



Market Announcement

27 March 2020

Advance Nanotek Limited (ASX: ANO) – Continued Suspension from Official Quotation

ASX Limited ('ASX') refers to:

- ASX's market announcement dated 16 March 2020 that ANO's shares would be placed into trading halt, at the request of ANO, pending release of an announcement;
- ASX's market announcement dated 18 March 2020 that ANO's shares would be suspended, at the request of ANO under listing rule 17.2, pending release of an announcement;
- ASX's market announcement dated 19 March 2020 that ANO's shares would be suspended from quotation under listing rule 17.3 pending further enquiries by ASX;
- ANO's announcement dated 26 March 2020 headed "Business Update" which included a section entitled "Update on Suspension".

ASX considers it appropriate and in the interests of an informed market to provide an update on the suspension from official quotation of ANO's shares.

On 19 March 2020, ASX issued a query letter to ANO in relation to the announcement proposed to be released by ANO. ASX's query letter and ANO's response dated 19 March 2020 are attached to this market release for the benefit of the market.

On 19 March 2020, 20 March 2020 and 23 March 2020, ASX advised ANO and its advisers that its response to ASX's query letter were incomplete and unsatisfactory and that ANO's shares would remain in suspension until they provide proper responses to ASX's queries. ANO has not provided an updated response.

ASX has today issued ANO with a further query letter outlining the further information ANO is required to provide and advising that they will remain in suspension until satisfactory responses have been received and ASX otherwise considers it appropriate to reinstate ANO to quotation.

Issued by

Adrian Smythe
Manager, Listings Compliance (Sydney)

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19 March 2020

Reference: 15749

Mr Geoff Acton
Managing Director
Advance Nanotek Limited

By email:

Dear Mr Acton

Advance Nanotek Limited ('ANO'): query letter

ASX refers to:

- A. ANO's request for a trading halt ('Trading Halt Request'), received by ASX on 16 March 2020, attaching an announcement for release on the ASX market announcements platform ('MAP') which included the following statements regarding the reasons for the request:

*"Astivita Limited (ASX:AIR), a customer of ANO, brought to the attention of ANO a highly progressed opportunity regarding the development of oral care products (**New Products**), which could prevent the coronavirus cells multiplying. ANO have decided that it intends to file a patent application in respect of the New Products on Tuesday, 17 March 2020. Given the substantial involvement of AIR in bringing the New Products opportunity to ANO, both companies have agreed that arrangements need to be entered into between them regarding ownership of intellectual property in the New Products and/or commercial arrangements regarding commercialisation of the New Products (**IP Ownership**). The trading halt is needed to afford both companies the time to seek legal advice in respect of IP Ownership, as both boards have common directors."*

- B. ANO's announcement, released on MAP on 17 March 2020, titled "Clarification on Trading Halt Letter" ('17 March Announcement'), which included the following statements:

"ANO clarifies that there was a typo in the letter yesterday. The letter should have read:

'The patent is looking at a range of oral care products that could inhibit the replication of the novel coronavirus inside the cells of the oral cavity / mouth.'

Further, the IP lawyers have reviewed the patent and confirmed the novelty of the patent idea and are looking to finalise and file the patent today."

- C. ANO's request for its securities to be suspended from official quotation, received by ASX on 18 March 2020.

- D. ANO's draft announcement entitled 'Antiviral Composition for Oral Care Patent # 2020900820' lodged with ASX on 18 March 2020 ('Draft Announcement'), which included the following statement:

"we came across a potential antiviral solution on Saturday March 14, 2020 (Patent application attached). The work on this patent was started on Saturday March 14, 2020 and the Boards have agreed to a trading halt on Sunday morning. The initial sales are contemplated on the Amazon EU platform as no regulatory approvals are needed."

and which purported to attach a patent application ('Patent Application').

- E. ANO and Astavita Limited's ('AIR') common directors. Specifically:

- a. Geoff Acton;

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- b. Lev Mizikovsky; and
- c. Rade Dudurovic,

comprise all of AIR's directors, and three out of four of ANO's directors.

- F. The Appendix 3Y – Change of Director's Interest Notice, released by ANO on MAP on 19 March 2020, disclosing the acquisition by:
- a. Ankla Pty Ltd of 69,881 ordinary shares in ANO;
 - b. Rainrose Pty Ltd of 58,036 ordinary shares in ANO; and
 - c. Winothai Pty Ltd of 1,600 ordinary shares in ANO,
- representing the acquisition on 12 March 2020 of an indirect interest by Mr Mizikovsky in 129,517 ordinary shares in ANO for a total consideration of \$490,724.34.

Questions and requests for information

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

1. Please provide a full account and detailed timeline of how ANO came to be aware of the "highly progressed opportunity" referred to in the Trading Halt Request. In your answer, please address ANO's understanding regarding:
 - a. Who brought the opportunity to AIR and when?
 - b. Specific details of how "highly progressed" the opportunity was at the time it was presented to AIR, given the statement in the Draft Announcement that "*we came across a potential antiviral solution on Saturday March 14, 2020 ... The work on this patent was started on Saturday March 14, 2020*".
 - c. Why AIR, as a customer of ANO, considered it necessary or desirable to progress the opportunity in partnership with ANO rather than in its own right.
 - d. The basis for the statement in the Trading Halt Request that AIR's involvement in bringing the New Products opportunity to ANO was "substantial", again given the statement in the Draft Announcement that "*we came across a potential antiviral solution on Saturday March 14, 2020 ... The work on this patent was started on Saturday March 14, 2020*".
2. Who are the "IP lawyers" referred to in the 17 March Announcement?
3. Has the Patent Application been finalised and lodged with IP Australia? If so, by whom and when?
4. Who are the "current inventors" referred to in page 4 of the Patent Application?
5. Please outline in detail the evidence that ANO has that supports the statement on page 2 of the Patent Application:

"The composition of the present invention is expected to show anti-viral properties."
6. Please outline in detail the evidence that ANO has that supports the postulation on page 4 of the Patent Application:

"The present inventors have postulated that zinc ions derived from a zinc compound or a zinc salt inhibit the replication machinery of RNA viruses, and as such can help control illness and spread of the diseases."

7. Please outline in detail the evidence that ANO has that supports the statement in the Trading Halt Request that the New Products:

“could prevent the coronavirus cells multiplying.”

8. Please outline in detail the evidence that ANO has that supports the statement in the 17 March Announcement that the oral care products in question:

“could inhibit the replication of the novel coronavirus inside the cells of the oral cavity / mouth.”

9. Please explain why ANO is seeking to make the statements referred to in paragraphs 5 - 8 above now in relation to the New Products when according to the Draft Announcement:

“A standard organism feline coronavirus test of the product will be completed in approximately 3 weeks, by the UK based laboratory (MSL Solution Providers), at which stage ANO will confirm if the concept is successful against COVID-19.”

10. Please explain why ANO believes the information regarding its intention to file the Patent Application is information that a reasonable person would expect to have a material effect on the price or value of ANO’s securities, given a patent application confers no rights unless and until the patent is granted.¹

11. Please provide a copy of the advice received from the IP lawyers and referred to in the 17 March Announcement confirming the novelty of the patent idea (not for release to the market).

12. Please advise whether ANO has received any legal advice regarding the statement in the Draft Announcement that: *“The initial sales are contemplated on the Amazon EU platform as no regulatory approvals are needed.”* If it has, please provide a copy of the advice (not for release to the market). If it has not, please explain its basis for making this statement.

13. Please advise whether the products which are the subject of the Patent Application have been the subject of any clinical or other trials for their effectiveness in inhibiting Covid-19, and if so:

- a. the nature of the trial; and
- b. its outcome.

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 9:00 am AEST on Monday, 23 March 2020.

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, ANO’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 MAP 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. It should not be sent directly to the ASX Market Announcements Office. This is to allow

¹ “The fact that a patent application has been filed is seldom material, it is generally only after grant that a patent right becomes a material asset, which should be disclosed”: Code of Best Practice for Reporting by Life Sciences Companies (second edition), published May 2013, page 16 https://www.asx.com.au/documents/research/Code_of_Best_Practice_for_Reporting_by_Life_Science_Companies.pdf

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me to review your response to confirm that it is in a form appropriate for release to the market, before it is published on MAP.

Enquiries

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

Yours sincerely

Lauren Osbich
Adviser, Listings Compliance (Sydney)



19 March 2020

Response to ASX Query Letter

A copy of the ASX Query Letter is included with this release.

The Company response to each of the queries in the order of the ASX query letter is as follows:

- 1a. The CEO of Astivita Limited ("AIR") as part of his mandate to develop new personal care products.
- 1b. As per previous ASX releases for AIR the company continues to develop personal care products.
- 1c. AIR lacks the laboratories and technical capabilities to pursue the opportunity identified by the AIR CEO. Advance NanoTek Limited ("ANO") has both the laboratories and the technical capabilities to execute on this opportunity.
- 1d. On Saturday, 14 March 2020 the ANO and AIR team identified an agent capable of delivering zinc into the Virus.
2. Gary Nock.
3. Yes, by Gary Nock on Tuesday 17 March 2020 application number 2020900820 ("Patent Application").
4. Refer to the Patent Application emailed to ASX officers on Wednesday, 18 March 2020.
5. Refer to the research and patents listed in the Patent Application.
6. Refer to the research and patents listed in the Patent Application.
7. Typo was fixed and released in the subsequent ASX release.
8. Refer to the research and patents listed in the Patent Application.
9. This is commonly used test as referred to in the ASX release by ZNO.
10. This information is considered market sensitive by the Board due to the current health crisis.
11. Gary Nock confirmed the novelty of the Patent Application during a telephone call to Geoff Acton.
12. No.
13. Refer to the research and patents listed in the Patent Application.

Most of the above information was already in the releases available to the ASX. The balance of information sort by the ASX is in the opinion of the Board is not material.

Authorised by:
Geoff Acton (B.Com CA)
Managing Director

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TITLE

Antiviral composition for oral care

TECHNICAL FIELD

[0001] The present invention relates to the field of anti-viral products for the oral cavity. Specifically, it relates to an anti-viral composition which can be widely used in oral care products for the prevention and treatment of viral infections.

BACKGROUND ART

[0001] Viral infections of the oral mucosa (lining of the oral cavity) are commonly encountered in general practice. In addition to viruses which specifically infect the oral mucosa, such as the herpes simplex virus, many common respiratory viruses, such as the influenza virus, also infect the oral mucosa during their pathogenesis. The replication and release of respiratory viruses in the oral cavity contributes both to their pathogenesis and their contagion.

[0002] Despite the importance of the oral cavity in the pathogenesis and contagion of respiratory viruses, there are very few anti-viral products for the treatment of the oral mucosa available. Existing anti-viral products are only suitable to target localized infections, such as cold sores caused by the herpes simplex virus. Moreover, the anti-viral products are often specific to the condition – i.e. will only function for the herpes simplex virus. Finally, they may only be used after an infection has developed.

[0003] Therefore, a need exists in the field for a composition to be widely used in oral care products with broad anti-viral properties. There further exists a need for a composition that could be utilized preventatively, in addition to in response to an infection. In this niche, the composition must be safe for frequent and continuous use, with minimal risks and side-effects.

[0004] It will be clearly understood that, if a prior art publication is referred to herein, this reference does not constitute an admission that the publication forms part of the common general knowledge in the art in Australia or in any other country.

SUMMARY OF INVENTION

[0005] In one aspect, the present invention provides a composition for use in oral care comprising at least one zinc compound or at least one zinc salt and hinokitiol or a salt thereof.

[0006] In one embodiment, the composition contains at least one zinc compound, or at least one zinc salt, or two or more zinc compounds and/or zinc salts.

[0007] In one embodiment, the at least one zinc compound or at least one zinc salt may be selected from one or more of zinc chloride, zinc oxide, zinc myristate, zinc citrate, zinc nitrate, or zinc sulfate, zinc chlorate, zinc phosphate, zinc molybdate, zinc chromate, zinc bromide and zinc iodide. Other zinc salts that are non-toxic may also be used. The zinc salts may be inorganic salts or organic salts.

[0008] In one embodiment, the composition comprises a therapeutically effective amount of at least one zinc compound or at least one zinc salt and hinokitiol. In one embodiment, the weight ratio of the zinc compound and/or zinc salt and the hinokitiol and salts thereof is within the range of 3:1 to 1:10.

[0009] The composition of the present invention is expected to show anti-viral properties. The composition of the present invention is suitable for use in oral care products, such as, but not limited to, mouth rinse, toothpaste, gargling solutions and mouth wash. In other embodiments, the composition may comprise a throat lozenge or a nasal spray or a topical oral mucosa treatment composition or a topical nasal mucosa treatment or an inhaler or a puffer or a treatment for the oro-pharynx. Products containing this composition may be used continuously and frequently, for the prevention and treatment of viral infections.

[0010] The composition takes advantage of the combinatorial effect of zinc ions, released from zinc compounds or from a zinc salt when dissolved, and hinokitiol, which promotes the uptake of zinc ions into cells.

[0011] Any therapeutically acceptable salt of hinokitiol or any pharmaceutically acceptable salt of hinokitiol may be used in the present invention. However, preferred embodiments may use hinokitiol. The IUPAC name of hinokitiol is 2-Hydroxy-6-propan-2-ylcyclohepta-2,4,6-trien-1-one.

[0012] In a second aspect, the present invention provides use of at least one zinc compound or at least one zinc salt and hinokitiol in the preparation of a medicament composition for treating viral infections. The medicament composition may comprise an oral care composition.

[0013] In a third aspect, the present invention provides a method for treating a viral infection by treating a patient with a composition as described reference to the first aspect of the present invention. The composition may comprise an oral care composition and the patient may use the

oral care composition by taking it into the mouth. In one embodiment, the oral care composition may be gargled, or used as a toothpaste or a mouthwash and subsequently spat out.

[0014] Any of the features described herein can be combined in any combination with any one or more of the other features described herein within the scope of the invention.

[0015] The reference to any prior art in this specification is not, and should not be taken as an acknowledgement or any form of suggestion that the prior art forms part of the common general knowledge.

BRIEF DESCRIPTION OF DRAWINGS

[0016] Various embodiments of the invention will be described with reference to the following drawings, in which:

[0017] Figure 1 depicts an illustration of the infection and replication process of an RNA virus, such as that of influenza. Zinc ions interact with the processing of viral polyproteins and the RNA dependent RNA polymerase (RdRp), inhibiting the replication of the viral genome and proteins. However, zinc ions are normally unable to pass through the membrane, due to possessing a charge. Hinokitiol promotes the uptake of zinc ions into cells through an uncharacterized mechanism, enabling maximal effect.

DESCRIPTION OF EMBODIMENTS

[0018] The terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting of the invention. As used herein, the term “and/or” includes any and all combinations of one or more of the associated listed items. As used herein, the singular forms “a”, “an”, and “the” are intended to include the plural forms as well as singular forms, unless the context clearly indicates otherwise. It will be further understood that the terms “comprises” and/or “comprising”, when used in this specification, specify the presence of stated features, steps, operations, elements, and/or components, but do not preclude the presence or addition of one or more other features, steps, operations, elements, components, and/or groups thereof.

[0019] Unless otherwise defined, all terms (including technical and scientific terms) used herein have the same meaning as commonly understood by one having ordinary skill in the art to which the invention belongs. It will be further understood that terms, such as those defined in commonly used dictionaries, should be interpreted as having a meaning that is consistent with

their meaning in the context of the relevant art and the present disclosure and will not be interpreted in an idealized or overly formal sense unless expressly so defined herein.

[0020] In describing the invention, it will be understood that a number of techniques and steps are disclosed. Each of these has individual benefit and each can also be used in conjunction with one or more, or in some cases all, of the other disclosed techniques. Accordingly, for the sake of clarity, this description will refrain from repeating every possible combination of the individual steps in an unnecessary fashion. Nevertheless, the specifications and claims should be read with the understanding that such combinations are entirely within the scope of the invention and claims.

[0021] The present disclosure is to be considered as an exemplification of the invention, and is not intended to limit the invention to the specific embodiments illustrated by the figures or description below.

[0022] The present invention will now be described. The composition is comprised of hinokitiol and a zinc salt or zinc compounds, including but not limited to zinc chloride, zinc oxide, zinc nitrate, zinc chlorate, zinc sulfate, zinc phosphate, zinc molybdate and zinc chromate. Other zinc compounds or zinc salts may also be used. Two or more zinc compounds or zinc salts may be used. This composition may be used as an anti-viral active agent in oral care formulations. The proportions of hinokitiol and zinc are not limited, but are especially preferable in a ratio of hinokitiol to zinc of 1:3 to 10:1.

[0023] The anti-viral action of the zinc salt and hinokitiol composition occurs through multiple mechanisms of action. The present inventors have postulated that zinc ions derived from a zinc compound or a zinc salt inhibit the replication machinery of RNA viruses, and as such can help control illness and spread of the diseases. Hinokitiol strongly promotes the transport of zinc into cells, making this mode of action more effective. Common RNA viruses include the influenza, which affects at least 9 million people a year. Another RNA virus is the COVID-19, the coronavirus which has currently caused a pandemic. COVID-19 is very similar to the virus which caused severe acute respiratory syndrome (SARS). It was found that the SARS virus entered and replicated inside the oral mucosa, and then was released into saliva, facilitating its spread. A similar process has been predicted to occur with COVID-19.

[0024] Viral infection of the oral mucosa (the lining of the oral cavity) is a common feature of many respiratory viruses that is central to pathogenesis and spread. Despite this, few anti-viral oral hygiene products exist. The present invention in some embodiments is a composition of a

zinc salt and hinokitiol to be used as an anti-viral agent in oral care products. The composition is extremely low risk for adverse effects and irritation, and as such can be used continuously and frequently as both a preventative measure and a treatment. Oral care products in which this composition may be used include, but are not limited to toothpaste, mouth rinse and gargling solution. The composition inhibits viral replication in the oral cavity through interacting with the replication machinery of the viruses.

[0025] In the present specification and claims (if any), the word ‘comprising’ and its derivatives including ‘comprises’ and ‘comprise’ include each of the stated integers but does not exclude the inclusion of one or more further integers.

[0026] Reference throughout this specification to ‘one embodiment’ or ‘an embodiment’ means that a particular feature, structure, or characteristic described in connection with the embodiment is included in at least one embodiment of the present invention. Thus, the appearance of the phrases ‘in one embodiment’ or ‘in an embodiment’ in various places throughout this specification are not necessarily all referring to the same embodiment. Furthermore, the particular features, structures, or characteristics may be combined in any suitable manner in one or more combinations.

[0027] In compliance with the statute, the invention has been described in language more or less specific to structural or methodical features. It is to be understood that the invention is not limited to specific features shown or described since the means herein described comprises preferred forms of putting the invention into effect. The invention is, therefore, claimed in any of its forms or modifications within the proper scope of the appended claims (if any) appropriately interpreted by those skilled in the art.

CITATION LIST

PATENT LITERATURE

Otsu, Yoshiro, Yaeno Arima, and Yoriko Nakai. 1997. "Antibacterial and Antifungal Activity Method, Therapeutic Method of Infectious Diseases and Preserving Method of Cosmetics." - US5696169A

Fukui, Atsuko and Takuya Nakatsubo. 2019. "Antiviral Agent and Throat Candy, Gargle, and Mouthwash Using the Same." - JP2019077617A

Dong, Liang, Steven Espinal, Patrick Wong, and Paul Magruder. 2007. "Antiviral Medication." - ES2236012T3

NON PATENT LITERATURE

Krenn, B. M. et al. 2009. "Antiviral Activity of the Zinc Ionophores Pyrithione and Hinokitiol against Picornavirus Infections." *Journal of Virology* 83(1):58–64.

Te Velthuis, Aartjan J. W. et al. 2010. "Zn²⁺ Inhibits Coronavirus and Arterivirus RNA Polymerase Activity in Vitro and Zinc Ionophores Block the Replication of These Viruses in Cell Culture." *PLoS Pathogens* 6(11):1–10.

Wang, Wei Kung et al. 2004. "Detection of SARS-Associated Coronavirus in Throat Wash and Saliva in Early Diagnosis." *Emerging Infectious Diseases* 10(7):1213–19

Xu, Hao et al. 2020. "High Expression of ACE2 Receptor of 2019-NCoV on the Epithelial Cells of Oral Mucosa." *International Journal of Oral Science* 12(1 PG-8):8. Retrieved (<https://doi.org/10.1038/s41368-020-0074-x> NS -).

CLAIMS

1. A composition for use in oral care comprising at least one zinc compound or at least one zinc salt and hinokitiol or a salt thereof.
2. A composition as claimed in claim 1 wherein the composition contains at least one zinc compound, or at least one zinc salt, or two or more zinc compounds and/or zinc salts.
3. A composition as claimed in claim 1 or claim 2 wherein the at least one zinc compound or at least one zinc salt is selected from one or more of zinc chloride, zinc oxide, zinc myristate, zinc citrate, zinc nitrate, or zinc sulfate, zinc chlorate, zinc phosphate, zinc molybdate and zinc chromate.
4. A composition as claimed in any one of the preceding claims wherein the composition comprises a therapeutically effective amount of at least one zinc compound or at least one zinc salt and hinokitiol.
5. A composition as claimed in any one of the preceding claims wherein the weight ratio of the zinc compound and/or zinc salt and the hinokitiol or salts thereof is within the range of 3:1 to 1:10.
6. A composition as claimed in any one of the preceding claims wherein the composition comprises a mouth rinse, toothpaste, a gargling solution or a mouth wash.
7. Use of at least one zinc compound or at least one zinc salt and hinokitiol or a salt thereof in the preparation of a medicament composition for treating viral infections.
8. Use as claimed in claim 7 wherein the medicament composition comprises an oral care composition.
9. A method for treating a viral infection by treating a patient with a composition as claimed in any one of claims 1 to 6.
10. A method as claimed in claim 9 wherein the composition comprises an oral care composition and the patient uses the oral care composition by taking it into the mouth.
11. A method as claimed in claim 10 wherein the oral care composition is gargled, or used as a toothpaste or a mouthwash and subsequently spat out.
12. A method as claimed in claim 9 wherein the composition comprises a throat lozenge or a

nasal spray.

13. A method as claimed in any one of claims 9 to 12 wherein the composition is used continuously or frequently, for the prevention and treatment of viral infections.

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ABSTRACT

Viral infection of the oral mucosa (the lining of the oral cavity) is a common feature of many respiratory viruses that is central to pathogenesis and spread. Despite this, few anti-viral oral hygiene products exist. The present invention is a composition of a zinc salt and hinokitiol to be used as an anti-viral agent in oral care products. The composition is extremely low risk for adverse effects and irritation, and as such can be used continuously and frequently as both a preventative measure and a treatment. Oral care products in which this composition may be used include, but are not limited to toothpaste, mouth rinse and gargling solution. The composition inhibits viral replication in the oral cavity through interacting with the replication machinery of the viruses.

DRAWINGS

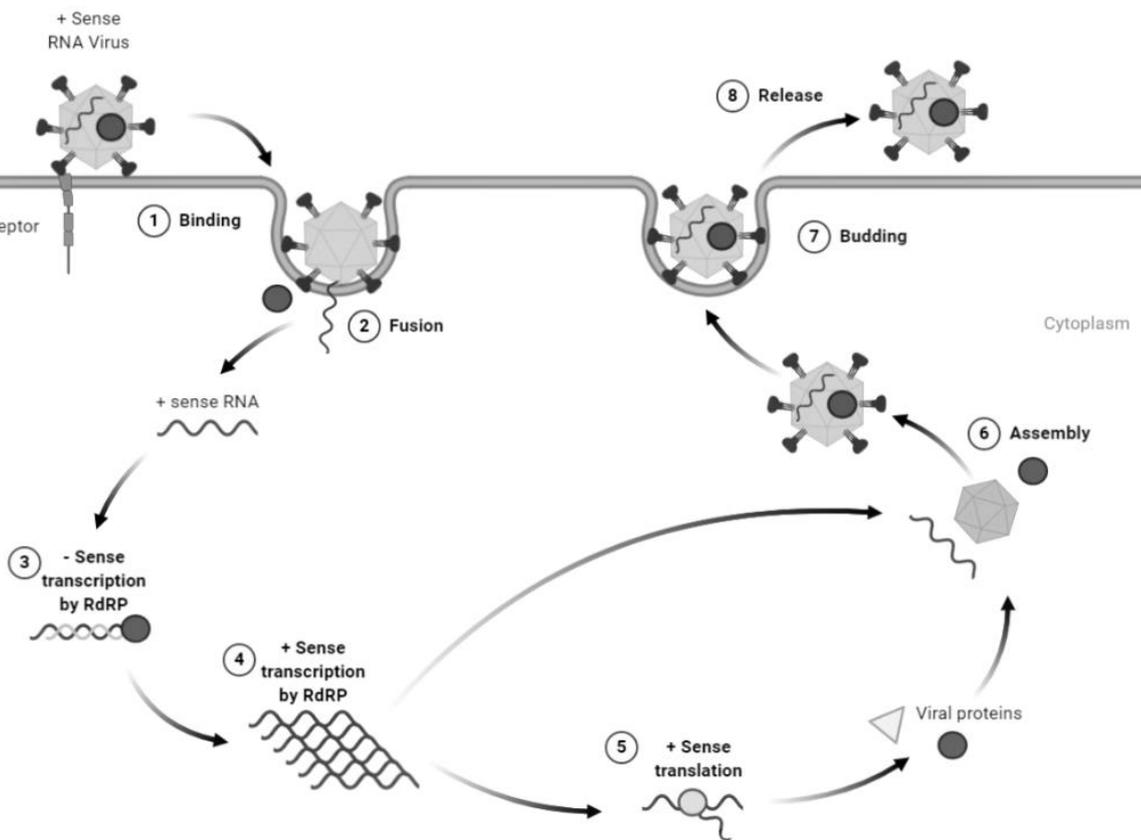


FIGURE 1