

BIOTRON LIMITED
(ASX:BIT)

AGM

23 November 2021



Forward Looking Statements

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Key Achievements 2020/2021 FY

- Key milestone for HIV-1 program:
 - Commenced two clinical trials of BIT225
 - Trials designed in consultation with international experts with key links to pharma
 - Designed specifically to solidify understanding of what BIT225 is doing and how it is doing it with focus on partner requirements
 - There is no roadmap to follow for HIV cure/eradication
 - Trials are being done to generate data to support future regulatory filings/use labels
 - Completed a new manufacturing of BIT225 clinical-grade (cGMP) drug for future trials
 - Progressed identification of next-generation HIV-1 drug candidate – candidates are currently undergoing preliminary safety testing



Key Achievements 2020/2021 FY (cont)

- Expanded the SARS-CoV-2 program
 - Testing in relevant, robust animal model of COVID in USA laboratory
 - Results are imminent
- Hepatitis B Virus (HBV) program
 - Progressed identification of potential lead to move into animal model(s)
- **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**
 - **Focus is on partnering**



HIV-1 Unmet Need

- Safe, effective antiretroviral drugs (ART) have been central to successfully keeping virus levels down in HIV+ people; Profound reductions in mortality, morbidity and transmission

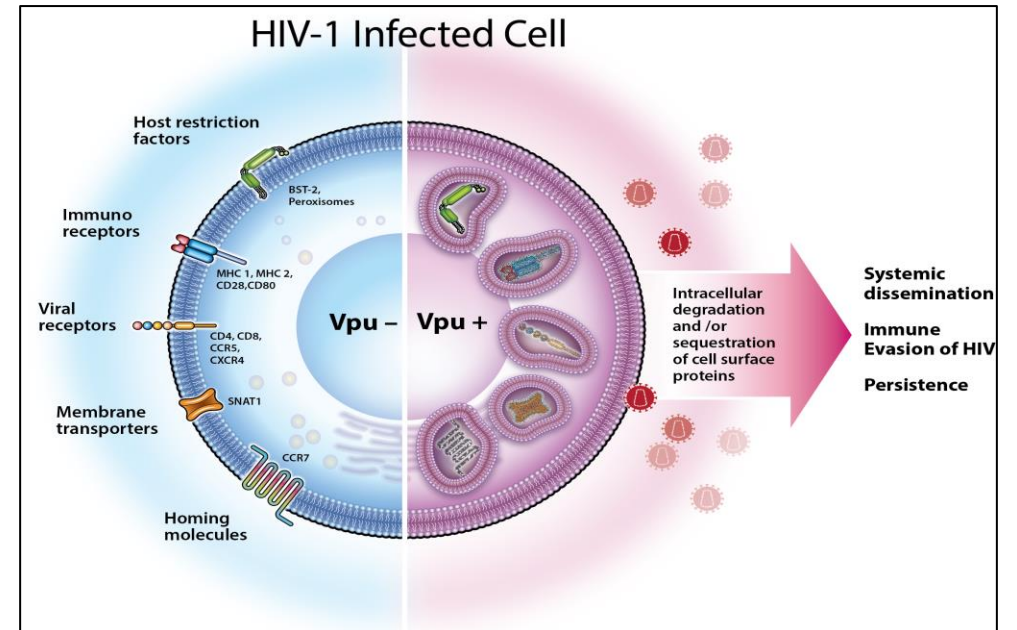
BUT

- **ART is not curative, latent viral reservoirs remain and reactivate**
- **Immune reconstitution is only partial and accompanied by a state of chronic inflammation**
- **A significant excess of chronic diseases, malignancy and neurocognitive deficits result in individual and societal burdens**
- **Global treatment costs are not remotely sustainable**



BIT225 – A new class of anti-HIV drug

- There is no roadmap for HIV-1 cure/eradication
- The BIT225-009 trial showed that there is a pathway to show clinical benefit for treating with BIT225
 - BIT225 a first-in-class drug that uniquely combines direct acting antiviral with immunomodulatory activities.
- BIT225 targets Vpu protein of HIV-1
 - Vpu is responsible for down-regulating key receptors on infected cells so that infected cells are hidden from the immune system
- Data from the completed Phase 2 clinical trial indicated that BIT225 reverses this process, resulting in “unmasking” of infected cells and reversing the suppression of the immune system



BIT225-010 and 011 HIV-1 Trials

- Two trials were designed to generate specific data to show a clinical benefit with BIT225, and further explore key observations related to inflammation and immune activation in both treatment naïve and experienced populations
- Assessing key biomarkers (immunological and virological) consistent with accepted clinical and commercial applications
- Aim is to determine impact on health-related outcomes that will be key to future regulatory filings
- Both trials have commenced, with completion scheduled mid-2022 and preliminary results 3Q2022



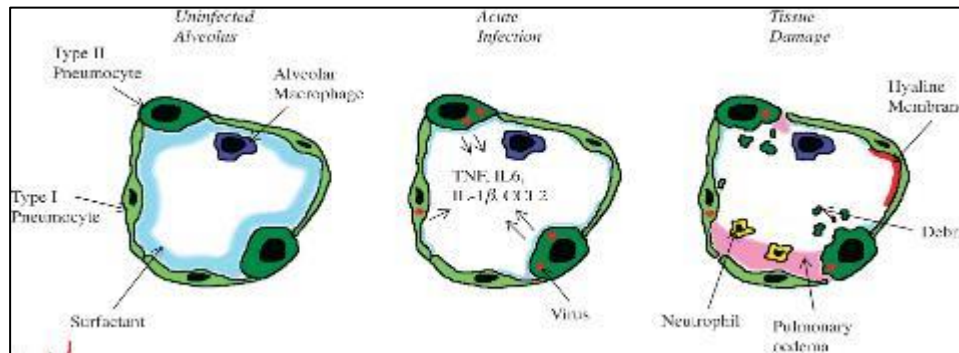
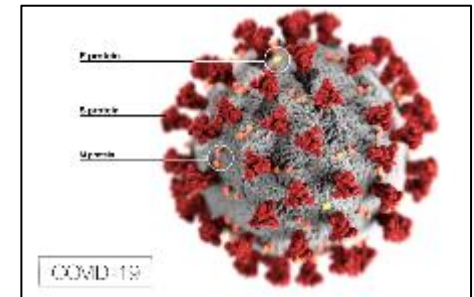
BIT225 and HIV-1 – Positioning

- A safe and effective agent that in conjunction with ART reduces inflammation and leads to fewer HIV comorbidities, improved health and lessened healthcare costs
- A safe and effective agent that in conjunction with ART leads to increased immune system recognition and eradication of HIV



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

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

- Designed and synthesised >100 new compounds to target the SARS-CoV-2 E protein (oral drugs)
- Screened for ability to inhibit replication of SARS-CoV-2 in a range of cell culture models
- Lead series identified based on these studies
 - Several compounds with good antiviral activity in these *in vitro* studies
- IN PROGRESS:
 - Testing key compounds in an animal model of SARS-CoV-2 in the USA
 - Assessing immunomodulatory activity in parallel with antiviral activity
 - Running preliminary preclinical safety studies in parallel
 - Data expected before end 2021



Hepatitis B Virus

- ~300 million worldwide chronically infected with HBV
- Increased risk of significant liver disease, including liver failure and cancer
- HBV causes up to 80% of liver cancers
 - 5 year survival of 15%
- >780,000 die every year
- as a consequence of HBV infection
- ***Current treatments suppress virus replication but do not deliver a cure***
- Cure will likely require attacking multiple targets of the HBV lifecycle
 - Aggressive suppression of replication
 - Inhibition of formation as well as elimination of cccDNA
 - Boost host immune response to chronic infection



Biotron HBV Program

- Over last 12 months Biotron has designed and tested a suite of new compounds to expand its portfolio of novel small molecule compounds with good activity against HBV
- Extensive package of preclinical *in vitro* data includes evidence of reduction in cccDNA, HBsAg, and other relevant HBV markers
- Biotron compounds have a unique mechanism of action with implications for HBV cure
- Preliminary safety testing is in progress with the top set of compounds, to identify a lead
- A confirmatory study to extensively assess impact on HBV in primary human cells will commence shortly, ahead of a study in an animal model of HBV infection



Summary

- HIV-1 program is the prime focus
 - Clear clinical development program designed to demonstrate to regulators and pharma how the drug may be used to improve health outcomes in combination with ART
- SARS-CoV-2 program is developing drugs with potential to reduce virus levels and immune dysfunction seen in moderate to severe COVID. Aim is to progress these as quickly as possible through relevant models and into formal safety studies.
- Hepatitis B (HBV) remains a promising and important early-stage program and good progress has been made to select a robust lead candidate
- **Biotron clearly has a portfolio of antivirals which uniquely combine antiviral inhibition with immunomodulatory activity.**
- **All activities are undertaken with aim of generating data for partners.**

