



July 2020

Dear Shareholders,

So far, 2020 has been an outstanding year for Biotron in the progress of BIT225 against HIV-1. The Company reported additional, important results in March from the Phase 2 clinical trial. This month, further data from ongoing research work were released to the market.

BIT225 is a first-in-class small-molecule anti-viral compound that works to inhibit the viroporin mechanism of Viral Protein U (Vpu). Vpu is a protein that HIV uses in the assembly of new virus particles and in the “budding” of new viruses from the host cell.

One of the main problems in trying to cure HIV is the nature of the immune cells the virus infects. Its major target is a type of white blood cell known as the CD4 cell that has several important roles in the immune system. These include marshalling immune responses to attack foreign agents such as viruses and “remembering” previous infections.

Subsets of CD4 cells can, in effect, store a record of known infections, but the problem is that these cells can become dormant and live in the body indefinitely. Once these cells are infected with HIV, the virus can continue to survive in the body by hiding in these dormant CD4 cells.

Other cells, such as macrophages, are also targets for HIV-1 infection. Virus in these macrophage cells as well as in the dormant CD4 cells is hidden from the immune system meaning that anti-HIV drugs can never truly eradicate the infection from these reservoirs. Patients infected with HIV-1 must remain on treatment for life.

In March, we reported that Biotron had discovered a way for these hidden HIV-infected cells to be found, allowing the immune system to attack and kill the virus.

We conducted a Phase 2 randomised placebo-controlled clinical trial on 36 HIV-1 infected patients in Thailand in which we tested BIT225 in combination with Atripla, an approved current anti-HIV drug (ART). As reported to the market in late 2018, we saw unexpected, unique changes in the profiles of key immune cell populations in the BIT225 + ART group.

Since completing the Phase 2 trial, we have extended studies on the samples from the trial to further understand how BIT225 is working.

The data that we reported in March this year showed that adding BIT225 to anti-HIV-1 drugs stimulates the immune system so that it can find HIV-infected reservoir cells and take the necessary steps to eliminate any residual virus.

This effect of “unmasking” infected cells within cellular reservoirs would solve a huge problem in treating HIV-1 by allowing the body's immune system to work together with the anti-HIV drugs to clear out inaccessible pockets of virus and annihilate the infection for good – opening up the potential for HIV-infected people to avoid lifetime drug treatment.

Since we reported the data in March, our team has been doing further work with research collaborators at The Scripps Research Institute in California. Together with the Immunology and Microbiology Department at Scripps Research, we have been studying further the effect of BIT225 on cells in culture in the laboratory.

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We presented a summary earlier this month at AIDS 2020, the 23rd International AIDS Conference.

The results tell us that BIT225 modifies and enhances the immune response to HIV by reversing the effect of Vpu on cells. It helps explain the immunologic changes that we saw in the Phase 2 clinical trial and gives us even more confidence in our drug.

In summary, we now know that BIT225 appears to:

- find, unmask and make accessible hidden HIV-infected cells that current anti-HIV-1 drugs do not reach;
- inhibit Vpu's role in making new HIV particles;
- reverse Vpu's sabotaging effects on the immune system response to HIV;
- stimulate the immune system to respond to HIV infection; and therefore
- may allow HIV to be destroyed.

The compound is the first of its kind to act as both a direct-acting antiviral drug and an immune enhancer.

We are close to putting together the complete picture showing BIT225's role in treating HIV-1. We now know what it does and what markers to look for. The next step for BIT225 is to refine how it should be used in the clinic. This will require a Phase 2b clinical trial to convert statistically significant changes in test results to statistically significant changes in clinical results. The recent completion of long-term toxicology studies of BIT225 is an important step as we will be able to design clinical studies in which it can be used for up to 6 months.

As announced to the market this week, Biotron has appointed Stephen Becker MD as Chief Medical Officer to oversee the next stage of BIT225's clinical development. Dr Becker has extensive experience as a product development executive, clinician and researcher with specific focus on the therapeutic areas of HIV, infectious diseases and immunology. Based in the USA, he brings solid clinical experience plus years of experience in a similar role in the industry, as well as time in a senior role with the Bill & Melinda Gates Foundation.

Dr Becker's connections with pharmaceutical companies, USA government organisations, philanthropic organisations, as well as his knowledge of regulatory and policy issues relating to development and approvals of new drugs bring essential skills at this critical stage of Biotron's development.

## **SARS-CoV-2**

As discussed in the January shareholder update, Biotron has a number of compounds in its library that have shown very good activity against a range of coronaviruses. This dates back to studies we undertook at the time of outbreak of severe acute respiratory syndrome (SARS-1), a coronavirus, back in 2002–2004. Some of Biotron's compounds showed antiviral activity against SARS. Because that virus disappeared relatively quickly and was not, in the end, a commercial target for therapeutics, Biotron did not pursue that work.

In February this year, Biotron began testing a range of its compounds against SARS-CoV-2, the causative agent of COVID-19, to assess whether they can inhibit this coronavirus. This work is progressing well in a series of different assays to assess the impact of the compounds on markers of virus replication as well as immune markers. These assays will provide the best overall understanding of the potential of Biotron's compounds to treat COVID-19.

## **Hepatitis B Virus**

Hepatitis B Virus (HBV) is another important early stage program for Biotron. We continue to design, synthesise and test new compounds with the aim of identifying a lead candidate. We are working with other experienced groups to access key assays and are fortunate that this work is not materially impacted by Covid-related shutdowns and continues to make good progress.

Biotron remains focused on progressing its antiviral programs directed at viroporins through to a commercial outcome. The current pandemic highlights the importance of novel approaches such as Biotron's with its potential to target a broad range of existing and emerging viruses.

Best regards,



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