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28 November 2024

The Manager Companies ASX Limited 20 Bridge Street SYDNEY NSW 2000

(20 pages by email)

Dear Madam,

#### PRESENTATION TO ANNUAL GENERAL MEETING

I attach a Chairman's Address and a PowerPoint presentation to be delivered at today's Annual General Meeting which is convened to be held at 11.00 am.

This announcement has been approved by the Company's Managing Director.

Yours faithfully

Peter J. Nightingale Company Secretary

pjn12420



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#### CHAIRMAN'S ADDRESS TO THE AGM

Again, welcome ladies and gentlemen.

At last year's AGM we discussed, at length, the Company's then recently completed trio of clinical trials. We believed, based on timelines from previous trials, that results would soon follow. In fact, we suggested they were imminent. That word 'imminent' is now permanently barred from Company discourse.

The trials were, as stated, complex. The analysis process was, as stated, also complex. In fact, far more complex and time consuming than anticipated. This process is conducted by qualified and independent third parties. Unfortunately, they, in turn, were overwhelmed by the number of clinical trials in post-COVID catch-up mode. Despite all efforts, nothing could be done to accelerate outcomes.

Frustration was widespread. Particularly so amongst Biotron shareholders. Crucially, primary endpoints in two of our three trials were not met. This does not mean the trials failed. Indeed, they did not. Clinical trial success is measured in many ways, as will be discussed further in the Managing Director's report. Nevertheless, questions remain and we are endevouring to find answers. At this meeting every opportunity will be offered to shareholders to better understand the results of the trials.

Commercialisation remains our primary objective. We remain in contact with major companies in the field. As you will have seen, we have also engaged a US-based consulting group to conduct a worldwide search for potential partners.

Today's meeting marks the resignation and departure of Stephen Locarnini and Susan Pond, two highly valued and long-standing directors of this Company.

Stephen faces a daunting health struggle and we sincerely wish him well in the difficult days ahead.

Susan is stepping down from all formal governance roles to focus on personal responsibilities.

I thank them both for their enduring support and unwavering efforts on the Company's behalf over the past several years. Both will be greatly missed.

In closing, I wish to thank Biotron's small team of management, staff, consultants, advisors and fellow directors for their tireless efforts over the past, testing, 12 months.

It is my intention to now move to the business of the meeting after which I shall invite our CEO, Michelle Miller, to deliver the Managing Director's report.

We will allow as much time as is needed for questions.

Sincerely

Michael J. Hoy

Chairman

# ANNUAL GENERAL MEETING

**ASX:BIT** 

28 November 2024





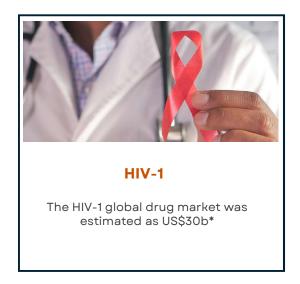
## **Forward Looking Statements**

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

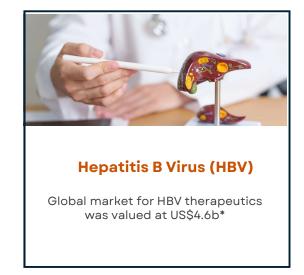
### Biotron

# Industry-leading experts focused on transformative viral treatments

- Experienced Board & Management team with pharma, finance and VC backgrounds
- Clinical stage company with portfolio of small molecule drugs targeting viral diseases with major health problems and large international markets









## 2024 in Review

- Readout of the results from three Phase 2 clinical trials
  - This is a remarkable achievement for any organisation in a relatively short period of time
- Progressed early-stage programs
  - Hepatitis B virus
  - Dengue virus
- Progressed next-generation drugs for HIV-1 and SARS-CoV-2 programs
- Focus is on achieving a commercial outcome



# BIT225-010 and -011 Phase 2 HIV Clinical Trials Met Primary End Points

## 01

Results from these two trials further our understanding of BIT225

## 02

Unique mechanism that combines immunomodulation combined with direct acting antiviral activity

 Current anti-viral drugs have direct acting antiviral activity i.e. stop viruses replicating, but do not on impact on the effect that viruses have on the immune system.

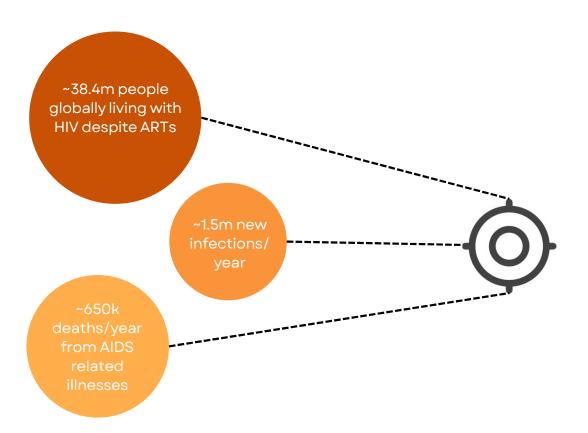
## 03

# Implications go beyond the Company's HIV Program

 The results provide evidence that targeting viroporins, found in a wide range of viruses, has the potential to translate into clinically meaningful outcomes.



## Why HIV-1?



The increased prevalence of HIV-1 infections, % of patients on treatment due to improved disease awareness and the need for treatments to improve quality of life are expected to drive market growth to over US\$50b by 2030

An estimated one third of the ART-treated HIV-infected population achieves only partial immune reconstitution

This population is at increased risk for serious comorbid conditions including neurocognitive, cardiovascular, renal and hepatic disorders that impair quality of life and drive healthcare expenditures.



# BIT225-010: Phase 2 Trial in Naïve, Acutely Infected HIV Population - OVERVIEW

BIT225 or placebo added to cART in HIV-positive individuals commencing cART treatment (n=27, randomised 2:1)

BIT225/cART or placebo/cART dosing continued for 24 weeks. At conclusion, everyone continued on cART

### Parameters measured throughout:

- Safety and tolerability
- Viral loads
- Immune cells, markers, cytokines etc to assess potential immunomodulatory activity of BIT225

Trial was run at several sites in Thailand



# BIT225-010: Phase 2 Trial in Naïve, Acutely Infected HIV Population – OUTCOMES vs OBJECTIVES

#### PRIMARY OBJECTIVES

1. Safety and tolerability

- 2. Impact on virus levels levels than
- 3. Change of immune cells, immune markers, etc

### **OUTCOMES**

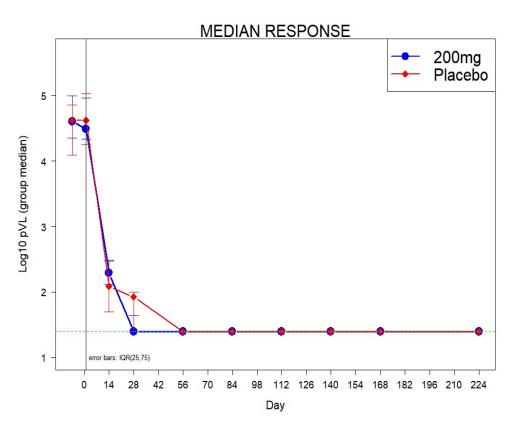
- Safe and generally well tolerated
- No deaths or drug-related SAEs
- AEs were similar to those seen in previous trials

BIT225/cART cohort had a faster decline in virus those on placebo/cART.

Statistically significant differences were observed between the two cohorts for several immune cell subpopulations/ markers/ cytokines



## BIT225-010 HIV-1 Phase 2 Trial – Reduction in Viral Loads Are Faster in BIT225 Group



- BIT225-treated cleared virus faster than those on ART alone
  - 72% of BIT225/ART group vs 33% of placebo/ART reached limited of detection by day 28
- Rate of decline of virus levels in critical second phase of decay was statistically higher in BIT225/ART group vs placebo/ART



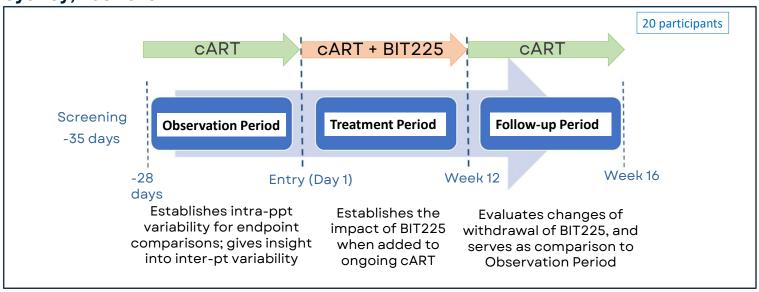
## **BIT225-010 HIV-1 Phase 2 Trial - Conclusions**

- The changes seen when BIT225 is added indicate that the drug has induced statistically significant changes in specific immune cell populations, markers, and cytokines.
- The immune results are consistent with those seen in earlier trials and suggest a
  possible immune modifying effect of BIT225 when used with cART.
- The blood (plasma) viral load data suggests that BIT225 is having an impact on a critical phase of viral decay when latent reservoirs are established.



# BIT225-011: Phase 2 Trial in Treatment-Experienced Immune Non-Responders

First time BIT225 has been trialed in this at-risk HIV population. Trial was run at sites in Sydney, Australia



#### Parameters measured throughout:

- Safety & tolerability
- Plasma viral loads
- Broad range of immune cell subtypes, cytokines, inflammation markers, cell activation and exhaustion markers to assess potential immunomodulatory effects of BIT225



# BIT225-011: Phase 2 Trial in Treatment-Experienced Immune Non-Responders – OUTCOMES vs OBJECTIVES

### PRIMARY OBJECTIVES

1. Safety and tolerability

2. Viral markers

3. Change of immune cells, immune markers, etc

### **OUTCOMES**

Safe and generally well tolerated No deaths or drug-related SAEs AEs were similar to those seen in previous trials

All participants maintained viral suppression throughout study

Statistically significant changes were observed for several immune subpopulations/markers/cytokines during the Treatment period compared to the initial Observation period.

### CONCLUSIONS

The changes seen when BIT225 is added indicate that the drug has induced statistically significant changes in specific immune cell populations, markers, and cytokines.

This HIV population is not well served with current cART; new mode of action drugs are needed to improve numbers and activity of immune cells and markers, leading to clinical benefits.



## **COVID-19 Clinical Program**

In 2022 BIT's lead antiviral drug was shown to:

- Prevent COVID-19,
- · Reduce virus levels, and
- Stop the cytokine storm in a relevant, robust, industryrecognised animal model of disease

As BIT225 had been tested in humans for other viral diseases it could move quickly into clinical testing, with the BIT225-012 trial commencing in May 2023

At that time there were limited treatment options, uncertainty around the robustness of vaccine-generated immunity, and concern regarding the emergence of new SARS-CoV-2 variants





## BIT225-012: Phase 2 COVID-19 Clinical Trial

#### PRIMARY OBJECTIVES

- 1. Safety and tolerability
- 2. Efficacy assessed by nasal viral loads

## **CONSIDERATIONS**

### **OUTCOMES**

- Safe and generally well tolerated
- No deaths or drug-related SAEs
- AEs were similar to those seen in previous trials

No statistically significant differences between drug and placebo groups based on change in SARS-CoV-2 nasal viral load, kinetics of change or time to negative SARS-CoV-2 PCR when compared to baseline values on Day 1 to dosing completion on Day 7.

However, *post hoc* analyses that excluded patients who did not have quantifiable nasal loads on Day 1 indicated that viral loads leveled off after Day 6 in placebo cohort while continuing to decline in BIT225-treated cohort.

- Overlap of BIT225 AEs and SARS-CoV-2 symptoms made assigning causality and efficacy difficult
- The high rate of community immunity to SARS-CoV-2 due to vaccination and natural infection makes determination of efficacy of new drugs challenging.
- Anyone deemed at risk of severe COVID or presenting with severe symptoms was excluded from the trial due to existence of an approved available treatment that could not be ethically withheld.
- Our animal model data remain compelling and among the best reported



## **EARLY-STAGE ANTIVIRAL PROGRAMS**

- Biotron remains focused on its platform of viroporin antagonists which uniquely combine direct-acting antiviral and immunomodulatory activities across numerous viruses responsible for important human disease.
- The results from BIT225 have important implications for Biotron's other antiviral programs targeting other viruses as they support the druggability of this new class of drugs
- Good progress continued with early-stage programs, in particular Hepatitis B virus and Dengue virus



## **SUMMARY**

- Preliminary analyses indicate that both HIV trials achieved their primary objectives
  - The data supports previous findings that BIT225 uniquely combines direct-acting antiviral and immunomodulatory activities
- The challenge for HIV therapies is demonstrating *clinical* benefit over and above current cART
  - Regulatory agencies e.g. FDA have been focused to date on direct-acting antiviral drugs
  - Pathways for immunomodulatory agents for viruses have lagged
  - BIT225-010 and BIT225-011 are important steps in the path to development of viroporin inhibitors as a new drug class BUT there is a high hurdle for new classes of drugs
- The results from BIT225 have important implications for Biotron's other antiviral programs targeting other viruses as they support the druggability of this new class of drugs
- Focus remains on achieving commercial outcome(s) for the Company's assets and programs
- The US-based C14 Consulting Group, LLC has been appointed to work with Biotron to refine its commercialisation strategy and provide business development support at this important time



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