BIOTRON LIMITED
(ASX:BIT)

INVESTOR UPDATE
25 November 2021

Forward Looking Statements

This presentation may contain forward-looking statements with respect to the financial condition, results and business achievements/performance of Biotron Limited (ACN 086 399 144) and certain of the plans and objectives of its management. These statements are statements that are not historical facts. Words such as “should”, “expects”, “anticipates”, “estimates”, “believes” or similar expressions, as they relate to Biotron Limited, are intended to identify forward-looking statements. By their nature, forward-looking statements involve risk and uncertainty because they reflect Biotron’s current expectations and assumptions as to future events and circumstances that may not prove accurate. There is no guarantee that the expected events, trends or results will actually occur. Any changes in such assumptions or expectations could cause actual results to differ materially from current expectations.

Biotron Limited (ASX:BIT) Overview

- Clinical stage company developing small molecule drugs targeting viral diseases with major health problems:
  - HIV-1 , COVID-19, Hepatitis B virus and others
- **Unique approach to tackling virus infections**
  - **Combining direct antiviral and immunomodulatory activities to knock down virus levels and boost the body's immune system to fight the infection**
- Experienced Board and management team with pharma, financial and VC backgrounds
- Headquartered in Sydney, Australia
- Portfolio of clinical and preclinical antiviral drugs

Biotron

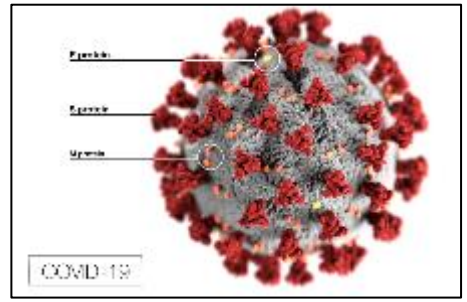
Biotron's Core Technology/Expertise

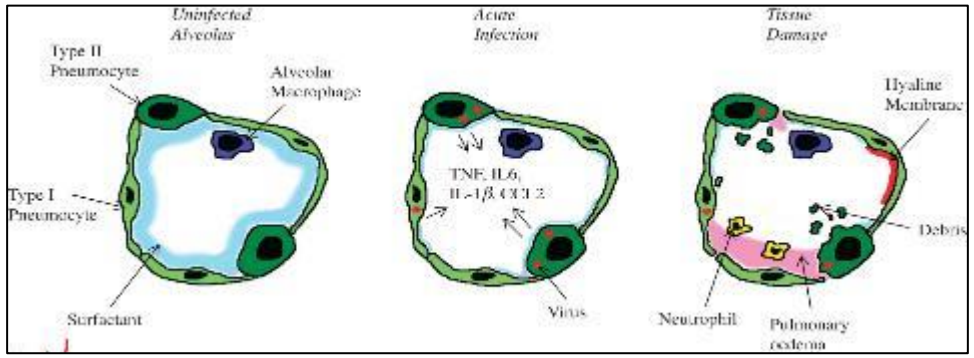
- Targeting a key viral protein class found on a range of different viruses
  - Known as viroporins – these proteins determine how efficiently a virus infects cells and evades the immune system
- The HIV-1 program, including a successful, completed, Phase 2 HIV-1 clinical trial, demonstrates proof of concept of Biotron's approach
  - Provides clinical validation of Biotron's approach to treating serious virus infections
- During 2020/2021 Biotron extended its technology to target SARS-CoV-2
  - Long standing interest and expertise in coronaviruses dating back to the SARS-1 outbreak
  - Biotron scientists were the first to identify the CoV E protein as a viroporin and a good target for drugs

Biotron

SARS-CoV-2

- Biotron's approach has been to design new small molecule drugs that target the SARS-CoV-2 viroporin(s)
  - E protein is a viroporin
  - Multiple roles in the virus lifecycle
    - Entry into cells and exit of new virus particles from infected cells
    - Pathogenesis of disease resulting from the infection
    - Triggers inflammatory cascade in the lungs leading to respiratory distress and failure





  - Deletion of E protein sequences attenuate infectivity and pathogenesis of CoVs
  - By targeting viroporins Biotron's anti-SARS-CoV-2 compounds are expected to impact on moderate/severe COVID

Biotron

SARS-CoV-2 Program

Vaccines remain central to control of the pandemic but there is an urgent need for effective drugs to treat COVID in at-risk populations

- Since start of pandemic Biotron's focus has been on designing and testing new compounds to target the SARS-CoV-2 E protein (oral drugs) based on SARS-1 program active compounds
- Lead series of new compounds identified based on these studies

- Included BIT225, Biotron's clinical stage anti-viral (HIV-1 and Hepatitis C virus) drug in *in vitro* cell based and and *in vivo* animal studies of SARS-CoV-2 infection.
- Studies undertaken in laboratory of collaborators at The SCRIPPS Research Institute, La Jolla, CA

Biotron

K18-hACE2: Mouse Model of COVID-19

- K18-hACE2 mouse model of COVID-19:
  - Mice engineered to express human ACE2 – the receptor used by SARS-CoV-2 to enter cells
  - Infection with SARS-CoV-2 results in a dose-dependent lethal disease
    - Rapid weight loss
    - Shed high levels of virus from respiratory tract
    - Develop pneumonia and pulmonary pathology similar to that seen in severe cases of COVID-19
    - Immune cell infiltrates and proinflammatory cytokine response is similar to that seen in COVID-19
  - Model is used to study pathogenesis of the disease and assess therapeutic agents.

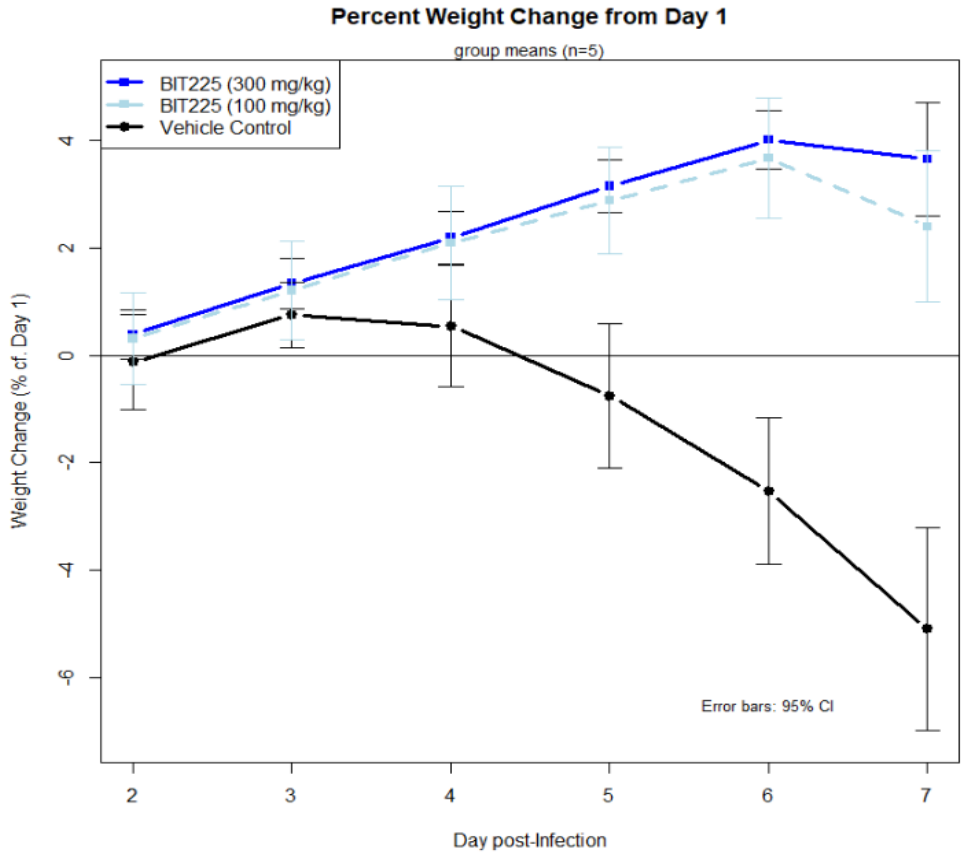
BIT225 – Mouse Model of COVID-19 Study

BIT225 (100mg/kg and 300 mg/kg) administered via oral gavage, BID for 7 days versus vehicle control the in K18-hACE2 transgenic mouse model:

- Virus strain: 2019n-CoV/USA-WA1/2020
- Infectious dose: 10^4 *pfu* intranasal, administered after second drug dose
- Number of mice: 5 mice per group (=20)
- Drug dosing schedule: 12 hourly for 14 doses
- Sacrificed day 7
- Endpoints:
    - Body weight and clinical observations
    - Viral RNA by q-RT-PCR in tissue homogenates
    - Infectious virus by plaque assay in tissue homogenates
    - Assessment of pro-inflammatory cytokines and chemokines in lung and blood

BIT225 Protected Against Severe Disease

Significant differences in % body weight change from Day 1



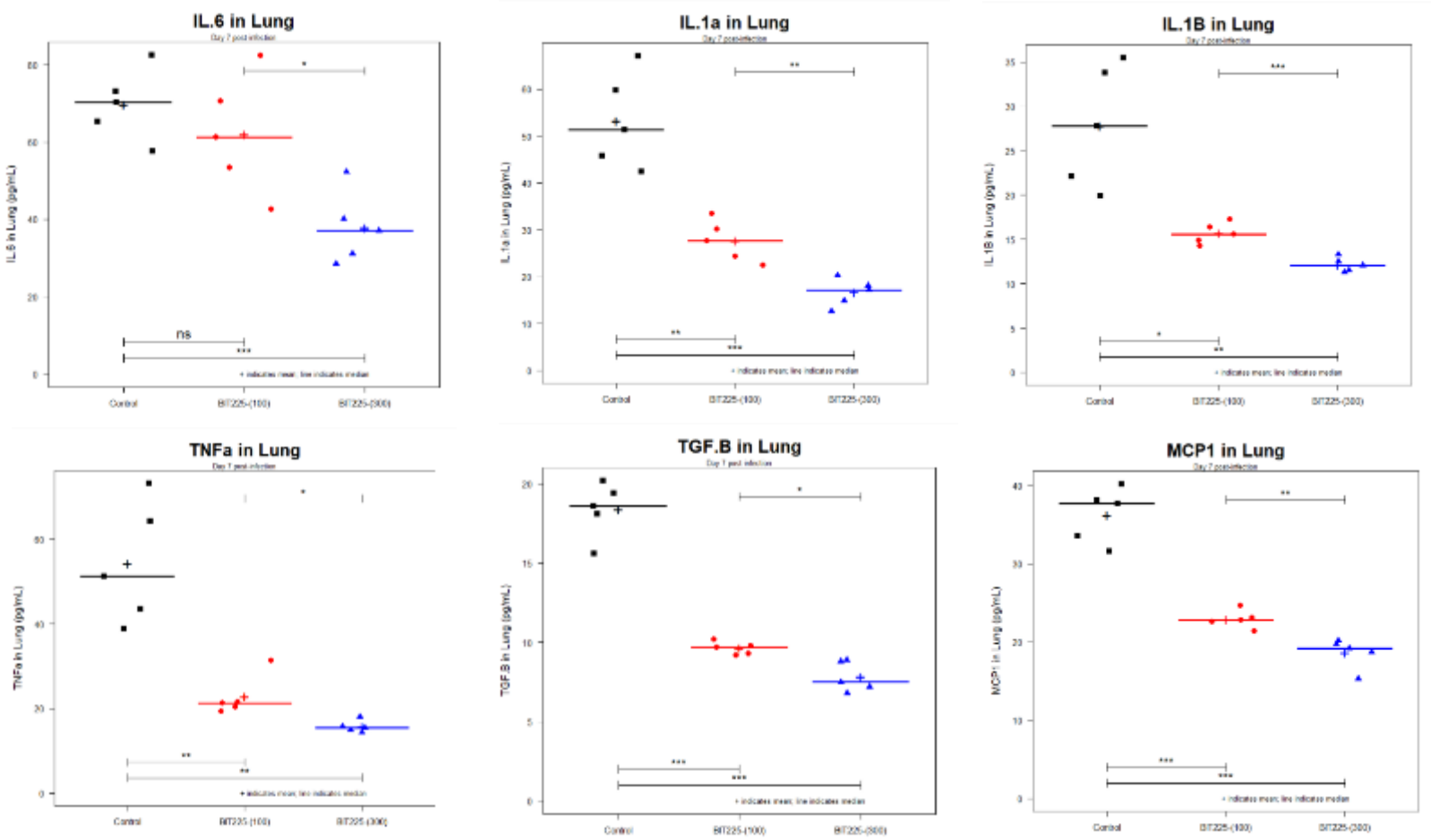
The increase in weight of mice treated with BIT225, compared to the decrease in weight of mice treated with vehicle control, indicates a reduction in the severity of disease and complications associated with SARS-CoV-2 infection.

Figure shows mean % weight change for mice treated with 300 mg/kg of BIT225 and mice treated with vehicle control. Between Day 0 and Day 7, mice treated with vehicle control showed a mean weight reduction of 5.1 % ($P = 0.005$), while mice treated with 300 mg/kg of BIT225 showed a mean weight increase of 3.7% % ($P < 0.01$).

Biotron

BIT225 Significantly Reduced “Cytokine Storm”

Assessment of pro-inflammatory cytokines/chemokines in lungs



For all six cytokines, the high dose of BIT225 is associated with significant reduction in lung tissue compared to mice treated with vehicle control. In addition, the high dose of BIT225 has greater effect than the low dose.

Increased levels of pro-inflammatory cytokines (‘cytokine storm’) are linked to severe illness and death in people infected with SARS-CoV-2 virus. Controlling this cytokine storm is essential for successful treatment of COVID-19.

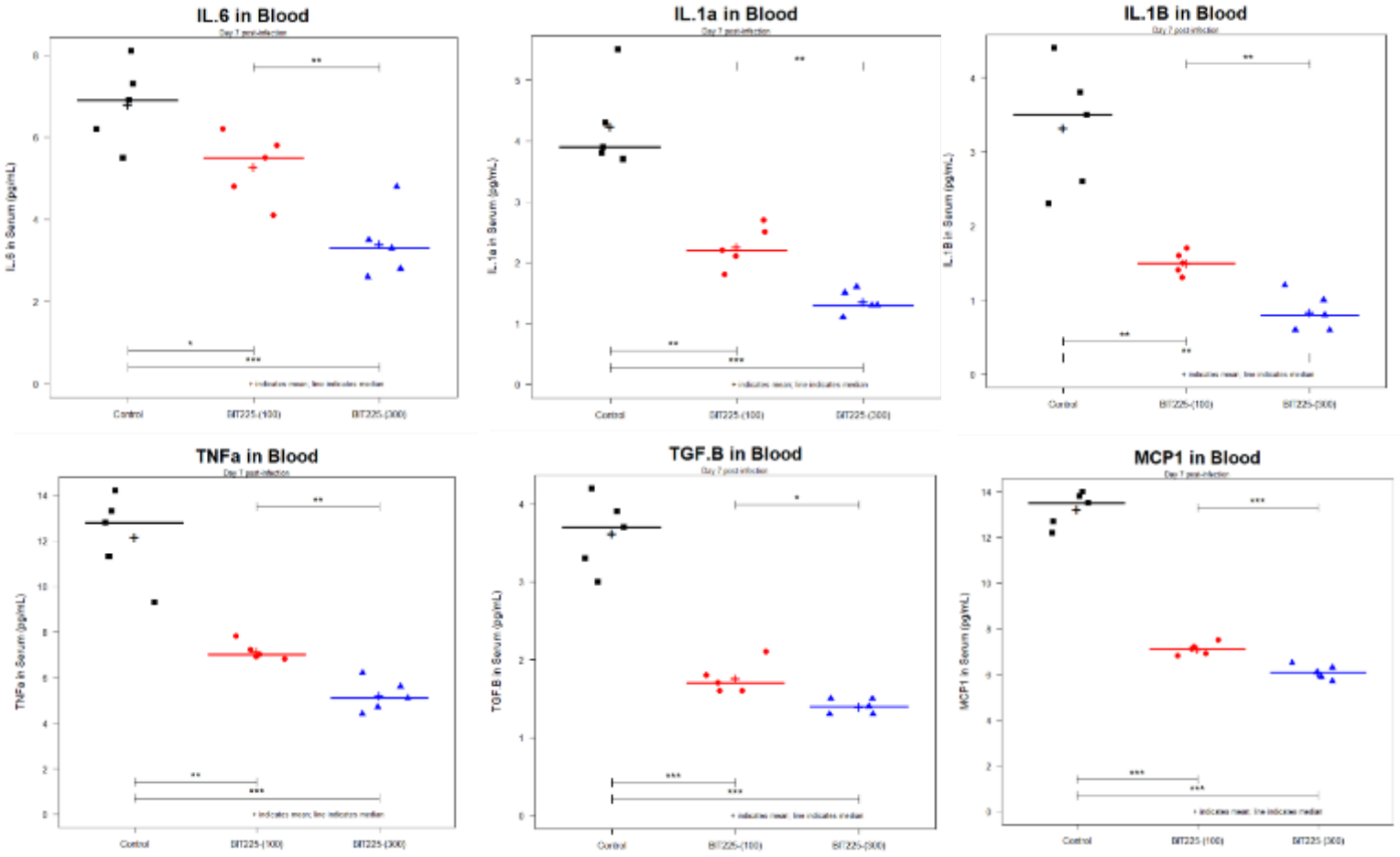
.

BIT225 treatment versus vehicle and BIT225 (300 mg/kg) versus BIT225 (100 mg/kg) statistical comparisons were by T-test (n = 5 per group). Asterisks indicate strength of statistical significance based on P-values (*** P<0.001, ** P<0.01; * P<0.05; ns P>0.05).

Biotron

BIT225 Significantly Reduced “Cytokine Storm”

Assessment of pro-inflammatory cytokines/chemokines in blood



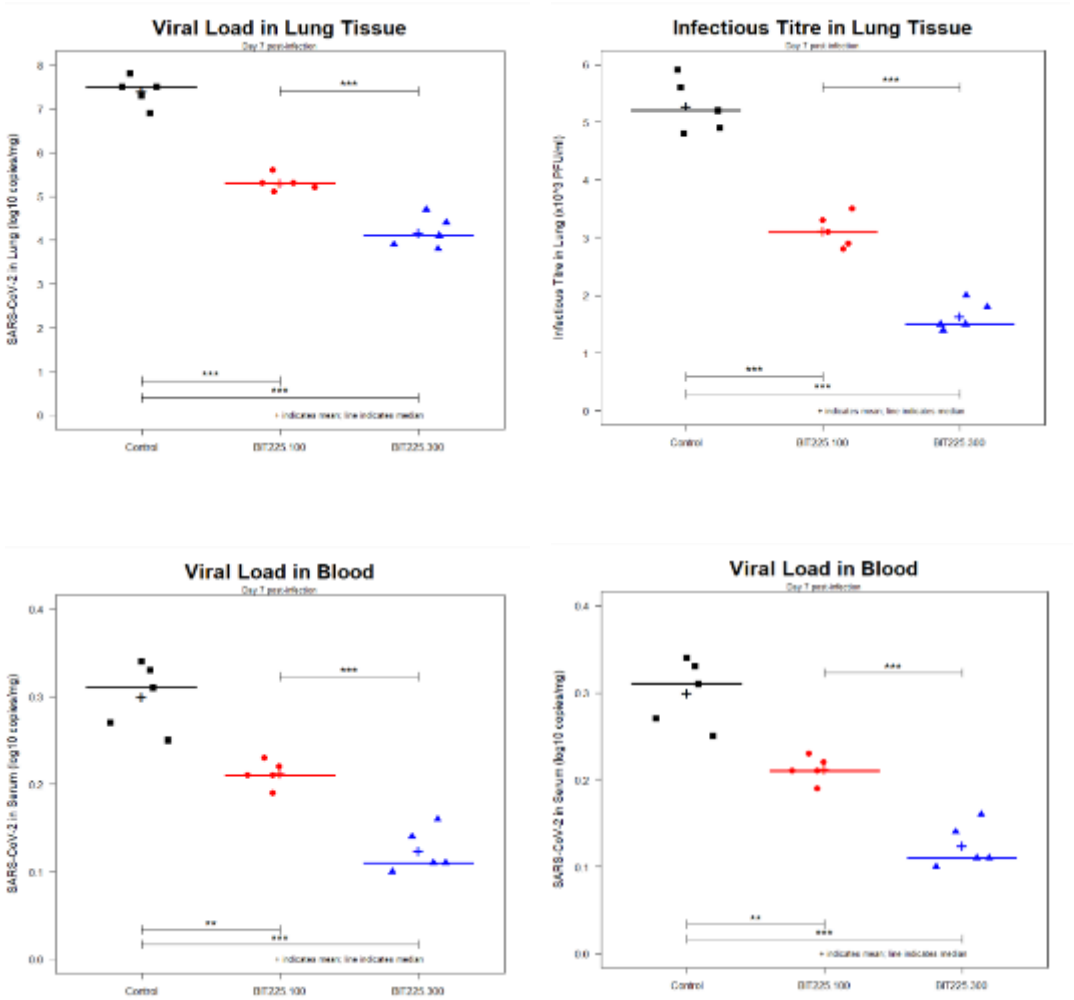
For all six cytokines, the high dose of BIT225 is associated with significant reduction in blood compared to mice treated with vehicle control. In addition, the high dose of BIT225 has greater effect than the low dose.

Increased levels of pro-inflammatory cytokines (‘cytokine storm’) are linked to severe illness and death in people infected with SARS-CoV-2 virus. Controlling this cytokine storm is essential for successful treatment of COVID-19.

BIT225 treatment versus vehicle and BIT225 (300 mg/kg) versus BIT225 (100 mg/kg) statistical comparisons were by T-test (n = 5 per group). Asterisks indicate strength of statistical significance based on P-values (*** P<0.001, ** P<0.01; * P<0.05; ns P>0.05).

Biotron

BIT225 Significantly Reduced Virus Levels in Lungs & Blood



Virus levels in lungs and blood showed that both doses of BIT225 significantly reduced viral load compared to vehicle control.

There was a dose-dependent effect with BIT225.

Plots show data values for each mouse, with median (line) and mean ("+") indicated by treatment group. Compound treatments versus vehicle and BIT225 (300 mg/kg) versus BIT225 (100 mg/kg) statistical comparisons were by T-test (n = 5 per group). Asterisks indicate strength of statistical significance based on P-values (*** P<0.001, ** P<0.01; * P<0.05; ns P>0.05). In all cases, the 300 mg/kg dose of BIT225 significantly reduced viral load compared to the 100 mg/kg dose.

Biotron

BIT225 – Summary of Mouse Study

- BIT225 demonstrated substantial and clinically meaningful efficacy against SARS-CoV-2 in this animal model of COVID-19:
  - Significantly inhibits SARS-CoV-2 replication and reduces infectious viral load in lungs and blood
  - Significantly reduces the production of pro-inflammatory cytokines and chemokines, and
  - Reduces the severity of complications associated with SARS-CoV-2 infection in this animal model of COVID-19.

Biotron

BIT225 – Extensive Clinical Trial Experience

- BIT225 is a small molecule, antiviral drug that is in capsule form for oral dosing
  - Suitable for once daily dosing
- BIT225 is in development for HIV-1 eradication and improving health outcomes associated with immune dysfunction
  - Two Phase 2 trials are currently recruiting in ART-treatment naïve (Thailand sites) and ART-treatment experienced (Australian sites) populations
- Over 200 people have been dosed in clinical trials to date, with up to 12 weeks dosing. Current trial approvals are for dosing out to 24 weeks.
  - Completed 9 clinical trials involving healthy volunteers, patients with HIV-1 infection, patients co-infected with Hepatitis C virus (HCV) and HIV-1 and patients with HCV (as monotherapy and in combination with pegylated interferon-alfa and ribavirin).
  - Well characterised safety and PK profile
- Completed formal pre-clinical studies include chronic (i.e. 24 weeks) safety studies
- Recently completed another cGMP manufacturing campaign of BIT225
- BIT225 is very stable over extended periods, including at room temperatures

Biotron

BIT225 – Moving Quickly to Assess in Human COVID Study(s)

- In discussions with international advisors to design clinical study(s) to assess efficacy against COVID
- Engaging with relevant regulators (FDA/CTAP) to facilitate fast assessment

- Aim is to progress BIT225 into trials to assess efficacy as therapeutic for COVID-19 as quickly as possible

Biotron

SUMMARY

- BIT225 demonstrated substantial and clinically meaningful efficacy against SARS-CoV-2 infection in an animal model of COVID-19
- It is active against the highly infectious delta strain in cell cultures
- BIT225 is a clinical stage drug in development for treatment of HIV-1, with over 200 people dosed in trials to date.
- BIT225 is an oral drug, suitable for once-a-day dosing and has a well characterised safety profile.
- BIT225 has a unique mode of action that differentiates it from other COVID drugs in development
    - It belongs to a new class of antiviral drugs known as viroporin inhibitors
    - Existing HIV-1 data has demonstrated that BIT225 uniquely combines direct-acting antiviral activity with immunomodulatory activity in clinical studies.
- Biotron Limited is now seeking to accelerate BIT225 into clinical trials in SARS-CoV-2-infected people.

Biotron

BIOTRON LIMITED
(ASX:BIT)

Michelle Miller, PhD
CEO & Managing Director
mmiller@biotron.com.au
www.biotron.com.au
+61 412313329