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The Manager Companies
ASX Limited
20 Bridge Street
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(5 pages by email)

Dear Madam

COMMENCEMENT OF TWO PIVOTAL BIT225 CLINICAL TRIALS

The Directors of Biotron Limited (ASX: BIT) are pleased to announce that the Company has commenced two clinical trials with its lead antiviral drug BIT225 in HIV-1-positive populations.

The trials build on favourable results from the completed BIT225-009 Phase 2 clinical trial in which BIT225 was shown to induce immunomodulation effects and key markers of improved health outcomes. The two new trials are designed to investigate further the immune changes observed in the BIT225-009 study.

For the first time, BIT225 will be tested in people who have been taking approved anti-HIV-1 treatment ('ART') for an extended period with well-controlled HIV-1 infection. Previously, BIT225 has been tested in newly infected, antiretroviral treatment-naïve people commencing treatment for the first time. Importantly, this new trial, BIT225-011, will be conducted at sites in Sydney, NSW, and will include people who have not achieved full immune reconstitution despite long term durably suppressive ART. This group, estimated to encompass more than one third of the HIV-treated population, is at an increased risk of clinical progression to AIDS and other morbidities and has higher rates of mortality than HIV-infected patients who have attained full immune reconstitution.

BIT225 will be added to the BIT225-011 subjects' ART for a period of 12 weeks, after which time they will remain on ART as per standard treatment protocols.

The Principal Investigators ('PIs') for the BIT225-011 trial are Professor Anthony Kelleher, St Vincent's Hospital, Darlinghurst, NSW, and Assoc/Professor Mark Bloch, Holdsworth House, Darlinghurst, NSW.

This trial has commenced at Holdsworth House, following receipt of approval for the study from the Bellberry Human Research Ethics Committee ('HREC') and the holding of the Site Initiation Meeting. The St Vincent's site is anticipated to commence enrolment once approvals have been received from additional HRECs.

Biotron's Managing Director, Dr. Michelle Miller said, "We are extremely pleased to be undertaking this study here in Sydney, Australia with such an experienced, internationally recognised team. Initiating this clinical trial is an important step towards demonstrating the clinical benefit that BIT225 could bring to the treatment of HIV-1, especially in a still at-risk group. BIT225's unique dual action in targeting HIV-1 in cellular reservoirs and improving immune functions has the potential to improve health outcomes in this population."

The other new trial, BIT225-010, has also commenced at two sites in Thailand. This study will include individuals newly diagnosed as being HIV-1 positive but who have not yet commenced ART.

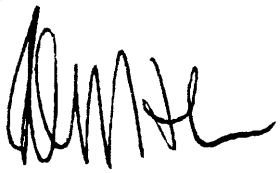
The study participants will have BIT225 or placebo added to the newly-approved standard of care ART at the beginning of treatment for a period of 24 weeks. The dosing period is twice as long as the previously successful BIT225-009 trial and allows for a more detailed investigation of immune changes observed in that study.

The PIs for the trial are Dr Anchalee Avihingsanon and Dr Khuanchai Supparatpinyo. Following the recent receipt of approval from relevant HRECs and holding Site Initiation Meetings, the trial has commenced at HIV-NAT, Thai Red Cross AIDS Research Centre, Bangkok and at the Research Institute for Health Sciences, Chiang Mai University.

The trials have been designed in consultation with Biotron's international Scientific Advisory Board and Chief Medical Officer, Dr Stephen Becker, as well as other experienced experts in the field. The purpose of undertaking these two studies is to generate the necessary data to demonstrate to the pharmaceutical industry and regulators the potential of BIT225, when used with ART, to improve patient outcomes and address currently unmet clinical needs in HIV-1 infected patients.

Additional details on the BIT225-010 and BIT225-011 clinical trials are set out in an Addendum below. The trials are expected to conclude in mid-2022 and data to be made available during the second half of 2022.

Yours sincerely



Peter J. Nightingale
Company Secretary

ADDENDUM

SUMMARY OF CLINICAL TRIAL DETAILS

1. **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.

   - 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.

2. **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:

   a. 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.
   b. Treatment with BIT225 plus cART for 12 weeks, measuring a panel of immune, immune activation, inflammation and viral markers throughout.
   c. 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 to 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.

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 by the Company's Managing Director.

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