when ACW became aware of the information; and**

*The Company first became aware of the information at 11.54 am AEDT on 15 February 2024*

**1.2 the circumstances under which ACW became aware of the information.**

*The Company was notified of the UK MHRA's decision by email from a regulatory agent based in the UK with an attached pdf letter of approval dated February 14, 2024*

**2. Does ACW consider the information to be information that a reasonable person would expect to have a material effect on the price of value of its securities?**

Yes.

**3. If the answer to question 2 is "no", please:**

*Not applicable. The answer to question 2 is Yes.*

**3.1 explain the basis for that view;**

**3.2 provide the Listing Rule or Corporations Act basis necessitating the disclosure of the information on MAP (as paragraph H);**

**3.3 explain why ACW indicated that the Announcement was 'market sensitive' when it was lodged on MAP; and**

**3.4 explain how ACW is of the view that it complied with ASX's guidance on 'ramping announcements' (see paragraph G).**

**4. If the answer to question 2 is "yes", please:**

**4.1 explain the basis for that view;**

*The UK Innovation Passport approval is a material form of validation for the Xanamem program in Alzheimer's disease, akin to the "Breakthrough" designation sometimes awarded by the FDA.*

**4.2 explain whether ACW is of the view that the information was kept confidential prior to its release, note the significant increase in the price of ACW securities; and;**

*The information was communicated to the market by ASX announcement less than 2 hours after receipt. Only the "need to know" group of the CEO, Head of Communications, Company Secretary, Regulatory associate and a small number of others knew of the award in the two hours prior to the ASX announcement.*

**4.3 explain the basis for ACW's view that it complied with Listing Rule 3.1 with respect to the information, including the steps taken by ACW to ensure that the information was released promptly and without delay.**

*See the answer to 4.2.*

**5. Does ACW have any other explanation for the increase in the price of its securities prior to the publication of the announcement on MAP?**

*Yes. Firstly, we note that the increase in share price on the day of the announcement only occurred after the announcement at approximately 2pm, increasing from 2:25 pm. Previously, the Company made a series of announcements over the period 24 January to 15 February. Notably, the non-price sensitive ASX announcement of 24 January advising that a peer reviewed manuscript of a PET brain scan study had been published in a medical journal led to an increase in share price and volume from a base of approximately 2.7 cents (the announcement was deemed non-price sensitive because the same data had previously been presented multiple times in external corporate presentations over more than two years). Subsequently, a notice on 9 February regarding the issue of 18 million restricted long term incentive shares issued to our new CFO, William Souter, appears to have triggered gradual price and volume increases from 3 cents to 4.3 cents on 14 February.*

**6. Please confirm that ACW is complying with the Listing Rules and, in particular, listing rule 3.1.**

*We confirm that the Company is in compliance with the Listing Rules and, in particular, Listing Rule 3.1.*

**7. Please confirm that ACW'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 the Company with delegated authority from the board to respond to the ASX on disclosure matters.**

*Confirmed.*

Yours sincerely



Peter Webse  
Company Secretary

## ENDS

### Investors

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***Authorised by the Board of Directors of Actinogen Medical***

### About Actinogen Medical

Actinogen Medical (ACW) is an ASX-listed, biotechnology company developing a novel therapy for neurological and neuropsychiatric diseases associated with dysregulated brain cortisol. There is a strong association between cortisol and detrimental changes in the brain, affecting cognitive function, harm to brain cells and long-term cognitive health.

Cognitive function means how a person understands, remembers and thinks clearly. Cognitive functions include memory, attention, reasoning, awareness and decision-making.

Actinogen is currently developing its lead compound, Xanamem, as a promising new therapy for Alzheimer's Disease and Depression and hopes to study Fragile X Syndrome and other neurological and psychiatric diseases in the future. Reducing cortisol inside brain cells could have a positive impact in these and many other diseases. The cognitive dysfunction, behavioural abnormalities, and neuropsychological burden associated with these conditions is debilitating for patients, and there is a substantial unmet medical need for new and improved treatments.

### Current and Upcoming Clinical Trials

The **XanaCIDD Phase 2a depression trial** is a double-blind, six-week proof-of-concept, placebo-controlled, parallel group design trial in 160 patients. Patients are evenly randomized to receive Xanamem 10 mg once daily or placebo, in some cases in addition to their existing antidepressant therapy, and effects on cognition and depression are assessed.

The **XanaMIA Phase 2b Alzheimer's disease trial** is a double-blind, 36-week treatment, placebo-controlled, parallel group design trial in 220 patients with mild to moderate AD and progressive disease, determined by clinical criteria and confirmed by an elevated level of the pTau181 protein biomarker in blood. Patients receive Xanamem 10 mg or placebo, once daily, and effects on cognition, function and progression of Alzheimer's disease are assessed. Thus, Xanamem is being assessed in this trial for its potential effects as both a cognitive enhancer and a disease course modifier.

### About Xanamem

Xanamem's novel mechanism of action is to block the production of cortisol inside cells through the inhibition of the 11 $\beta$ -HSD1 enzyme in the brain. Xanamem is designed to get into the brain after it is absorbed in the intestines upon swallowing.

Chronically elevated cortisol is associated with cognitive decline in Alzheimer's Disease and excess cortisol is known to be toxic to brain cells. Cognitive impairment is also a feature in Depression and many other diseases. Cortisol itself is also associated with depressive symptoms and when targeted via other mechanisms has shown some promise in prior clinical trials.

The Company has studied 11 $\beta$ -HSD1 inhibition by Xanamem in more than 300 volunteers and patients, so far finding a statistically significant improvement in working memory and attention, compared with placebo, in healthy, older volunteers in two consecutive trials and clinically significant improvements in functional and cognitive ability in patients with biomarker-positive mild AD. Previously, high levels of target engagement in the brain with doses as low as 5 mg daily have been demonstrated in a human PET imaging study. A series of Phase 2 studies in multiple diseases is being conducted to further confirm and characterize Xanamem's therapeutic potential.

Xanamem is an investigational product and is not approved for use outside of a clinical trial by the FDA or by any global regulatory authority. Xanamem® is a trademark of Actinogen Medical.

#### **Disclaimer**

This announcement and attachments may contain certain "forward-looking statements" that are not historical facts; are based on subjective estimates, assumptions and qualifications; and relate to circumstances and events that have not taken place and may not take place. Such forward looking statements should be considered "at-risk statements" - not to be relied upon as they are subject to known and unknown risks, uncertainties and other factors (such as significant business, economic and competitive uncertainties / contingencies and regulatory and clinical development risks, future outcomes and uncertainties) that may lead to actual results being materially different from any forward looking statement or the performance expressed or implied by such forward looking statements. You are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof. Actinogen Medical does not undertake any obligation to revise such statements to reflect events or any change in circumstances arising after the date hereof, or to reflect the occurrence of or non-occurrence of any future events. Past performance is not a reliable indicator of future performance. Actinogen Medical does not make any guarantee, representation or warranty as to the likelihood of achievement or reasonableness of any forward-looking statements and there can be no assurance or guarantee that any forward-looking statements will be realised.

**ACTINOGEN MEDICAL ENCOURAGES ALL CURRENT INVESTORS TO GO PAPERLESS BY REGISTERING THEIR DETAILS WITH THE DESIGNATED REGISTRY SERVICE PROVIDER, AUTOMIC GROUP.**



16 February 2024

Reference: 88788

Mr Peter Webse  
Company Secretary  
Actinogen Medical Limited

By email:

Dear Mr Webse

**Actinogen Medical Limited ('ACW'): Aware Query**

ASX refers to the following:

- A. ACW's announcement titled "Actinogen awarded UK Innovation Passport for Xanamem" lodged on the ASX Market Announcements Platform ('MAP') on 15 February 2024 (the 'Announcement'), which disclosed that approval had been granted by the UK Medicines and Healthcare products Regulatory Agency ('MHRA') in relation to ACW's application for an Innovation Passport as part of the ILAP for Xanamem in the treatment of Alzheimer's disease. ('Information').

ASX notes the announcement was indicated by ACW to be 'market-sensitive' when it was lodged on MAP.

- B. The increase in the price of ACW's securities in the trading sessions prior to the publication of the Announcement on MAP. Specifically, ASX notes the 38.7% increase from the closing price of \$0.031 on 9 February 2024 to \$0.043 on 14 February 2024.
- C. 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.
- D. 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."*
- E. 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.”
- F. 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.”*
- G. Section 7.10 of Guidance Note 8, which states (relevantly):
- “ASX is alive to listed entities making market announcements with a view to “ramping up” the price of their securities. Ramping announcements come in many forms, including:*
- *the release of a “business update” or something similar, which will typically be worded in an exuberant fashion but which on closer examination contains little in the way of substance that has not already been disclosed to the market;”*
- ...
- “Whenever ASX detects what it suspects to be a ramping announcement, it will give careful consideration to suspending the entity’s securities from trading and issuing a query letter to the entity asking the entity:*
- *if it marked the announcement as market sensitive when it was lodged on MAP, to identify what information in the announcement the entity considered was market sensitive and why;”*
- H. Section 14 of Guidance Note 14, which states (relevantly):
- “MAP should only be used to publish information that is appropriately given to ASX under the Listing Rules or the Corporations Act for publication to the market. It should not be used as a guise to publish material that is really promotional, political or tendentious in nature.”*

### Request for information

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

1. Please outline:
  - 1.1 when ACW became aware of the Information; and
  - 1.2 the circumstances under which ACW became aware of the Information.
2. Does ACW consider the Information to be information that a reasonable person would expect to have a material effect on the price or value of its securities?
3. If the answer to question 2 is “no”, please:
  - 3.1 explain the basis for that view;

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- 3.2 provide the Listing Rule or Corporations Act basis necessitating the disclosure of the Information on MAP (as per paragraph H);
  - 3.3 explain why ACW indicated that the Announcement was 'market-sensitive' when it was lodged on MAP; and
  - 3.4 explain how ACW is of the view that it complied with ASX's guidance on 'ramping announcements' (see paragraph G)
4. If the answer to question 2 is "yes", please:
    - 4.1 explain the basis for that view;
    - 4.2 explain whether is ACW of the view that the Information was kept confidential prior to its release, noting the significant increase in the price of ACW's securities; and
    - 4.3 explain the basis for ACW's view that it complied with Listing Rule 3.1 with respect to the Information, including the steps taken by ACW to ensure the Information was released promptly and without delay.
  5. Does ACW have any other explanation for the increase in the price of its securities prior to the publication of the Announcement on MAP?
  6. Please confirm that ACW is complying with the Listing Rules and, in particular, Listing Rule 3.1.
  7. Please confirm that ACW'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 ACW 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 **9.30 AM AEDT Tuesday, 13 February 2024**. 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, ACW'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 and may require ACW to request a trading halt immediately.

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.

#### **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 ACW'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.

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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 ACW's securities under Listing Rule 17.3.

**Listing Rules 3.1 and 3.1A**

In responding to this letter, you should have regard to ACW'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 ACW'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.

**Release of correspondence between ASX and entity**

ASX reserves the right to release all or any part of this letter, your reply and any other related correspondence between us to the market under Listing Rule 18.7A.

Kind regards

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ASX Compliance