BIOTRON LIMITED (ASX:BIT)

BIO2019 Philadelphia, PA





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, viroporintargeting 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



Viroporins

- Virus-encoded proteins, mainly found in RNA viruses
- Form hydrophilic pores in host cell membranes
- Involved in key stages of the viral cycle, including:
 - Virus entry and uncoating,
 - Transport through cellular compartments, and
 - Maturation, budding and release of infectious virus
- Crucial for viral pathogenicity due to involvement in various steps of virus life cycles
- Evidence that they play a role in innate immune modulation





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	$ \longrightarrow $				
Dengue M	Potential Leads Identified	$ \longrightarrow $				
"Pan" Respiratory (incl Corona, rhino, adeno, RSV)	Screening	\implies				





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 unmasks 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



