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2 May 2022

The Manager Companies
ASX Limited
20 Bridge Street
SYDNEY NSW 2000 (6 pages by email)

Dear Madam

BIT225 EFFECTIVE AGAINST ESTABLISHED SARS-CoV-2 IN ANIMALS

The Directors are pleased to advise that the Company's lead clinical drug, BIT225, has demonstrated effective protection from severe disease in mice with established SARS-CoV-2 infection in a new animal study performed at The SCRIPPS Research Institute, La Jolla, CA, USA.

- **In a significant step forward, new data shows that BIT225 protects from severe disease even when started once there is an established infection.**
- **Mice commencing treatment with BIT225 after infection with SARS-CoV-2 had similar levels of protection against severe disease as mice commencing treatment with BIT225 prior to infection.**
- **The results are important as they provide key information that will assist in determining the dosing regimen for BIT225 in planned human clinical studies.**
- **The results further extend the robust *in vivo* data package that shows statistically and clinically significant efficacy of BIT225 in both treatment and prevention in murine models of COVID-19.**

In previously reported studies (17 March 2022 and 25 November 2021), animals were dosed with BIT225 12 hours before infection with SARS-CoV-2. In this new study, the animals were infected with SARS-CoV-2 up to 48 hours before starting treatment with BIT225.

This is a more challenging model and creates a high hurdle to demonstrate efficacy of the drug.

In all studies, BIT225 was tested in a human-adapted COVID-19 mouse model (K18-hACE2) that is routinely used to assess the ability of drugs to target SARS-CoV-2 and treat COVID-19 disease.

The experimental details, set out in the Addendum below, show that BIT225 can both prevent and treat SARS-CoV-2 disease – necessary requirements for successful product development in this therapeutic area.

All BIT225 pre-dosed mice (n=5) and 24-hour post-dose mice (n=5) remained healthy and continued to gain weight as per age expectations through to Day 12 when the study was terminated. One of the five animals in the 48-hour post-dosing cohort died on Day 11 of the study. As in previous studies all vehicle-control mice showed an inexorable downward trend in body weight, and all control mice (n=5) died by Day 8 (Figure 1 below).

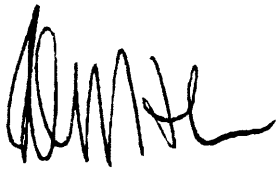
Group mean body weights of BIT225-treated mice throughout the studies (a reflection of COVID-19 disease) were statistically different to vehicle control mice throughout the study (Figure 2 below). While there appears to be a trend for less weight gain if initiation of BIT225 dosing is delayed, the trend lines are statistically the same regardless of whether drug treatment was initiated pre-infection or post-infection.

Biotron's Managing Director, Michelle Miller, said.

"The results from this new study are important as they show a clear clinical benefit for BIT225 regardless of time of commencement of treatment. We believe that BIT225's extended therapeutic protection window sets it apart from other approved or in-development agents and further strengthens our confidence in this valuable clinical asset."

In March 2022 the Company submitted a proposal to the USA Food and Drug Administration (FDA) to conduct a human clinical trial to assess the efficacy of BIT225 for the treatment of COVID-19 under the Coronavirus Treatment Acceleration Program, a special emergency program for potential coronavirus therapies. A response is expected shortly and, once received, the Company will be in a position to determine its capital requirements for the human clinical program funding which will be sought from potential partners and non-equity funding sources.

Yours sincerely



Peter J. Nightingale
Company Secretary

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About Biotron
Biotron Limited is engaged in the research, development, and commercialisation of drugs targeting significant viral diseases with unmet medical need. The Company has BIT225 in clinical development for HIV-1 and promising preclinical programs for SARS-CoV-2 and HBV. In addition, Biotron has several earlier stage programs designing drugs that target a class of virus protein known as viroporins which have a key role in the virus life cycle of a very broad range of viruses, many of which have caused worldwide health issues such as Coronavirus, Dengue, Ebola, Middle East Respiratory virus, Influenza and Zika viruses.

This announcement has been approved for release by the Company's Managing Director.

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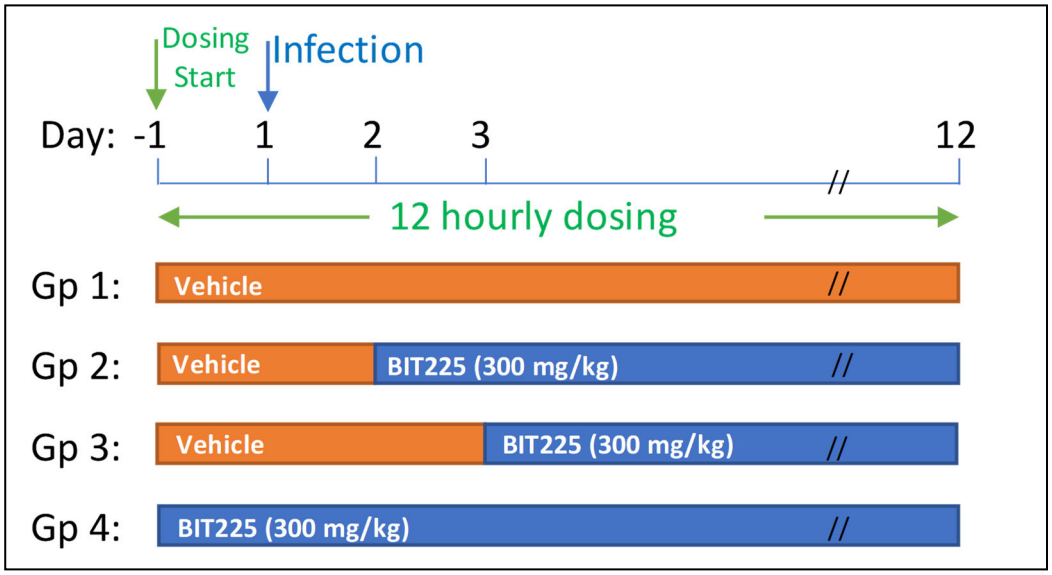
ADDENDUM - EXPERIMENT DETAILS

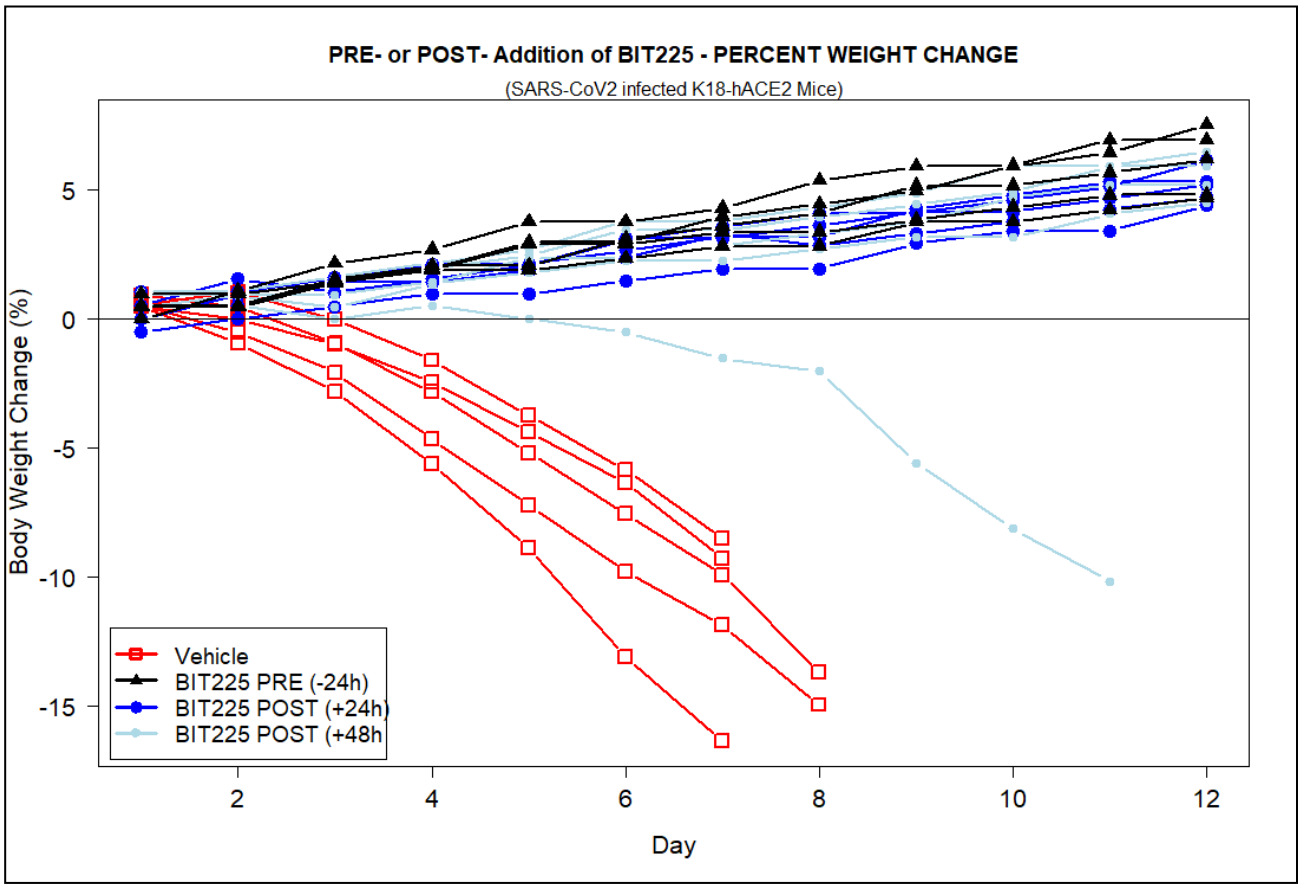
Transgenic mice expressing human ACE2 under the control of the cytokeratin 18 promoter (K18-hACE2 mice) were inoculated intranasally with 10^4 PFU of SARS-CoV-2 (2019n-CoV/US-WA1/2020). The mice were dosed by oral gavage as follows (as per schematic):

- Group 1: 5 mice dosed twice day for 12 days with vehicle control (i.e. drug-free control).
- Group 2: 5 mice dosed twice daily for 2 days with vehicle control, then 10 days with 300 mg/kg BIT225 (24 hour post-dosing group).
- Group 3: 5 mice dosed twice daily for 3 days with vehicle control, then 9 days with 300 mg/kg BIT225 (48 hour post-dosing group).
- Group 4: 5 mice dosed twice daily for 12 days with 300 mg/kg BIT225 (pre-dosing group).



Body weight and general health were monitored daily. The primary outcomes and endpoints measured were survival time and body weight. Mice losing >30% body weight compared to their baseline pre-infection weight were euthanized and counted as a death due to virus event. All surviving mice were sacrificed on Day 12.

Figure 1 (below) shows show data values of weights for each mouse, expressed as percentage change in weight from baseline (pre-infection) weight.



All mice in the vehicle group (unfilled squares) died or had reached the humane endpoint of >30% body weight loss from baseline at days 7 or 8 post-infection. In contrast, body weights for mice in all the BIT225 dosage groups – except for one mouse in Group 3 - steadily increased over the duration of the study to Day 12. The Group 3 mouse that lost weight died during the night of Day 11. All other mice in Groups 2, 3 and 4 survived.

Figure 2 (below) shows group mean trendlines for percent weight change from Day 1 (error bars indicate 95% confidence interval: n=5). There appears to be a trend for less weight gain as initiation of BIT225 dosing is further delayed. The difference between the pre-dosing and 48-hour post-dosing groups is not statistically significant at Day 11 (P=0.03, T-test).

Stars indicate P-values (adjusted by the Bonferroni method) for 8 T-tests comparing mean body weights for the vehicle group versus the combined BIT225-treated groups at Days 1-8: * P < 0.05; ** P < 0.01; *** P < 0.001. (note: Group 3 mouse that died is absent from Day 12 mean).

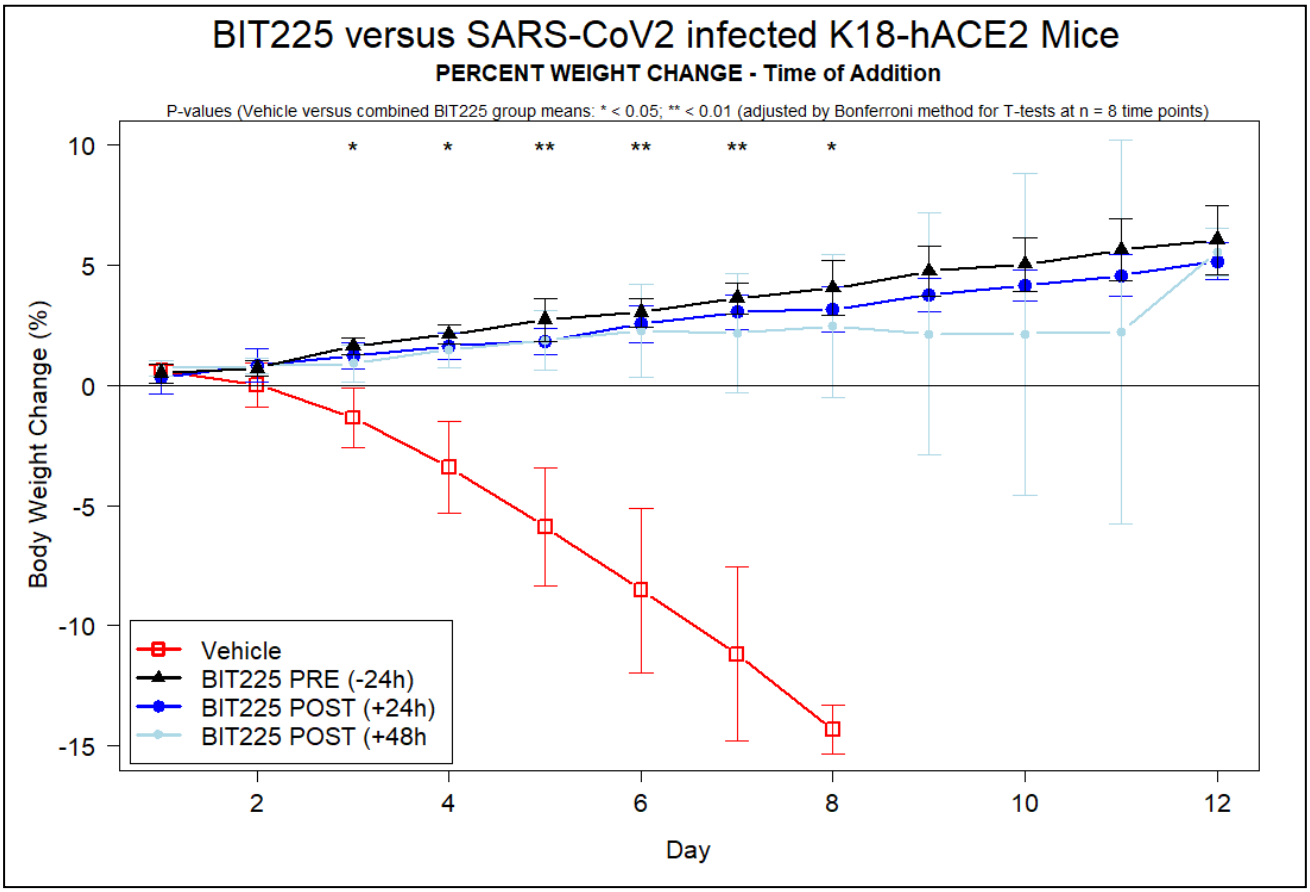


Figure 3 (below) shows the Kaplan Meier mortality curves for Groups 1 to 4. The curve for the vehicle control group is statistically different by the Log-rank test (P<0.001).