

BIOTRON LIMITED
(ASX:BIT)

Biotech Showcase 2018

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A decorative horizontal bar at the bottom of the slide. It features a dark blue background with a lighter blue and yellow liquid-like graphic on the left side, resembling a stylized wave or a splash of liquid.

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.

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- Biotron is designing, developing and commercialising a platform of antiviral drugs with a novel mode of action – able to target a wide variety of viral infections
- Pipeline of programs in high value, high need markets
- Progress in clinical lead program (BIT225) provides strong validation for entire platform

Biotron Limited – Snap Shot

BROAD PLATFORM WITH NEW CLASS OF ANTIVIRAL DRUGS		
HIV-1 ERADICATION	HEPATITIS C VIRUS (HCV)	HBV & EARLY STAGE PROGRAMS
<ul style="list-style-type: none">- Targeting HIV-1 in long-lived reservoirs- Phase 2 trial in progress during 2017; dosing complete	<ul style="list-style-type: none">- New class of HCV drug- Phase 2 completed- Seeking partnerships in China	<ul style="list-style-type: none">- Pipeline of early stage programs, including:<ul style="list-style-type: none">- Hepatitis B virus- Respiratory viruses- Flaviviruses (Dengue)
ROBUST CLINICAL VALIDATION – COMPLETED 8 CLINICAL TRIALS WITH STRONG SAFETY & EFFICACY OUTCOMES		

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Key Achievements 2017

- Commenced Phase 2 HIV-1 clinical trial of BIT225 and Combination Antiretroviral Therapy (cART) in Feb'17
 - Dosing with BIT225/placebo completed; data pending (anticipated 1Q18)
- Demonstrated significant and accelerated reduction in HIV-1 viral load following addition of BIT225 in humanised mouse model of HIV-1 infection in Feb '17
- Independent Nature publication validated Biotron's approach of targeting HIV-1 in macrophages as a key step in HIV-1 eradication in May '17
- Appointed a Corporate Advisor for China – assisting with executing HCV regional partnering strategy in June '17
- Raised \$1.56 million via rights issue in June '17
- Received \$1.6 million R&D tax refund in Nov '17

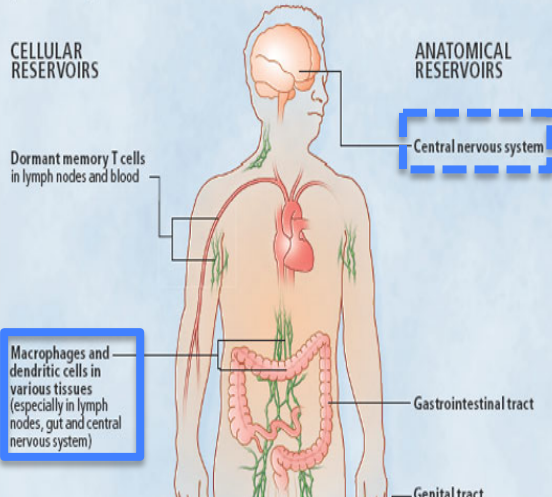


HIV-1 Eradication

[WHERE THE VIRUS HIDES]

HIV'S MANY RESERVOIRS

Beyond lying in wait in dormant memory T cells, HIV may reproduce at a low rate in certain other immune system cells—particularly macrophages and dendritic cells that seem inherently able to ward off immune defenses and anti-HIV drugs to some extent. Further, HIV-infected cells in a few parts of the body may be physically shielded to a degree from the immune system and certain drugs. HIV made in cellular and anatomical reservoirs does not reach the blood readily in aggressively treated patients but might generate a vigorous infection if treatment stops.



Current drugs do not eradicate HIV-1 virus

- HIV-1 remains hidden in reservoirs, leading to chronic, life-long infection
 - Invisible to body's immune defenses
 - Not sensitive to 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
- Cost of treatment
 - ~ \$20 billion p.a. world wide
 - Major burden on healthcare systems

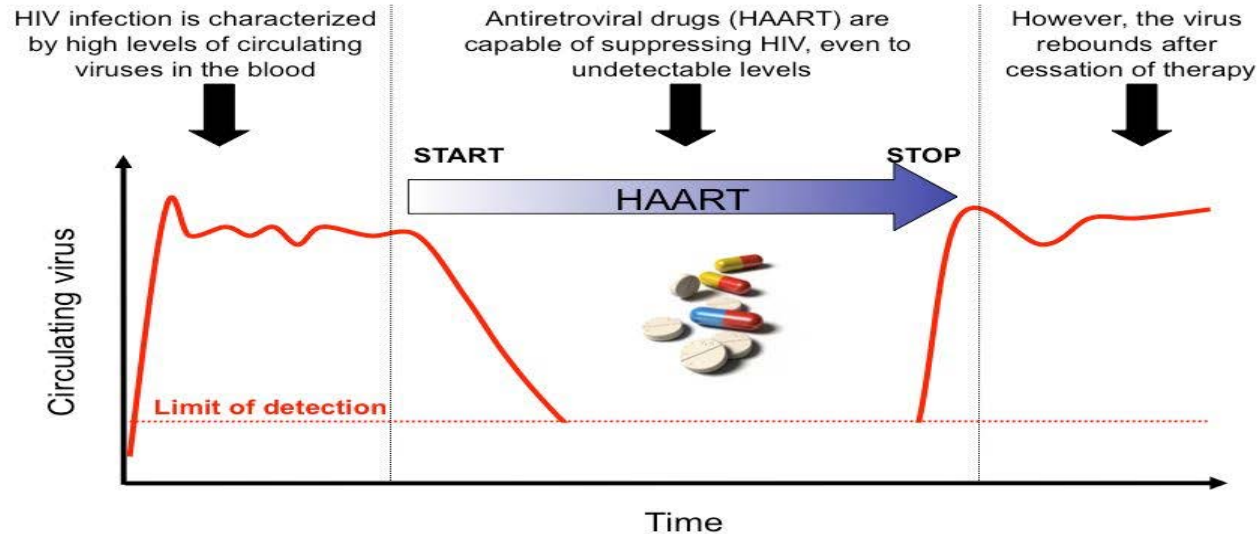
BIT225 has potential to be used in combination with other drugs to eradicate HIV-1 reservoirs

Mario Stevenson
Scientific American **299**, 78 - 83 (2008)

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Current Drugs Do Not Eradicate HIV-1

Current Anti-HIV Drugs do not Eradicate HIV



➡ HIV hides in reservoir that are not sensitive to current therapies

Macrophages are Key HIV-1 Reservoirs

Study published in Nature Medicine in April 2017 confirmed that macrophages are key viral reservoirs

**nature
medicine**

HIV persistence in tissue macrophages of humanized myeloid-only mice during antiretroviral therapy

Jenna B Honeycutt¹, William O Thayer¹, Caroline E Baker¹, Ruy M Ribeiro², Steven M Lada³, Youfang Cao², Rachel A Cleary¹, Michael G Hudgens⁴, Douglas D Richman^{3,5,6} & J Victor Garcia¹

News and Views

HIV persistence in macrophages

Mario Stevenson 

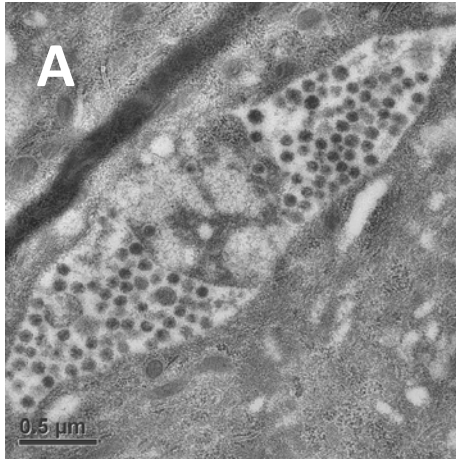
A recent study using a humanized mouse model shows that HIV-1 can persist in macrophages during antiretroviral therapy (ART), and suggests that macrophages may represent an obstacle to efforts to cure HIV-1 infection.

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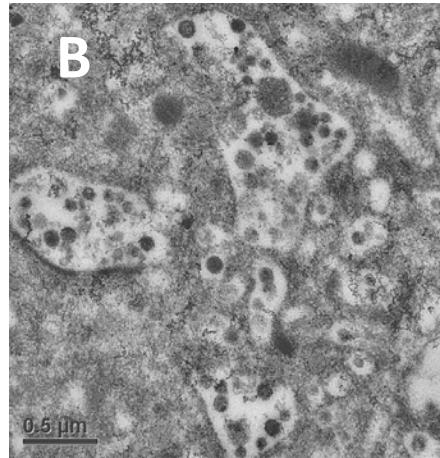


BIT225 Targets HIV-1 in Reservoir Cells

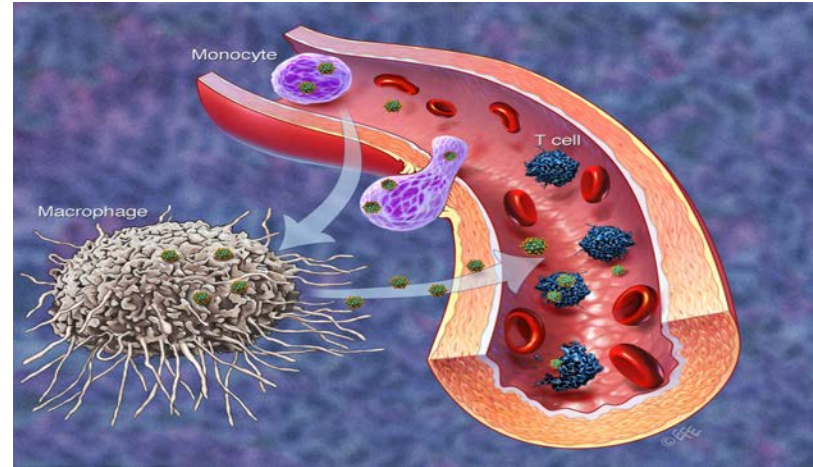
- BIT225 inhibits assembly and budding of new virus in macrophage reservoirs
- Phase 1b/2a trial (004) demonstrated that BIT225 can reduce HIV-1 levels in macrophage cells *in vivo*, paralleling *in vitro* studies (Wilkinson *et al*, J Antimicrob Chemother. 2015)
- Phase 2 trial (009) in progress (BIT225 in combination with ART) during 2017



(A) Untreated Controls



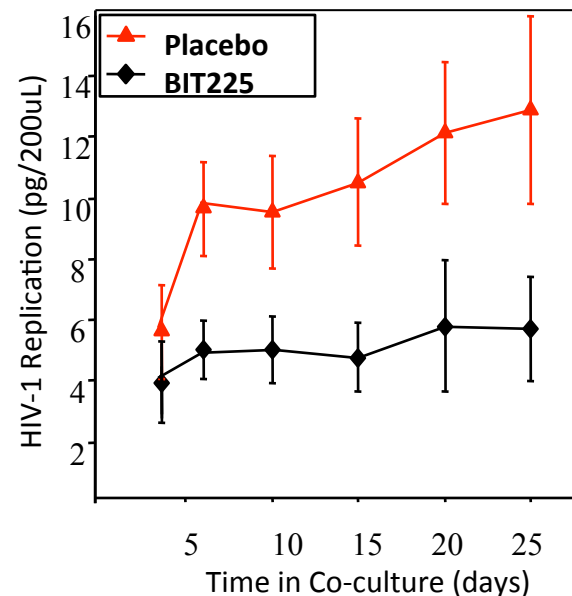
(B) BIT225 treated cells



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BIT225 – Proven Clinical Activity Against HIV-1

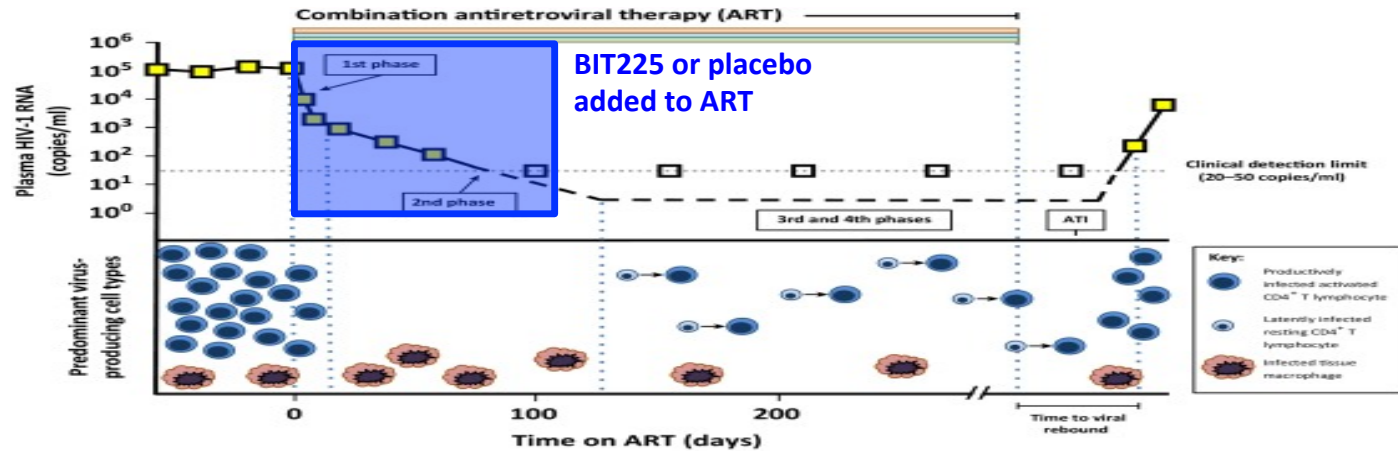
- BIT225-004: Phase 1b/2a randomised, placebo controlled, double-blind trial
 - 21 patients, HIV-1 positive, treatment-naïve; 10 days dosing with BIT225 (monotherapy)
- **Results demonstrated that BIT225:**
 1. **Targets HIV-1 in blood reservoir cells, and significantly reduces virus in these cells**
 2. **Crosses the blood-brain barrier, opening up the possibility of treatment of AIDS-related dementia**
 2. **Reduced myeloid-specific immune activation markers during trial**



Potential role for BIT225:

- Addition to current ART to eradicate key reservoirs, impacting immune activation
- Key component of cure/eradication strategies

HIV-1 Eradication: BIT225-009 Trial



Trends in Molecular Medicine

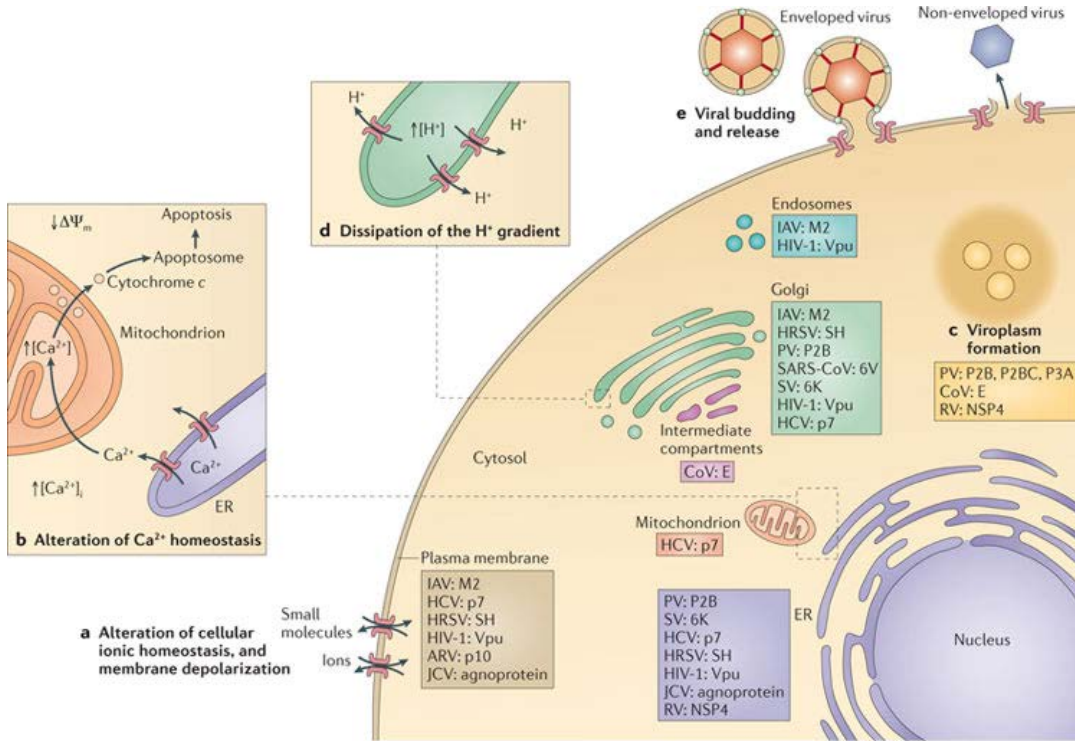
- 36 HIV-1⁺, treatment-naïve subjects commencing ART
- Randomised 2:1 (drug:placebo)
- BIT225 or placebo added to ART for first 12 weeks of treatment
- Read-out
 - Impact on virus levels; reduction of immune activation markers
- **Fully recruited; completed dosing with BIT225/placebo. Anticipate data in 1Q18**

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Biotron – New Approach to Anti-Viral Drug Development

- Core expertise is design and development of a new class of antiviral drugs targeting viral-encoded viroporin proteins
- Viroporins are present in wide range of viruses: Influenza (M2), HIV-1 (Vpu), HCV (p7), Dengue and West Nile (M protein), SARS (E protein) and others
- Broad platform:
 - Rapid, proprietary primary bacterial cell-based screening assays for target proteins
 - Focused library of compounds that target these viral proteins
 - Pipeline of internally-generated, first-in-class small molecule viroporin inhibitors for key markets

Viroporins



- Small hydrophobic proteins with ion channel activity
- Form hydrophilic pores in host cell membranes
- Key stages of the viral cycle such as virus uncoating, transport and maturation are ion-influenced processes in many viral species
- Crucial for viral pathogenicity due to involvement in various steps of virus life cycles
- **Ideal therapeutic targets; exemplified by Biotron's HIV-1 program (BIT225)**

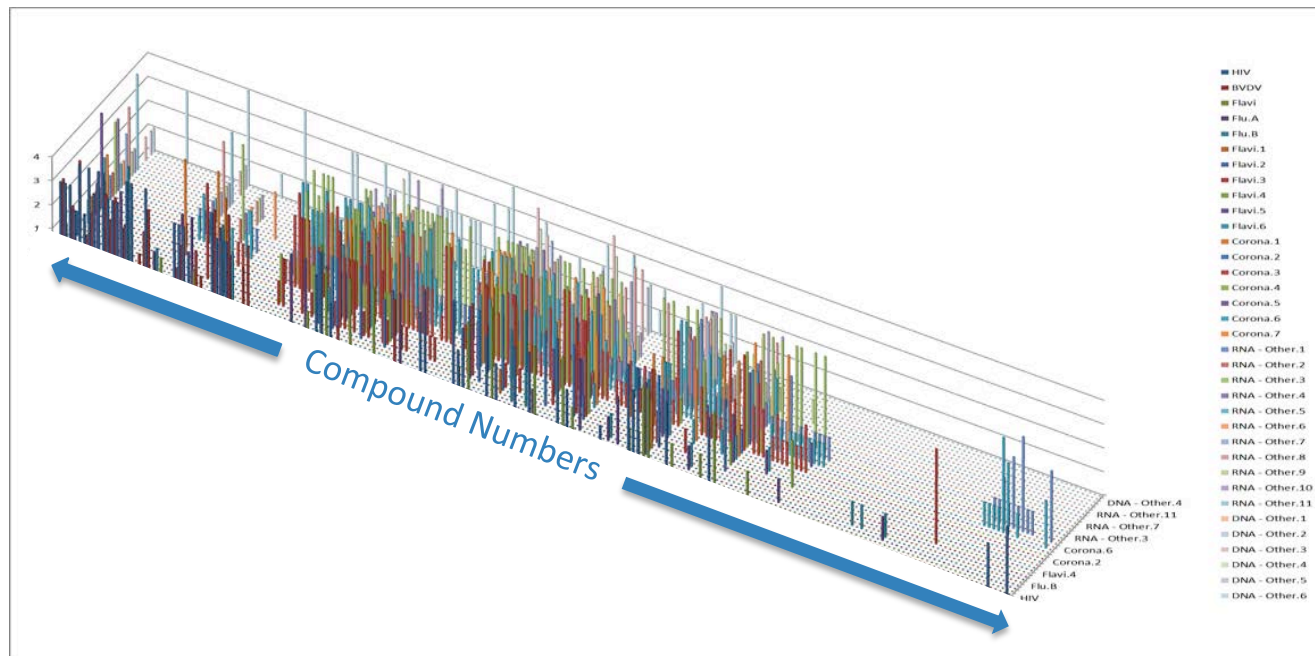
Unlocking Value for Other Virus Targets

Library of compounds designed to target viroporins found in some viruses:

Initially >250 compounds designed and synthesised; library now ~350

OTHER “HITS” IN LIBRARY include:

- Influenza A and B
- Hepatitis B virus (HBV)
- Coronaviruses (Including SARS)
- Epstein-Barr virus (EBV)
- Zika virus
- Dengue virus
- Herpes viruses
- BK virus



Unlocking Value for Other Virus Targets

Biotron's Viroporin approach enables the targeting of a wide range of viral diseases; examples include:

- Respiratory Viruses such as Respiratory Syncytial Virus (RSV), Influenza, & Coronaviruses (leading cause of “common cold”)
- Flaviviruses such as Zika Virus and Dengue
- Transplant viruses such as BK virus
- Epstein Barr virus (EBV) - particular interest in Asia where it is causative agent of Nasopharyngeal Carcinoma

Biotron's Viroporin-targeting platform has the potential to become an important tool in the development of antiviral therapies

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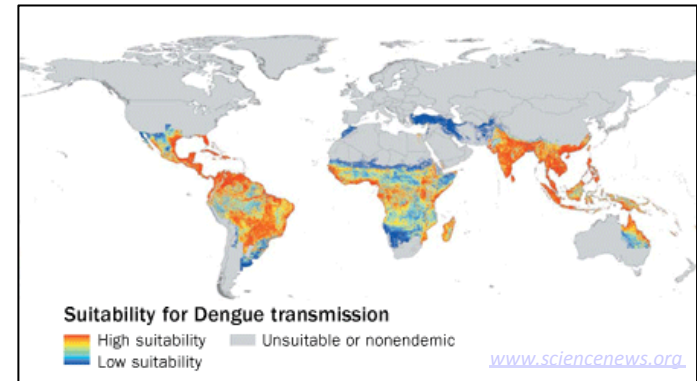
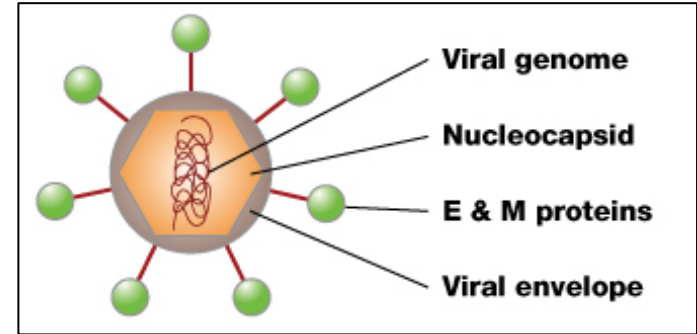
Hepatitis B Virus Program

- Hepatitis B virus (HBV) therapeutic space has significant interest from pharma & biotech companies
- Screening of Biotron's compound library has identified several compounds with activity against HBV
 - ***Screening in Hep G2 and AD38 cell lines, as well as studies in primary human hepatocytes (PHH)***
 - ***In vitro*** data includes evidence of reduction of industry recognised markers, including cccDNA
- Biotron compounds appear to have a novel mechanism of action
 - Potential for use in combination approaches to treatment of HBV
- Expands Biotron's partnering opportunities – potential for early stage co-development / collaboration agreement



Dengue Virus Program

- 2.5 billion people (40% world population) live in areas at risk of Dengue
- ~100 million people infected yearly
- A leading cause of illness and death in tropics and subtropics
- Transmission is by mosquito; most prevention programs target the vector
- No approved Dengue-specific therapeutic drug
- Vaccine trials have had disappointing results
- Biotron is targeting Dengue M protein – Similar target to HIV-1/Vpu and HCV/p7
 - Several compounds with promising activity have been generated; tests are on-going
 - Potential for pan-Flavivirus therapeutic



HCV – Remains an Opportunity

- The new HCV drugs may cause reactivation of HBV in HCV/HBV coinfecting patients
 - Resulted in US FDA “Black Box” Warning on new HCV drugs
- 30 million HCV-infected people in China, compared to 3-5 million in USA
- 93 million chronically infected with HBV in China, compared to 2.2 million in USA
 - High HCV/HBV co-infection rate in China (estimated to be 10 million)
 - Reactivation of HBV has potential to be a major health & economic issue in China
- BIT225 has been shown in clinical trials to significantly improve clinical outcome in HCV GT1-infected patients in combination with Interferon & Ribavirin (IFN/RBV)
- IFN/RBV have several potential advantages over new HCV drugs in some settings
 - IFN/RBV is significantly cheaper than the new HCV drugs
 - HBV reactivation is less common and less severe in HCV/HBV co-infected patients with IFN/RBV
- Seeking partnerships for Biotron’s HCV program in China



Commercialisation and Partnering

- **HIV-1 Program** - Significant value inflection points around HIV-1 program data expected in 2018
- **HCV Program** - BIT225 particularly well suited to Asia, with high numbers of HCV-infected patients including a high proportion of HCV/HBV co-infected patients
- Early stage collaboration opportunities for pre-clinical targets, such as:
 - Hepatitis B
 - Dengue
- Additional development collaboration potential for “other” pharma targets
- Seeking partners for individual targets or entire platform

Corporate Snapshot

Key Financial Metrics

Ticker Code	ASX: BIT
Share Price (09 Jan 18)	A \$0.03
Market capitalisation	A \$11.4 million
12 Month Trading Range	A \$0.016 – 0.046
Shares Outstanding	392 million
Cash Position (09/2017)	A \$0.83 million*
	*Excludes A\$1.6 m R&D tax rebate received in Nov '17

Brief Biotron Overview

- Spun out from John Curtin School of Medical Research at the Australian National University in 1999
- Listed on ASX in Jan 2001 (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

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Investment Highlights

NOVEL ANTIVIRAL PLATFORM

Targeting viroporin proteins with a rapid screening proprietary primary bacterial cell-based platform - a library of over 350 compounds with activity against a range of viruses.

BROAD ANTIVIRAL PIPELINE

Clinical and Preclinical programs in indications with high unmet clinical need or large patient populations such as HIV-1, HCV & Dengue, HBV, Zika & Influenza

ROBUST CLINICAL VALIDATION

Completed 7 human Clinical Trials with promising safety and efficacy outcomes

STRONG INTELLECTUAL PROPERTY POSITION

Portfolio of patents and patent applications directed to the Company's anti-viral drug portfolio

Biotron

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