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11 July 2024

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

pjn12248

July 2024

Dear Shareholders

Recently, Biotron released headline results from the two Phase 2 HIV-1 trials that have been in progress with the Company's lead antiviral drug BIT225.

These two trials build on previous studies with BIT225 for treatment of HIV. Once again BIT225 was found to have statistically significant impact on important immune and inflammation biomarkers.

These positive results are important as they provide further evidence that BIT225 is acting in a unique way against HIV.

Current anti-HIV drugs (also known as antiretroviral treatment or ART) have come a long way since the early days of AIDS. However, while ART is generally very effective at stopping replication of the virus, these existing drugs have no impact on reservoirs of HIV that are laid down early in infection and cannot be cleared out with ART.

These reservoirs are problematic. They mean lifelong treatment is required to keep the virus in check.

No current or new experimental treatments have successfully cleared out these reservoirs.

These reservoirs also mean that HIV can continue to negatively impact on the immune system. It is estimated that 20% - 40% of people infected with HIV and receiving ART have not achieved full immune reconstitution. These immune non-responders (INRs) are at increased risk for serious comorbid conditions including neurocognitive, cardiovascular, renal, and hepatic disorders that impair quality of life, and drive healthcare costs.

The BIT225-011 trial (the Sydney trial) was the first time BIT225 had been tested in an INR population. These people were long-term infected with HIV and on treatment with ART. Yet despite having been on ART for an average of 21 years their immune systems had not fully returned to normal. Everyone enrolled into the 011 trial received daily doses of BIT225 for 12 weeks in addition to their standard ART.

So what we were looking for in this trial?

In simple terms, we were hoping to see changes in the blood that indicate BIT225 may be unmasking and clearing virus hiding in reservoir cells.

Did we see any such changes?

Yes – statistically significant changes were seen in several immune biomarkers during the 12 weeks on BIT225/ART treatment compared to before starting on BIT225 i.e. when on ART alone.

We included a very broad range of different immune biomarkers (including different immune cell types, cytokines, inflammation markers, etc). It is worth noting that trials in INR populations with other therapeutics have not successfully modified immune outcomes.

What do the results mean?

The changes that we saw in the 011 trial are consistent with previous studies of BIT225. The results from the HIV clinical trials as well as non-clinical studies support BIT225 acting to unmask virus hidden in reservoirs and flush it out.

Why can't we just measure the reservoirs and show they've decreased?

Unfortunately, there are currently no validated assays that allow this to be done in an accurate and meaningful way. Reservoirs exist within various body organs where they cannot be readily accessed or measured.

This means that we are reliant on changes in biomarkers to indirectly show that reservoirs may have been impacted.

What about the BIT225-010 Phase 2 HIV trial?

The BIT225-010 trial (the Thai trial) was based on the previous successful 009 HIV trial. Both included people who were HIV positive and just starting on standard ART. BIT225 was added in for the first three months in 009, and for the 010 trial we extended this out to six months BIT225 treatment.

The 010 trial set out to further characterise the immune biomarkers changes that were seen in 009, and the trial successfully achieved this.

Importantly, in the 010 trial blood virus levels decreased more quickly in people on BIT225+ART compared to ART alone. This suggests that BIT225 is having an impact on a critical phase of viral decay when reservoirs are established.

What do the results mean for Biotron?

These positive findings have important implications for all Biotron's antiviral programs. Biotron's core expertise is designing drugs that work against viroporin proteins. These are parts of viruses that are responsible for modifying the body's immune system, thus allowing the viruses to evade the body's defences and cause disease.

Many viral infectious diseases including HIV, hepatitis B virus (HBV), hepatitis C virus (HCV), SARS-CoV-2, and dengue are characterised by significant immune dysregulation and severe clinical disease; a clear need exists.

There is a real interest internationally in new classes of antiviral drugs.

BIT225 uniquely combines direct antiviral activity with restoration of normal immune regulation through its targeting of viroporin activity. This potential is understood by pharmaceutical companies active in the infectious disease space.

The space in which we are working is complex scientifically and medically, and Biotron is at the cutting edge with this dual approach to treating viral infections.

Biotron's portfolio extends beyond BIT225. We have been working on next generation drugs for HIV and SARS-CoV-2. We have promising early stage programs against other key infectious diseases such as HBV and dengue. Good progress continues to be made on all fronts.

The completed trials were undertaken after extensive consultation with pharma and international immunology/virology experts.

We are now in the process of sharing the data and results from the trial with pharma and key opinion leaders.

The Company remains wholly focused on doing all it can to achieve a commercial outcome to benefit shareholders. Drug development is not fast and is inherently risky. But we have come a long way, with positive outcomes at every stage to date, and we remain optimistic.

We would like to thank shareholders for their patience and support in recent months while we finished post-trial activities and worked our way through extensive, time-consuming detailed analyses of very large data sets across the trials.

Best regards,

Michelle Miller
CEO & Managing Director

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