Biotron Limited
A.B.N. 60 086 399 144

Level 2, 66 Hunter Street
Sydney NSW 2000
Tel: (61-2) 9300 3344
Fax: (61-2) 9221 6333
E-mail: pnightingale@biotron.com.au
Website: www.biotron.com.au

4 May 2023

The Manager Companies
ASX Limited
20 Bridge Street
SYDNEY NSW 2000 (4 pages by email)

Dear Madam,

COMMENCEMENT OF PHASE 2 COVID-19 CLINICAL TRIAL

The Directors of Biotron Limited ('Biotron' or 'the Company') (ASX: BIT) are pleased to announce that the Company has commenced a clinical trial with its lead antiviral drug BIT225 for treatment of COVID-19.

The Phase 2, double blind, placebo-controlled clinical trial (BIT225-012) aims to determine if 7 days of treatment with BIT225 commenced within 3 days of onset of COVID-19 symptoms results in reduction in SARS-CoV-2 blood viral load, clinically favourable changes in viral, inflammatory and immune activation markers, as well as improvement in clinical symptoms of COVID-19.

The design of the trial was based on guidance received during 2022 from the USA Food and Drug Administration (FDA) and took into consideration the continually changing landscape of COVID-19.

The Company has consulted with international clinicians, clinical research organisations and other relevant experts to design a study aimed to be recruited quickly and generate meaningful data in a tight timeframe.

In addition to its unique clinical activity against HIV- 1, BIT225 has shown very good activity against SARS-CoV-2 and prevented development of disease in a COVID-19 mouse model. As previously announced (ASX announcements 25 November 2021, 17 March 2022 and 2 May 2022) BIT225 demonstrated both antiviral, immune modulatory and clinical benefit against SARS-CoV-2 in an accepted murine model of disease. The SARS-CoV-2-infected mice quickly die from respiratory disease very similar to human COVID-19. However, BIT225 very efficiently reduced levels of SARS-CoV-2 virus and stopped the life- threatening cytokine storm. BIT225-treated mice did not develop any signs of disease and remained healthy throughout the several studies that were conducted.

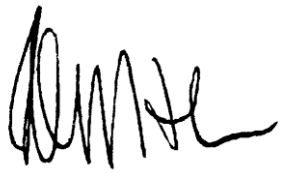
Despite the availability of SARS-CoV-2 vaccines, there remains a need for oral drugs to treat the infection and prevent severe disease, especially in at-risk individuals. BIT225 has an established human safety profile and the potential to be an important first in class drug for COVID-19 treatment.

The trial will be run at several sites in Thailand. The first trial site, HIV-NAT, Thai Red Cross AIDS Research Centre, Bangkok, has commenced the study after receipt of ethics approval from the Institutional Review Board (IRB), Faculty of Medicine, Chulalongkorn University and holding the Site Initiation Meeting. Additional sites are expected to commence enrolment once approvals are received from additional IRBs.

The trial is expected to be fully recruited in mid-2023 with data available early in the second half of 2023.

Additional details on the BIT225-012 Covid-19 clinical trial are set out in an Addendum below.

Yours sincerely



Peter J. Nightingale
Company Secretary

pjn11658

ADDENDUM: SUMMARY OF CLINICAL TRIAL DETAILS

BIT225-012 (ACTRN12623000035628/ UTN U1111-1286-7528): A Phase 2, Double Blind Placebo-Controlled Study of BIT225, an Orally Administered SARS-CoV-2 Viroporin Inhibitor, to Evaluate Antiviral Activity, Safety, and Immune Biomarkers in Non-Hospitalised Vaccinated and Unvaccinated Adults with COVID-19.

The primary objectives of the study are to:

- Determine the safety and tolerability of BIT225 when dosed at 200mg or 400 mg per day, or matching placebo administered for 7 consecutive days in individuals newly diagnosed with SARS-CoV-2 within 3 days of the first onset of symptoms. Safety will be assessed by the frequency of adverse events.
- Determine the efficacy of BIT225 when dosed at 200 mg, 400 mg per day, or matching placebo administered for 7 consecutive days in individuals diagnosed with SARS-CoV-2 within 3 days of the onset of symptoms, based on SARS-CoV-2 nasal viral load, kinetics of change, and time to negative SARS-CoV-2 PCR. Efficacy endpoints will include change in SARS-CoV-2 nasal viral load, kinetics of change, and time to negative PCR.

Secondary objectives of the study are to:

- Determine the efficacy of BIT225 when dosed at 200 mg, 400 mg per day, or matching placebo administered for 7 consecutive days in individuals diagnosed with SARS-CoV-2 within 3 days of the onset of symptoms, based on multiple clinical and immunological outcome measures as follows:
    - Time to sustained clinical recovery (targeted symptom resolution)
    - Time to clinical improvement
    - Rate of hospitalisation through Day 21
    - Rate of all-cause mortality through Day 21
    - Rate of recrudescent / recurrent SARS-CoV-2 infection
- Characterise disease-specific immune and inflammatory markers, including CD8 counts, CD4/CD8 ratio, pro-inflammatory cytokines, including IL-1β, IL-6, and markers of inflammation, such as sCD163.

Study Design:

BIT225-012 is a double-blinded, placebo controlled, randomised (1:1:1), multi-site Phase 2 trial designed to evaluate BIT225 at 200mg and 400 mg daily dose versus common placebo, to be conducted at approximately three sites in Thailand. The study will enrol both SARS-CoV-2 vaccinated and unvaccinated men and women, age < 60 years. Clinical, virologic and immunologic outcomes will be analysed by baseline SARS-CoV-2 nasal RNA and vaccine status. Individuals, 18 to 59 years of age who meet all inclusion criteria and no exclusion criteria, will be enrolled.

Up to 60 individuals, up to 20 in each of the BIT225 dosage arms, and up to 20 in the common placebo arm will be enrolled.

Treatment with either BIT225, as 100 mg capsules; 200 mg or 400 mg per day or matching placebo, will begin on Day 1 and continue for 7 consecutive days, followed by a fourteen (14) day follow-up period.

Study Population:

Up to 60 adult male and female individuals from ages 18 to 59 years, diagnosed with SARS-CoV-2 within 3 days of the onset of symptoms.

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

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 COVID-19, and additional promising preclinical programs including 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.

Enquiries

Dr Michelle Miller
Managing Director
Biotron Limited
+61-(0)412313329
mmiller@biotron.com.au

Rudi Michelson
Monsoon Communications
+61-3 9620 3333