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The Manager Companies
ASX Limited
20 Bridge Street
SYDNEY NSW 2000 (3 pages by email)

Dear Madam

POSITIVE OUTCOMES IN BIT225 PHASE 2 CLINICAL TRIAL IN HIV (BIT225-010)

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

  The results suggest that BIT225 is having a unique effect beyond that seen with current standard of care antiretroviral drugs.

- The data is consistent with BIT225 targeting virus present in reservoir cells.

The Directors of Biotron Limited (**the Company**) are pleased to advise that preliminary analyses of data from the BIT225-010 Phase 2 clinical trial of the Company's lead antiviral drug BIT225 provide confirmation, and extension, of the results of previous trials in people infected with HIV-1.

The double-blind placebo-controlled Phase 2 trial was designed to characterise the effect of BIT225 (200 mg, once daily for 24 weeks) added to a standard of care antiretroviral therapy (cART: 50 mg Dolutegravir (DTG), 300 mg Tenofovir disproxil fumarate (TDF) and 200 mg Emtricitabine (FTC)) in twenty-seven (18 BIT225 : 9 Placebo) treatment naïve people infected with HIV-1. Study participants were followed for a one-month period following 24-weeks of BIT225 or placebo dosing; all individuals continued on cART as per standard treatment guidelines post-study.

The primary objectives of the trial were to evaluate the safety, efficacy and impact of BIT225 administered with cART on selected inflammatory and immune markers in this patient population.

The primary objectives of the trial, which are set out in the attached Addendum, have been met:

1. **Safety and tolerability:**

   Preliminary analysis of the safety data has shown that BIT225 was safe and generally well tolerated at the 200mg once daily dose, with no deaths or drug-related serious adverse events. All participants achieved viral suppression and none were considered virologic failures.

   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 BIT-225 were of similar incidence, and severity, to those previously reported for the drug. Two people withdrew from the study; one withdrawal was not related to BIT225 or cART.

2. **Efficacy:**

   The efficacy of BIT225 was determined by an assessment of plasma viral loads, and changes to blood immune cell populations:

   a. Preliminary analyses of the HIV-1 plasma viral load (pVL) data (assessed at < 50 copies/ml and <200 copies/ml) for the BIT225-010 trial suggest that the addition of BIT225 to cART results in a more rapid reduction in plasma virus levels during the second phase of viral decay, compared to cART alone.

      The data indicated a more rapid viral clearance between days 14 and 56 in the BIT225 treatment group when compared to the group treated with cART alone. The rates of decline of the plasma HIV-1 viral loads were statistically greater in the BIT225 group compared to placebo (-0.047 & -0.022 log10/Day, respectively, $P < 0.02$ from T-test, Wilcox-test and ANCOVA models).

   b. Preliminary analyses of blood immune cell populations showed changes in specific immune cell populations in the BIT225 group compared to cART alone.

      Statistically significant differences ($P<0.05$) were observed between treatment groups in levels of subpopulations of CD4 and CD8 T cells as well as in CD16/56 NK cells, a key cell type combatting viral infection.

3. **"Characterise changes from baseline in an aggregate panel of immune activation and inflammatory markers in individuals receiving DTG-based cART with either active BIT225 or placebo":**

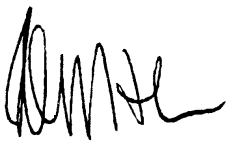
   Statistically significant differences ($P<0.05$) in the change from baseline were observed between the BIT225 and placebo (cART alone) for several immune activation and inflammatory markers including sCD14, sTNF-RII and IL-15. These changes are consistent with those seen in earlier trials and suggest a possible immune modifying effect of BIT225 when used with cART.

Dr Michelle Miller, Biotron's Managing Director, said; *"The positive outcomes from this trial further our understanding of BIT225. The blood (plasma) viral load data in particular should be highlighted, as it suggests that BIT225 is having an impact on a critical phase of viral decay when latent reservoirs are established. Current cART is efficient at rapidly and durably reducing virus levels in the blood, but this does not translate into clearance of latent reservoirs. The observed changes to immune markers and cells further the results from the previous 009 trial and suggest the utility of targeting viroporins as a new class of antiviral drugs.*

The results reported here are preliminary, and ongoing analysis of the BIT225-010 study, as well as its companion study, BIT225-011 in HIV-1 chronically infected individuals, will be reported when complete.

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

Yours sincerely



Peter J. Nightingale
Company Secretary

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ADDENDUM
SUMMARY OF CLINICAL TRIAL DETAILS

BIT225-010 (ACTRN12621000937819p/UTN U1111-1266-9893): A Phase 2 Study of BIT225, an HIV-1 Vpu Inhibitor, in Treatment Naïve HIV-1 Infected Individuals Commencing Dolutegravir-based Combination Antiretroviral Therapy (cART): Evaluation of Safety, Efficacy and Inflammatory and Immune Activation Markers.

The primary objectives of the study are to:

- Determine the safety, tolerability and efficacy of 200 mg BIT225 QD administered for up to 24 consecutive weeks in HIV-1 infected treatment naïve participants commencing antiretroviral therapy with standardised dolutegravir (DTG)-based cART. Efficacy will be determined by HIV-1 RNA at two different levels, <50 copies/mL and <200 copies/mL, and changes to blood immune cell populations. Safety will be determined by the incidence and severity of adverse events (AEs) using the DAIDS HIV grading severity of AEs.

- To characterise changes from baseline in an aggregate panel of immune activation and inflammatory markers in individuals receiving DTG-based cART with either active BIT225 or placebo. Biomarkers in this panel include: sCD163, sTNFR I and II, IL-6, IL-21, IL-15, IL-10, activated CD4+ and CD8+ T cell subsets (CD28+, CD27+, CCR7+) and changes in NK cells.

The secondary objectives of this study are to:

- Determine if the addition of BIT225 to DTG-based cART results in changes, compared with placebo, in low-level i.e. sub-50 copies/ml HIV-1 viral load and the HIV reservoir. Additional pro- and anti-inflammatory markers, cytokines, cellular exhaustion markers, cellular activation markers, and T-cell phenotypes as well as other immune cell populations will be measured.

Study Design:

The study will enrol 27 adult male and female participants who will be randomised in a 2:1 double-blinded fashion for 24 weeks, with one group receiving BIT225 (18 individuals), and one group receiving placebo (9 individuals). All participants will receive standard of care cART. An eight (8) week follow-up period on cART alone will follow the active treatment, or placebo portion of the study. At the conclusion of the trial, participants will remain on cART as per standard treatment protocols.

Study Population:

The treatment naïve target population is males and females, aged 18 to 65 years inclusive, with HIV-1 infection that are intending to initiate cART. Recruited individuals will have a CD4+ count between 50 and 350 cells/mm^3 and HIV-1 RNA > 5000 copies/mL. determined at the time of screening.