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The Manager Companies
ASX Limited
20 Bridge Street
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Dear Madam

BIT225-011 Phase 2 HIV Exploratory Efficacy Trial Meets Primary Objectives

- Preliminary analyses indicate that the primary objectives of the trial have been met.

- The results extend the previously reported effects of BIT225 to an HIV-infected population that has not achieved full immune reconstitution despite long-term suppressive antiretroviral treatment.

The Directors of Biotron Limited (the Company) are pleased to advise that preliminary analyses of data from the BIT225-011 Phase 2 clinical trial of the Company's lead antiviral drug BIT225 indicate that the primary objectives of the trial have been met.

This longitudinal, open-label Phase 2 trial was designed to characterise the effect of BIT225 (200 mg, once daily) added to ongoing, suppressive standard of care antiretroviral therapy (**cART**) for twelve weeks in twenty HIV-1 infected, treatment-experienced participants who had achieved only partial immune reconstitution. Trial details are set out in the attached Addendum.

The primary objectives of the trial were to evaluate the safety and tolerability of BIT225 in this patient population, as well as to determine the impact of the addition of BIT225 to cART on immune activation, inflammation and viral markers.

A summary of the preliminary results is set out below:

1. **Safety and tolerability:**

   Preliminary analysis of the safety data has shown that BIT225 was safe and generally well tolerated at the 200 mg once daily dose, with no deaths or drug-related serious adverse events.

   The safety and tolerability profile of BIT225 in the current trial was congruent with that seen in previous trials. Observed Adverse Events (**AEs**) attributed to BIT225 were of similar incidence, and mild severity, to those previously reported for the drug. One person withdrew from the study following the first dose of study drug during the treatment period.

2. Determine change of immune activation, inflammation and viral markers:

Baseline values for a range of immune activation, inflammation and viral assays were determined for each person during an initial 4-week Observation Period. Subsequent values of the same markers were assessed during the 12-week treatment period with BIT225, as well as during a 4-week Follow-up Period after completion of BIT225 treatment. Analyses of Treatment and Follow up values were compared to those obtained during the Observation period.

All participants maintained viral suppression throughout the study. Statistically significant differences ($P<0.05$) in the change from baseline were observed during the BIT225 treatment period for several pre-specified immune markers and cell populations. These included NK cells, a key cell type involved in combating viral infection, and T-regulatory cells. Changes in these cell populations have been noted in previous trials with BIT225 and suggest a possible immune modifying effect of BIT225 when used with cART.

Professor Anthony Kelleher, Director, Kirby Institute, University of NSW, said:

*"Individuals who do not achieve full immune reconstitution following fully suppressive antiviral therapy represent an important portion of those with HIV infection. Studies suggest that immune non-responders (**INR**) represent 20% - 40% of those on current antiviral therapy. These individuals are at enhanced risk for serious comorbid conditions including neurocognitive, cardiovascular, renal and hepatic disorders that impair quality of life and drive healthcare expenditures.*

Development of therapies for the INR is a clear unmet need and therapeutic approaches including HIV-1 viroporin antagonism, such as BIT225, require testing in the clinic. The laboratory changes seen in this exploratory study, while not demonstrating a rise in CD4 cells, are of interest and may portend clinical impact."

Michelle Miller, Biotron's Managing Director, said:

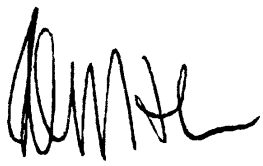
"This trial extends our understanding of BIT225 and complements the results from the previous HIV trials. Viroporin-targeting drugs such as BIT225 uniquely combine immune modulation with antiviral activity and have the potential to address both the immune and viral pathogenesis of numerous viral infections in a clinically-relevant fashion.

This study was a particularly complex and time-consuming trial. The results reported here are preliminary, and ongoing analysis of this BIT225-011 trial and the BIT225-010 HIV-1 trial in a treatment-naïve population will be reported when complete.

The Company would like to thank the principal investigators, trial sites, CROs, and most importantly, the trial participants who enrolled in the study."

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

Yours sincerely



Peter J. Nightingale
Company Secretary

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ADDENDUM – Summary of Clinical Trial Details

BIT225-011 (ACTRN12621001354875p/UTN U1111-1268-6150): A Phase 2 Study of BIT225, an HIV-1 Vpu Inhibitor, in HIV-1 Infected, Treatment Experienced Individuals, Attaining only Partial Immune Reconstitution on a Durable, Suppressive Combination Antiretroviral Therapy (cART) Regimen: An Open-Label Exploratory Evaluation of Changes in Inflammatory, Immune, Immune Activation and Viral Markers.

The primary objectives of the study are to:

- Determine change of immune, immune activation, inflammation and viral markers with the addition of BIT225 200mg QD, to stable, suppressive cART, for 12 weeks in HIV-1 infected, treatment experienced participants, who have achieved only partial immune reconstitution. Partial immune reconstitution is defined as a screening CD4 ≤ 350 cells/μL, or < 500 cells/μL with a CD4/CD8 ratio ≤ 0.6

- Assess safety and tolerability of BIT225 using the DAIDS Table for grading the severity of AEs (version 2.1, July 2017).

The secondary objectives of the study are to:

- To characterise changes from baseline Observation to those noted during active Treatment and Follow up Periods. The markers for these analyses include: low-level HIV viral load and the functional HIV reservoir. Additional pro- and anti-inflammatory markers, cytokines, cellular activation and exhaustion markers, and T cell phenotypes as well as other immune cell populations will be measured.

Study Design:

The study will enrol 20 adult male and female participants. All will continue their ongoing cART regimen, and all will receive 12 weeks of BIT225. Each participant will serve as their own control. The study has three distinct periods: Observation, Treatment and Follow-up:

- During the initial 4-week Observation period on cART alone repeated measurements of selected immune activation, inflammation and viral assays will be determined to generate baseline values for subsequent comparison to values obtained during, and following, BIT225 treatment period.
- Treatment with BIT225 plus cART for 12 weeks, measuring a panel of immune, immune activation, inflammation and viral markers throughout.
- After completing 12 weeks of BIT225 treatment, a 4-week Follow-up period will allow for evaluation of changes of immune, immune activation, inflammation and viral markers when compared to the Observation and Treatment periods.

Study Population:

The treatment-experienced population consists of adult males and females with HIV-1 infection, aged 18 - 65 years inclusive, who have been maintained on suppressive cART, with HIV RNA < 50 copies/mL for ≥ 24 months but have only achieved partial immune reconstitution.