BIOTRON LIMITED
(ASX:BIT)

AGM

26 November 2019

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.

Key Achievements 2018/2019 FY

- Completed Phase 2 HIV-1 clinical trial of BIT225 & reported positive results
- **Raised $5.7 million after costs in late 2018, including $4.7 million for 30 Nov '18 $0.06 options**
- Set up a world-class advisory group of international HIV-1 experts in 2H2019
- Focus on translational and commercialisation activities for HIV-1 program
- Setting up technology for Phase 3 and beyond

Phase 2 HIV-1 Clinical Trial - Recap

- BIT225-009 Phase 2 HIV-1 clinical trial:
  - 3 months once a day dosing of BIT225
  - HIV-1-positive, treatment naïve people starting standard antiretroviral drugs
  - Placebo-controlled, double-blind study
- Data from the clinical trial indicated that:
  - BIT225-treated subjects had statistically significant changes in immunological markers compared to those only dosed with standard antiretroviral drugs.
  - Most of these changes were unique i.e. never seen with any other anti-HIV-1 treatments
  - Profound implications for future HIV-1 treatment strategies

Outcomes & Implication from 009 Trial Data

Trial data showed us that something quite extraordinary had happened to the immune system in these patients.

BUT

- *How exactly had BIT225 induced these immunological changes?*
- *What do these changes mean clinically?*
- *What are the implications of this data for use of BIT225 in HIV-1-treatment landscape?*

FOCUS HAS BEEN ON WORKING OUT THE ANSWERS TO THESE QUESTIONS

HIV-1 Challenge

- Biotron is working with a very complex, difficult virus
- Globally, 75 million people have been infected with HIV; 32 million have died of HIV
- ~38 million are currently infected worldwide
- Between 2000 and 2015 over US$560 BILLION was spent globally on HIV/AIDS
- In the history of HIV-1 treatment, only ONE person has ever been “cured”
  - i.e. ***ONE in 75 million cases***

WHY is HIV-1 ERADICATION so HARD

- Current antiretroviral drugs stop the replication of HIV-1 in T cells
- ***BUT there are reservoirs of HIV-1 infection that are not cleared with current drugs***
  - ***Located in sanctuary sites***
  - ***Hidden in non-replicating cells (latently infected T cells)***
  - ***Hidden in macrophages where HIV-1 replicates slowly and with a different method than in T cells***
- Viruses can make changes to cells to avoid immune cell recognition and destruction

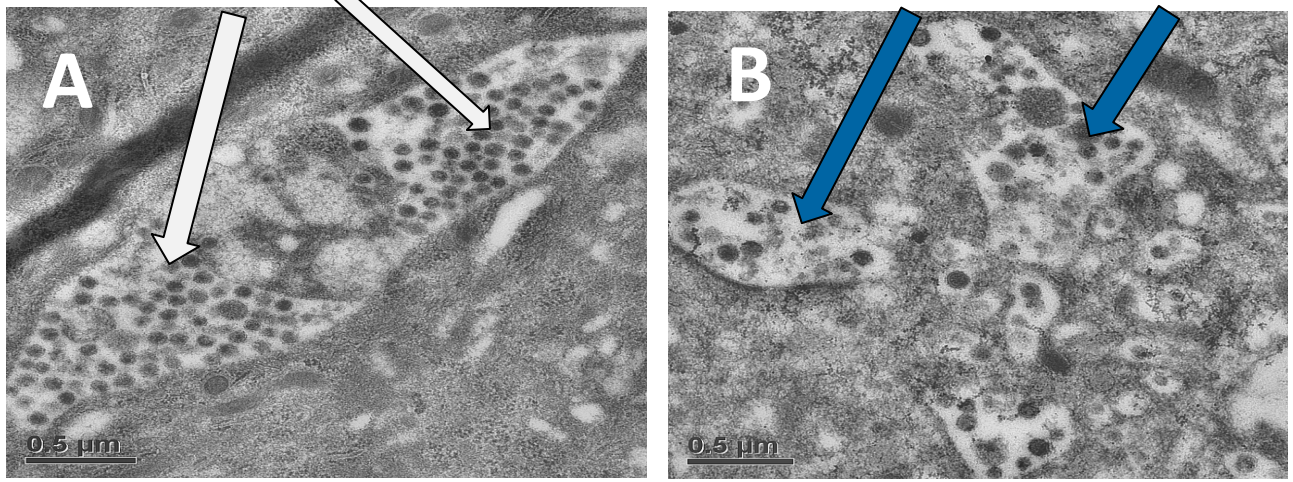
WHY is HIV-1 ERADICATION NECESSARY

- Long-term health implications e.g. HAND, immune activation, drug-drug interactions in an aging population
- Compliance issues/drug holidays can lead to viral rebound
- Cost of treatment
  - ~ $20 billion p.a. world wide
  - Major burden on healthcare systems
- *Those on therapy still suffer from an enhanced risk of morbidities and mortalities that is caused, at least in part by, overactivation of the immune system*

HIV-1 & BIT225

- BIT225 is a new mode of action anti-HIV-1 drug
  - Targets HIV-1 replication/assembly in macrophage reservoir cells

Infectious HIV-1 | **Non-infectious HIV-1**



(A) Untreated Controls | **(B) BIT225 treated cells**

  - Robust, stepwise translational R&D focused on the direct action of BIT225 on HIV-1 in these long-lived cells leading up to the Phase 2 trial

BIT225-009 Phase 2

BIT225 ANTIVIRAL DATA (PRECLINICAL & BIT225-004 PHASE 1B/2A TRIAL)

- Inhibition of HIV-1 in monocyte-derived macrophages (MDMs) (key reservoirs of HIV-1 infection)
- Targets HIV-1 Vpu
- Assembly/budding inhibitor
- Activity against broad range of viral isolates

HOW DOES THIS TRANSLATE INTO IMPROVED CLINICAL OUTCOMES?

BIT225-009

Designed Phase 2 trial to see impact of BIT225 over and above current anti-HIV drugs

HOW HAS BIT225 INDUCED THESE CHANGES?

BIT225-INDUCED IMMUNE CHANGES IN BIT225-009 PHASE 2 TRIAL

- Modification of various T cell responses
- Reduction of inflammatory marker sCD163

Data was unexpected i.e. significant immune changes with a non-vaccine, oral drug treatment

Understanding BIT225-009

- The last 12 months has seen an extraordinary scientific detective investigation to piece together how a small molecule antiviral drug has caused a vaccine-like effect
- Required in-depth understanding of very complex immunology
  - Reviewing relevant HIV-1/immunology literature
  - Consultation with relevant international expert HIV immunologists (KOLs recognised by pharma); discussions with pharma; discussions with academic collaborators
- Developed an hypothesis of how it was happening
- Undertook post-trial detailed, sophisticated laboratory analyses of patient samples to further characterise the changed immune responses in specialist laboratories in the USA and Australia
    - Stepwise, sequential testing of small volumes of limited patient samples to generate a clear, rational, scientifically sound explanation of how the results from BIT225-009 came about

BIT225-009 Data Today

- As a result of this detailed, post-trial analyses, we are forming a clear picture of how BIT225 induced the immune changes and what this means for potential eradication of HIV-1
- The time and effort to do this is of real benefit to the company and its shareholders:
  - This will form the basis of new intellectual property i.e. patent(s), to be filed by the company
    - Patents form tangible, saleable assets at the heart of biotechnology companies
    - Expected to expand the utility and patent life of BIT225 and other related compounds
  - We have continued dialog and engagement with pharma throughout the year, receiving valuable, positive feedback re data and our approach
  - The information is central to designing the next trials through to Phase 3 and beyond to regulatory approvals

Advisory

- We recently established a formal advisory board of the best international HIV-1 experts (all key opinion leaders) to guide and advise the company at this important stage of development
  - Extensive experience in clinical development within HIV-1 treatment and eradication field
  - Recognised and used by pharma as KOLs for HIV-1 drug treatment/eradication programs
  - Their involvement sends a powerful message to potential partners

Next Steps for HIV-1 Program

- Filing new patent(s) based on new information on molecular mechanism of BIT225 in the Phase 2 trial
  - Publication of trial data in peer-reviewed scientific journal(s)
  - Presentation of additional data from post-trial analyses at key international conference(s) in 2020
- Finalise clinical strategy for next stage of development with SAB in 1Q2020
- Development of next generation HIV-1 drugs – this is in progress

HIV-1 Program Summary

- The initial data from the 009 Phase 2 trial showed that BIT225 induced profound, unique changes to the immune system
- After extensive, detailed post-trial laboratory analyses of trial samples we now have an understanding of how BIT225 has generated these positive, vaccine-like changes
  - This information will further strengthen the company's robust intellectual property position
  - The data is key to designing the next stage of clinical development, leading to Phase 3 and regulatory approval processes
- **BIT225 is well positioned to play a central role in HIV-1 eradication**
- **We are focused on a commercial outcome; we are engaged with key pharma and have made excellent progress throughout 2019. BUT it is not a fast process.**

Biotron

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

- Hepatitis B virus (HBV) therapeutic space has generated significant interest from pharma & biotech companies
  - Oct ‘18 – J&J/ Arrowhead in deal worth up to US$3.7 billion
  - Aug 19 – GSK/Ionis Pharmaceuticals HBV antisense deal worth up to US$200 million in milestones
  - Nov 19 – Roche/Dicerna HBV RNAi deal worth up to US$1.5 billion in milestones
- Biotron has several compounds with good activity against HBV
  - Biotron drugs reduce levels of cccDNA as well as other key HBV markers and have a unique MoA
- Expands Biotron’s partnering opportunities – potential for early stage co-development /collaboration agreement

Commercialisation & Outlook for 2019/2020 FY

- *Aim is to achieve commercial outcomes for the company's programs*
  - **Prime focus is partnering the HIV-1 program**
    - Progressing discussions with potential partners
    - Ongoing analyses of clinical trial samples is adding to the data package/IP position
    - Conferring with advisory group to map out late-stage clinical development
  - Hepatitis B (HBV) remains a promising early stage program. Additional resources are being committed to progress this to partner-ready status
- **Multiple partnering opportunities across Biotron's portfolio**
- **Stock has shown that it moves significantly on the back of good news**
- **Strong financial position; exercise of 12 Dec 2019 $0.05 options expected to bring in an additional ~$5.6 million**

Biotron

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