

10 May 2018

The Manager Companies  
ASX Limited  
20 Bridge Street  
SYDNEY NSW 2000

(23 pages by email)

Dear Madam

### **RENOUNCEABLE RIGHTS ISSUE**

- **Renounceable rights offered at 1.5 cent per share to raise up to \$1.47 million.**
- **1 attaching option (5 cent expiring 12 December 2019) offered for every new share to be listed.**
- **Partially underwritten up to \$800,000.**
- **Directors will participate in the rights issue.**
- **Attractive pricing – 42% discount to 1 month VWAP of 2.6 cent.**
- **Shareholders can renounce their rights or apply for additional shares and attaching options.**
- **Rights to start trading from 15 May 2018.**

**Sydney, Australia, 10 May 2018** – Australian drug development company Biotron Limited (ASX:BIT) today announced a partially underwritten renounceable rights issue to raise up to approximately \$1.47 million. Net proceeds, in conjunction with existing cash reserves, will be used:

- For expansion of the Company's Hepatitis B virus (HBV) program, including testing of promising compounds in new models of infection.
- Continued evaluation of additional Biotron compounds against an expanded range of viral diseases including respiratory viruses, Dengue virus, and others.
- For commercialisation and negotiation activities, legal fees, travel and personnel costs.
- For general working capital.

The offer of securities will be made to eligible shareholders on the basis of one (1) new share and one (1) attaching listed option for every four (4) existing shares held on the record date (16 May 2018) at an issue price of 1.5 cent per share, which represents a 42% discount to the 1 month volume weighted average price (VWAP) of 2.6 cent.

Shareholders will be given the opportunity to apply for additional securities in excess of their entitlement, however, allocations are not guaranteed. The issue is renounceable and shareholders will be able to guarantee an increase to entitlements by the purchase of additional rights.

Directors have indicated they intend to participate in some or all of their entitlement under the rights issue.

CPS Capital Group Pty Ltd acts as Lead Manager and the Underwriter.

The proposed timetable\* for the offer is as follows:

Shares trade ex-entitlement (Ex Date) Rights trading starts	15 May 2018
Record date to determine Entitlements (Record Date)	16 May 2018
Prospectus with Entitlement and Acceptance Form dispatched Offer opens for receipt of Applications	21 May 2018
Rights trading ends	30 May 2018
Deferred settlement trading starts	31 May 2018
Closing date for acceptances	6 June 2018
Notify ASX of under-subscriptions	12 June 2018
Issue of New Shares Deferred settlement trading ends	14 June 2018
Dispatch of shareholding statements	14 June 2018
Normal trading of New Shares expected to commence	15 June 2018

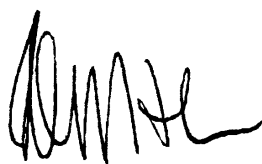
\*The above timetable is indicative and may change, subject to the Corporations Act and Listing Rules.

A prospectus for the offer and a personalised entitlement and acceptance form will be sent to eligible shareholders in accordance with the above timetable. Furthermore, from 21 May 2018, eligible shareholders can view their personalised entitlement and acceptance form online at [www.investorcentre.com](http://www.investorcentre.com).

Shareholders should consider the disclosure document in deciding whether to acquire the securities. Anybody wanting to acquire securities will need to complete the application form that will be in or will accompany the disclosure document.

This announcement lifts the trading halt entered on 8 May 2018.

Yours sincerely



Peter J. Nightingale  
Company Secretary

#### **Enquiries**

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### **About Biotron and BIT225**

A presentation on the Company's activities is attached.

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.

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

**Investor Update, May 2018**

*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

- 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 validation for Biotron's broader antiviral 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"><li>- Targeting HIV-1 in long-lived reservoirs</li><li>- Phase 2 trial complete; data anticipated mid-2018</li></ul>	<ul style="list-style-type: none"><li>- New class of HCV drug</li><li>- Phase 2 completed</li><li>- Seeking partnerships in China</li></ul>	<ul style="list-style-type: none"><li>- Pipeline of early stage programs, including:<ul style="list-style-type: none"><li>- Hepatitis B virus</li><li>- Respiratory viruses</li><li>- Flaviviruses (Dengue)</li></ul></li></ul>
CLINICAL VALIDATION – COMPLETED 8 CLINICAL TRIALS WITH GOOD SAFETY & EFFICACY OUTCOMES		

*Biotron*

# Key Recent Achievements

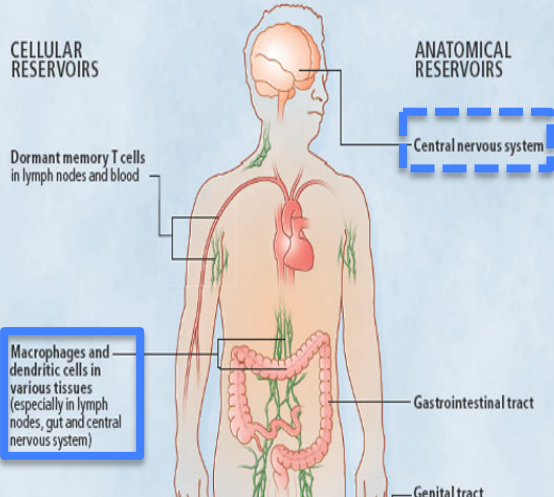
- Phase 2 HIV-1 clinical trial of BIT225 and Combination Antiretroviral Therapy (cART) complete
  - Post-trial analyses of patient samples in progress; data pending (anticipated mid-2018)
- BIT225 demonstrated significant and accelerated reduction in HIV-1 viral levels in a humanised mouse model of HIV-1 infection
- Independent Nature publication validated Biotron's approach of targeting HIV-1 in macrophages as a key step in HIV-1 eradication
- Compounds with good activity against Hepatitis B Virus (HBV) identified
  - Reduce levels of key HBV proteins; compounds appear to target a critical part of the HBV life cycle

# 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

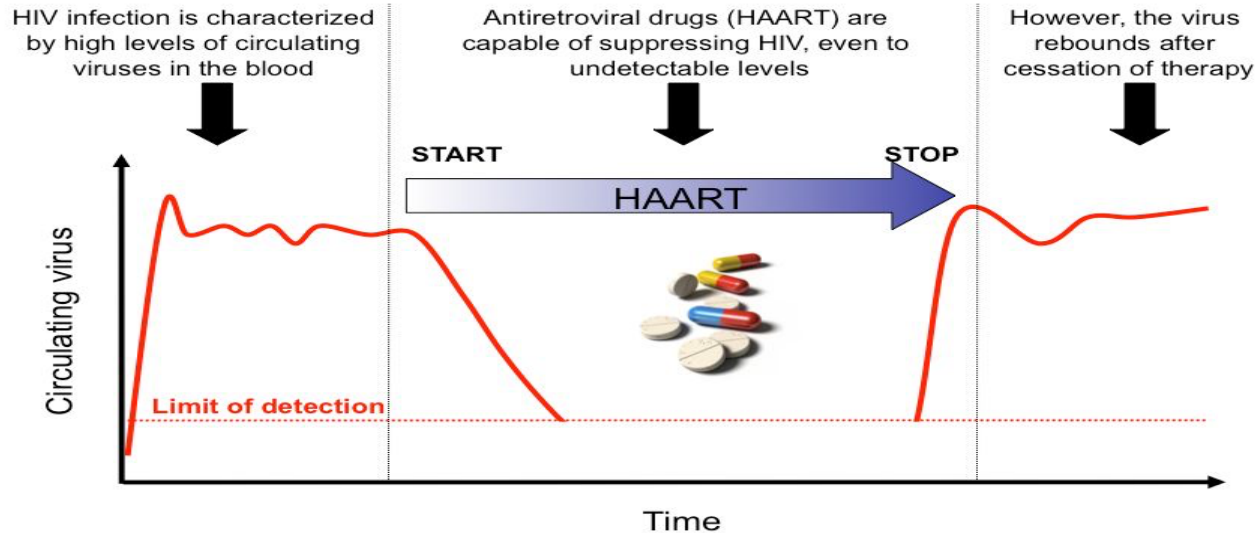
**BIT225 has potential to be used in combination with other drugs to eradicate HIV-1 reservoirs**

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 Honeycutt<sup>1</sup>, William O Thayer<sup>1</sup>, Caroline E Baker<sup>1</sup>, Ruy M Ribeiro<sup>2</sup>, Steven M Lada<sup>3</sup>, Youfang Cao<sup>2</sup>, Rachel A Cleary<sup>1</sup>, Michael G Hudgens<sup>4</sup>, Douglas D Richman<sup>3,5,6</sup> & J Victor Garcia<sup>1</sup>

News and Views

## HIV persistence in macrophages

Mario Stevenson 

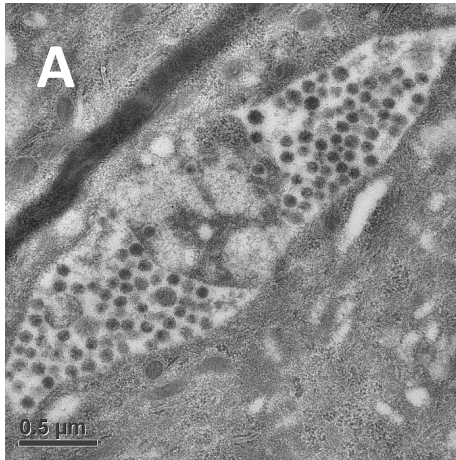
**A recent study using a humanized mouse model shows that HIV-1 can persist in macrophages during antiretroviral therapy (ART), and suggests that macrophages may represent an obstacle to efforts to cure HIV-1 infection.**

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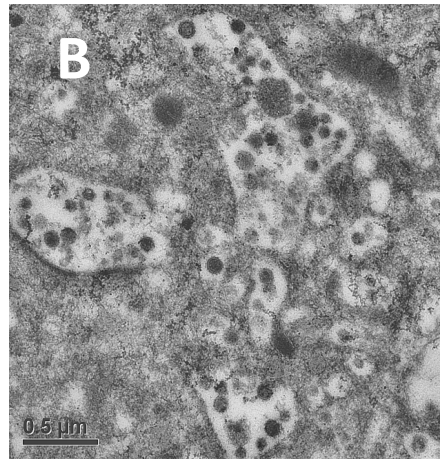


# BIT225 Targets HIV-1 in Reservoir Cells

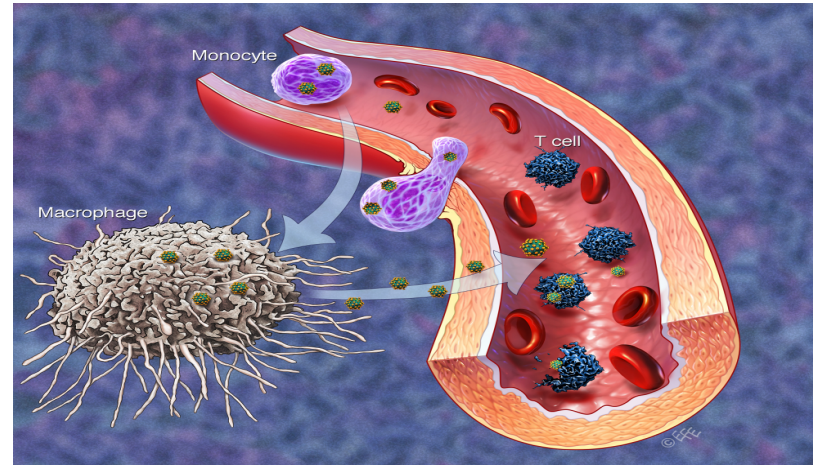
- BIT225 inhibits assembly and budding of new virus in macrophage reservoirs
- Phase 1b/2a trial (004) demonstrated that BIT225 can reduce HIV-1 levels in macrophage cells *in vivo*, paralleling *in vitro* studies (Wilkinson *et al*, J Antimicrob Chemother. 2015)
- Phase 2 trial (009) complete (BIT225 in combination with ART); data anticipated mid-2018



(A) Untreated Controls



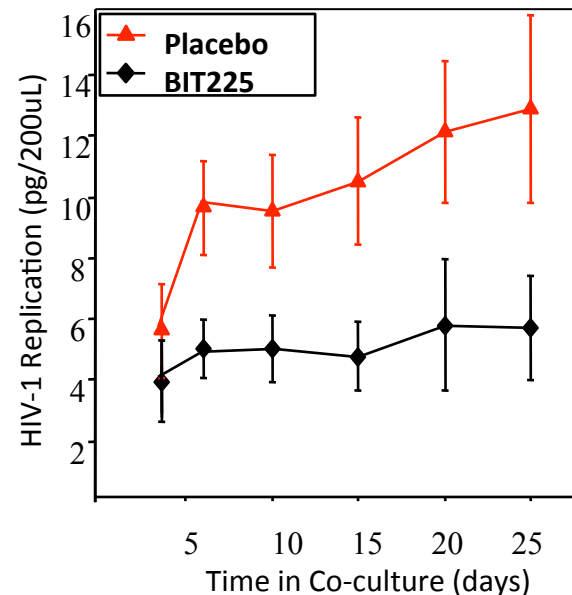
(B) BIT225 treated cells



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# BIT225 – Proven Clinical Activity Against HIV-1

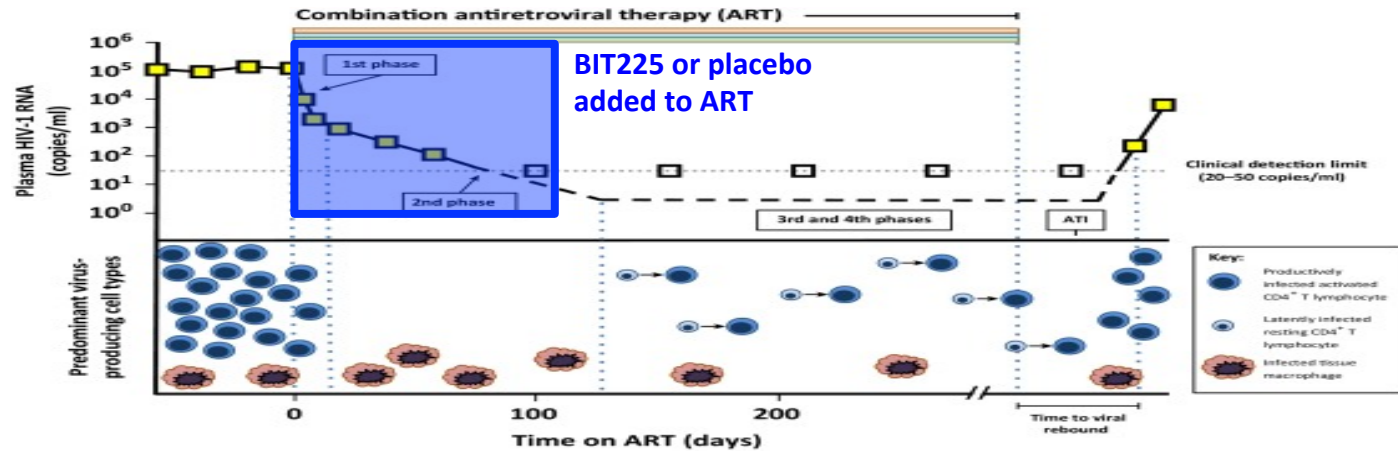
- BIT225-004: Phase 1b/2a randomised, placebo controlled, double-blind trial
  - 21 patients, HIV-1 positive, treatment-naïve; 10 days dosing with BIT225 (monotherapy)
- **Results demonstrated that BIT225:**
  1. **Targets HIV-1 in blood reservoir cells, and significantly reduces virus in these cells**
  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

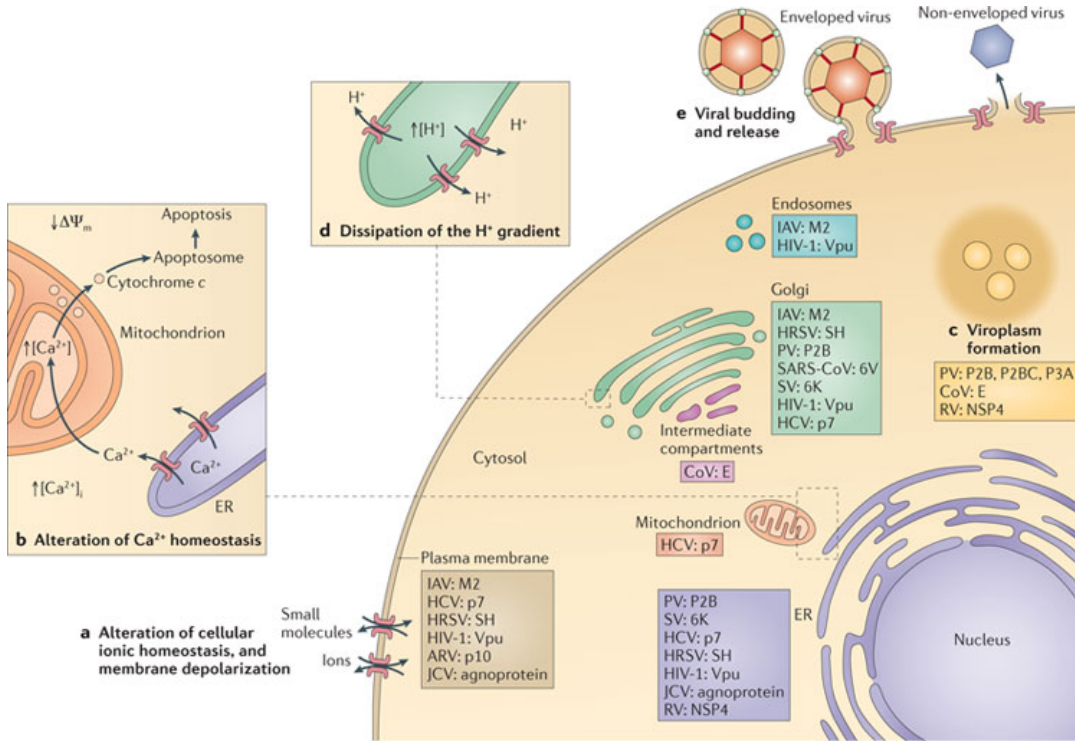
- 36 HIV-1<sup>+</sup>, treatment-naïve subjects commencing ART
- Randomised 2:1 (drug:placebo)
- BIT225 or placebo added to ART for first 12 weeks of treatment
- Read-out
  - Impact on virus levels; reduction of immune activation markers
- **Fully recruited; completed dosing with BIT225/placebo. Anticipate data mid-2018**

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# Biotron – New Approach to Anti-Viral Drug Development

- Focused on the 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

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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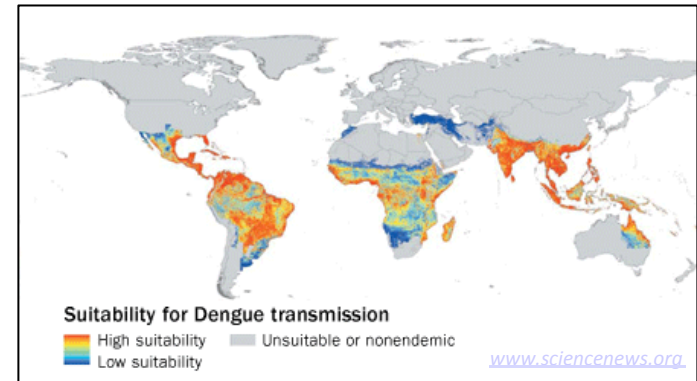
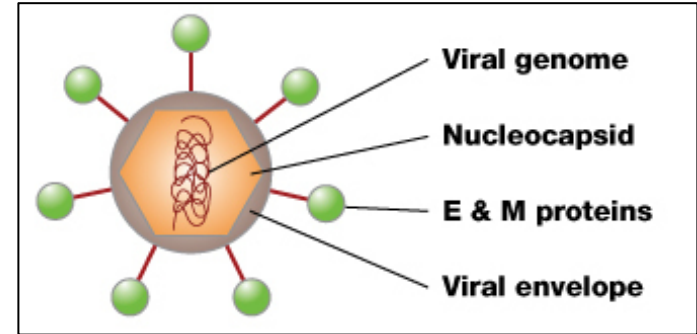


# Hepatitis B Virus Program

- 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

# 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** - 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

# Investment Highlights

## VIROPORIN-TARGETING 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

## CLINICAL VALIDATION

Completed 8 human Clinical Trials with promising safety and efficacy outcomes; 1 additional trial recently completed with data pending (mid-2018)

## INTELLECTUAL PROPERTY POSITION

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

*Biotron*

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