

Level 2, 66 Hunter Street  
Sydney NSW 2000  
Tel: (61-2) 9300 3344  
Fax: (61-2) 9221 6333  
E-mail: [pnightingale@biotron.com.au](mailto:pnightingale@biotron.com.au)  
Website: [www.biotron.com.au](http://www.biotron.com.au)

26 September 2023

The Manager Companies  
ASX Limited  
20 Bridge Street  
Sydney NSW 2000

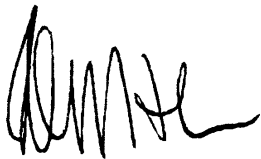
(3 pages by email)

Dear Madam

**SHAREHOLDER UPDATE**

In accordance with Listing Rule 3.17, I attach a copy of a document as sent to the Company's shareholders.

Yours sincerely



Peter J. Nightingale  
Company Secretary

pjn11877



September 2023

Dear Shareholders

I am pleased to report that Biotron is in the final stage of three Phase 2 clinical trials for HIV-1 and COVID-19. This is a pivotal time for the Company as it completes data collection and analyses of samples and information collected during the trials ahead of release of headline data in coming weeks.

Phase 2 trials provide key value inflection points. They are designed to provide information on safety and efficacy of new therapies and to demonstrate to potential partners and regulatory agencies how drugs may be used to treat specific diseases.

Biotron expects to have data from three such trials available in the very near term which puts the Company in a very strong position. These data, if positive, will be central to successfully negotiating and completing a commercial transaction for the Company's HIV-1 and COVID-19 clinical programs.

### **Two HIV-1 Phase 2 Clinical Trials**

BIT225 uniquely combines antiviral activity with immune enhancement. The two HIV-1 Phase 2 trials were designed to assess the impact of BIT225 on immune biomarkers in two groups of HIV-positive individuals.

The BIT225-010 trial included people newly diagnosed as being HIV-1 positive and commencing anti-retroviral treatment (ART) for the first time. The BIT225-011 trial enrolled people who had been taking ART for several years but had not achieved full immune reconstitution.

The data collected during these two HIV-1 trials are expected to characterise and extend the positive findings from previous trials in which BIT225 had positive effects on key immunologic markers of improved health outcomes.

Despite the availability of effective ART, the prevalence of HIV-1 infections continues to grow. In 2021, 38.4 million people globally were living with HIV, 1.5 million were newly infected with the virus and an estimated 650,000 people died from AIDS-related illnesses.

The global HIV drug market in 2021 was estimated to be US\$30 billion. The increased prevalence of HIV-1 infections, percentage 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\$50 billion by 2030.

### **COVID-19 Phase 2 Clinical Trial**

In addition to its unique clinical activity against HIV-1, BIT225 has shown very good activity against SARS-CoV-2 and prevented development of disease in a COVID-19 mouse model. SARS-CoV-2-infected mice quickly die from respiratory disease very similar to human COVID-19.

BIT225 very efficiently reduced levels of SARS-CoV-2 virus in mice and stopped the life-threatening cytokine storm. BIT225-treated mice did not develop any signs of disease and remained healthy throughout the several studies that were conducted.

On the basis of these animal studies, Biotron commenced a Phase 2 trial of BIT225 for COVID-19 in May this year. The trial was very quickly enrolled and the clinical phase completed in August. We are now completing laboratory and other data analyses, ahead of the anticipated release of headline data in coming weeks.

There is an international focus on preparation for future pandemics and new classes of effective, safe treatments for coronaviruses such as SARS remain high on the list of viruses of interest.

#### **Publication of BIT225 COVID-19 Animal Data**

The importance of Biotron's COVID-19 program is highlighted by the recent publication of a peer-reviewed paper containing mouse data in a prestigious journal.

The peer-reviewed paper, entitled "Post-infection treatment with the E protein inhibitor BIT225 reduces disease severity and increases survival of K18-hACE2 transgenic mice infected with a lethal dose of SARS-CoV-2" has been published as an open access online article in PLoS Pathogens. The paper, written in collaboration with international scientists in the USA and Denmark, underscores the high efficacy of BIT225 and its potential to treat COVID-19.

A link to the article can be found on Biotron's website homepage at [www.biotron.com.au](http://www.biotron.com.au).

The three current Phase 2 trials for HIV-1 and COVID-19 are the culmination of years of careful, stepwise, iterative, commercially focused drug development. All activities have been undertaken with the sole purpose of obtaining convincing data for potential partners and international regulatory agencies. The Company has engaged with both of these audiences throughout the development of the Company's lead antiviral drug BIT225.

Biotron has allocated considerable resources into the development of BIT225. Development hurdles for any first-in-class drug are high. But we believe BIT225 is close to the finish line.

Throughout 2023, Biotron has been focused on its clinical programs. However, the Company has continued its work to develop new, next-generation drugs for Biotron's HIV-1 and COVID-19. These follow-on drugs will provide additional value and further de-risk the Company's antiviral portfolio.

The Company has also continued its research to develop a new class of drug to treat Hepatitis B virus (HBV). We have designed and tested a series of compounds with very promising activity against this important virus and which will shortly be assessed in an animal model of disease. HBV treatment is an unmet medical need of commercial interest.

Biotron is aware of shareholder interest in the progress of the clinical trials. It is, however, imperative that the remaining laboratory work is completed with all attention to detail and in accordance with international guidelines for undertaking such studies. They are complex and require careful handling in specialised facilities here in Australia and overseas. The work is in its final stage and everyone associated with the trials is focused on completing the analyses as fast as possible. Release of headline data is expected in coming weeks.

I'd like to remind you to ensure that your contact details and communication preferences are kept up to date via Computershare as we head toward this year's AGM. Contact details for Computershare are available on Biotron's website.

Best regards,



**Michelle Miller**  
**CEO & Managing Director**