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7 June 2019

The Manager Companies  
ASX Limited  
20 Bridge Street  
SYDNEY NSW 2000

(15 pages by email)

Dear Madam,

**PRESENTATION AT BIO 2019**

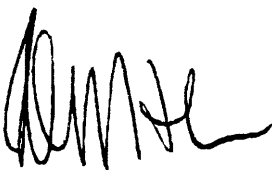
The Directors of Biotron Limited ('Biotron') are pleased to advise that the attached presentation titled "BIO2019" is being presented at the 2019 BIO International Convention held in Philadelphia, PA, USA. The annual BIO conference provides a unique opportunity to showcase the Company's product pipeline to the international biopharmaceutical industry.

The BIO conference also provides an opportunity to continue discussions with potential partners. As previously advised, the Company is seeking a collaboration or licensing deal with an international pharmaceutical company for late stage clinical development of its HIV-1 eradication program.

As highlighted in the presentation:

- The completed Phase 2 HIV-1 clinical trial demonstrated that Biotron's lead compound, BIT225, demonstrated significant, potentially beneficial immunological changes, not seen in patients only receiving current antiretroviral treatment.
- The results point to a potential role for BIT225 in improving patient health outcomes, as well as in future HIV-1 eradication strategies.
- The results support the ongoing clinical development of this important new class of anti-HIV drug.
- Additional analyses of patient samples from the Phase 2 HIV-1 trial are ongoing, to further characterise the observed immunological changes seen in the trial.
- Biotron's Hepatitis B virus (HBV) program is progressing well, with compounds reducing levels of HBV cccDNA, which is believed to be critical for eradication of this virus. Current treatments suppress virus replication but do not offer a cure.

Yours sincerely



Peter J. Nightingale  
Company Secretary

pjn9940

## **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 a promising preclinical program for 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 Dengue, Ebola, Middle East Respiratory virus, Influenza and Zika viruses.

## **Enquiries**

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**BIOTRON LIMITED**  
**(ASX:BIT)**

**BIO2019**  
Philadelphia, PA



***Biotron***

# 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.



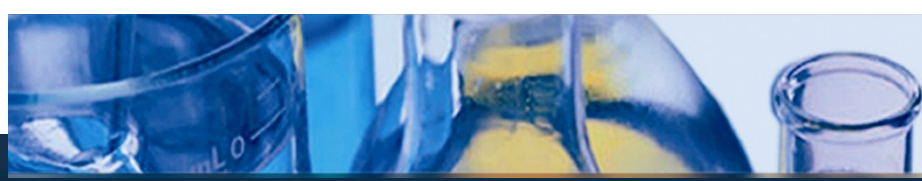
# Biotron Limited - Snapshot

- Spun out from John Curtin School of Medical Research at the Australian National University
- Listed on ASX (ASX:BIT)
- Headquartered in Sydney, Australia

## Board








Michael Hoy	Non-executive Chairman
Michelle Miller	Managing Director
Susan Pond	Non-executive Director
Rob Thomas	Non-executive Director
Stephen Locarnini	Non-executive Director

- Infectious disease focus
- **Pipeline of first-in-class small molecule, viroporin-targeting inhibitors for key viral infections**
- Phase 2 clinical program - HIV-1 eradication
- Preclinical Hepatitis B virus (HBV) program
- Pipeline of earlier stage anti-viral programs including respiratory viruses and Dengue virus





# Pipeline

INDICATION & TARGET PROTEIN	LEAD COMPOUND	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
HIV-1 Vpu	BIT225					
HIV-1 Vpu	Next Generation (Screening)					
HCV p7	BIT225					
HCV p7	BIT314 (next generation)					
HBV	Screening					
Dengue M	Potential Leads Identified					
"Pan" Respiratory (incl Corona, rhino, adeno, RSV)	Screening					





# HIV-1 Eradication

## Current antiretroviral drugs do not cure HIV-1 infection

- Current end points such as plasma viral load are inadequate
- HIV-1 reservoirs set up early, leading to chronic, life-long infection
  - Not sensitive to current anti-HIV-1 drugs
- ***New mode of actions drugs are needed to eradicate or cure HIV-1 infection***

## Why is HIV-1 eradication necessary?

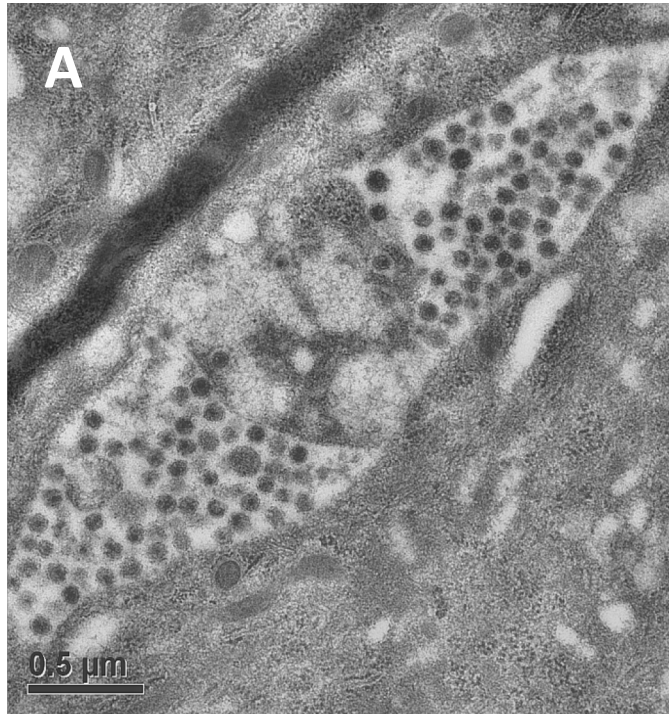
- Long-term health implications e.g. HAND, immune activation, drug-drug interactions
  - Immune activation and inflammation play a more important role among HIV-infected individuals than in the general population
- Compliance issues/drug holidays can lead to viral rebound
- Cost of treatment
  - ~ \$20 billion p.a. world wide
  - Major burden on healthcare systems



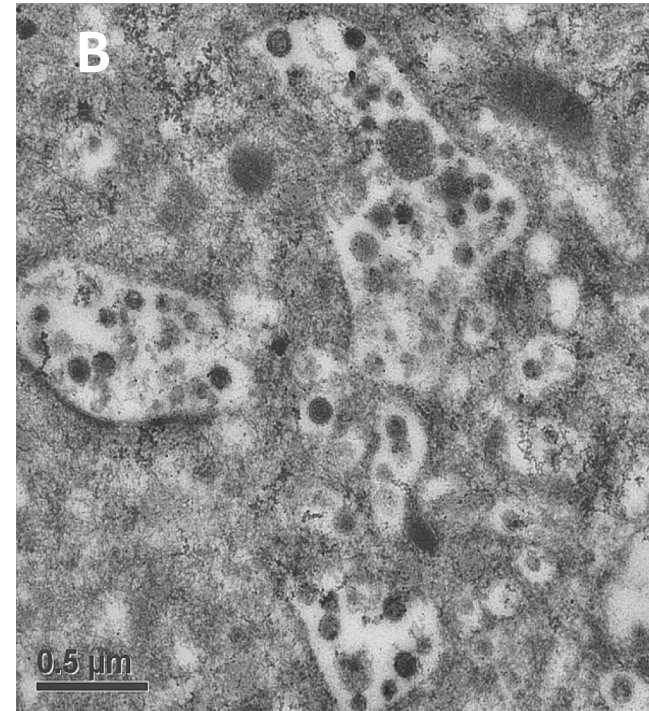


# BIT225 Targets HIV-1 in Reservoir Cells

**BIT225 targets HIV-1 Vpu protein, and inhibits assembly and budding of new virus in macrophage reservoirs**



**(A) Untreated Controls**



**B) BIT225 treated cells**



# BIT225-009 Phase 2 HIV-1 Trial

- Phase 2, 36 subject trial (placebo controlled, double-blinded trial, multisite trial)
  - HIV-1 positive, treatment-naïve commencing ART
  - BIT225 (200 mg once daily) or placebo added to treatment for 12 weeks
  - Completed in 2018

*To determine whether BIT225 has a clinical benefit over and above ART, and provide data to inform the drug's future development path.*



# Results from BIT225-009 Trial

Data from the BIT225-009 trial indicated that the antiviral effect of BIT225 resulted in:

1. Reduced macrophage-specific immune activation (sCD163)

- ***Via reducing infectious virus within this key reservoir, and/or***
- ***Direct effect on HIV-1 Vpu***
  - BIT225 inhibits Vpu function(s) which unmask the blockage of the innate immune system against HIV-1 infection mediated by Vpu

2. Significantly delayed decline in activated CD4 cell levels, suggesting that there may have been:

- Restoration of immune cell function, and/or
- A change in antigen presentation

Analyses of trial samples are ongoing to further characterize the observed immunological changes



# Significance of Results of BIT225-009 Trial

- Provides evidence of potential benefit over and above current approved antiretroviral drugs (ART)
- Evidence of immunological benefits that are not seen in subjects on ART alone
- Support ongoing development of BIT225
  - As a key component of future eradication strategies
  - As an add-in to ART to improve patient health outcomes



# 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





# Hepatitis B Virus

- Biotron compounds appear to have a novel mechanism of action against HBV
  - Antiviral activity results in reduction of **cccDNA** and **HBsAg** levels in robust cell culture assays

*Targeting HBV cccDNA is one of the Holy Grails in the race to HBV cure*

- Lead optimization and selection is in progress
  - Aim is to generate lead compound to progress to the clinic in 2020



# Summary

- Technology core is an antiviral platform with new class of small molecules with broad range of activities
- Demonstrated proof of concept of successful targeting of viroporins with BIT225
  - Significant value has been created, with completed Phase 2 trials
  - Solid package of data to support partnering/licensing for late-stage clinical development
- Promising preclinical HBV program, with evidence of reduction of cccDNA and HBsAg levels in infected cell cultures

**Biotron's Viroporin-targeting platform is an important tool in the development of a new class of direct-acting antiviral therapies with the additional potential to impact on immune activation linked to viral pathogenesis**

