Biotron Limited
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30 October 2024

The Manager Companies
ASX Limited
20 Bridge Street
Sydney NSW 2000 (8 pages by email)

Dear Madam

REPORT ON ACTIVITIES FOR THE QUARTER ENDED 30 SEPTEMBER 2024

Biotron Limited ('Biotron' or 'the Company') has achieved key outcomes including:

- Reported outcomes from the BIT225-012 Phase 2 COVID-19 clinical trial. The trial met the primary safety and tolerability end point but did not meet the primary efficacy end point.
- Continued the testing of new compounds with the aim of identifying next-generation lead anti-HIV-1 and anti-SARS-CoV-2 drugs and a lead candidate for HBV.
- Extended its early stage Dengue virus program to assess activity of a subset of Biotron's compounds against all four Dengue virus subtypes in cell cultures.
- Subsequent to the end of the reporting period, received an R&D Tax Incentive rebate of $1,814,495 for the 2023/24 financial year.

During the September quarter, the Company reported outcomes from the completed Phase 2 COVID-19 clinical trial (BIT225-012) with its lead antiviral drug BIT225.

As reported (6 September 2024), the trial met the primary safety and tolerability end point with observed adverse events congruent in severity and frequency with those seen in previous trials of BIT225.

The trial did not meet the primary efficacy end point in this population as assessed by the change in SARS-CoV-2 nasal viral load. There were 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.

The groups were similar in terms of time to sustained clinical recovery and time to clinical improvement.

Day 1 to Day 7 was selected as the timeframe for the primary efficacy analyses and was pre-specified in the Statistical Analysis Plan (SAP). Analyses were performed as set out in the SAP, in accordance with Good Clinical Practice (GCP) and international regulatory requirements.

Once the dataset was complete and unblinded, it was noted that four trial participants did not demonstrate quantifiable levels of nasal SARS-CoV-2 virus on Day 1. All participants had positive PCR at entry (Day 1), however, in these four individuals, levels of viral RNA were below the limits of quantification. A *post hoc*, exploratory evaluation from Day 3, when all participants had quantifiable viral load measurements, to Day 9 was performed.

In this analysis nasal viral load declines slowed in the Placebo group after Day 6, while continuing at a relatively consistent rate in the two BIT225 dosage groups, resulting in lower viral loads in the BIT225 dosage groups compared to placebo. The difference between the active (BIT225) and placebo arms was significant (P = 0.02), especially in those starting with higher initial viral loads.

While of interest, and potentially informing further study of BIT225 in SARS-CoV-2 infection, these *post hoc* exploratory analyses do not change the formal outcomes of the trial.

This double-blind, placebo-controlled Phase 2 trial was designed to characterise the effect of BIT225 (200mg or 400mg daily) administered for 7 consecutive days in sixty individuals newly diagnosed with SARS-CoV-2 infection at several sites in Thailand.

As reported (6 September 2024), the Company considers that the outcomes may have been adversely impacted by the widespread levels of immunity to SARS-CoV-2 infection in the community afforded by vaccination and prior infection as well as the exclusion from the trial of people at high risk of progression to severe COVID-19 (due to the availability of other treatment options for that population). The preclinical data of BIT225 in a mouse COVID-19 model that supported the BIT225-012 clinical study remain some of the best in the field.

The recently reported positive outcomes from the two Phase 2 HIV-1 trials, BIT225-010 and BIT225-011, added to the previous positive data of BIT225. The drug has demonstrated broad spectrum antiviral activity in preclinical and clinical studies.

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. Its portfolio extends beyond BIT225 and includes next-generation compounds for its HIV-1 and SARS-CoV-2 programs, as well as compounds with activity across a broad range of viruses including Hepatitis B virus (HBV), influenza, Dengue virus and others.

Viroporin inhibitors such as BIT225 uniquely combine direct-acting antiviral (DAA) and immunomodulatory activities, in contrast to existing antiviral drug classes that focus on DAA only.

During the quarter under review, the Company has continued to characterise the antiviral activity of its anti-HBV compounds in cell-based assays. In addition, several compounds were assessed for their ability to inhibit all four Dengue virus subtypes in cell-based assays. These investigations are ongoing, with the aim of identifying a lead series for progression into formal preclinical studies.

In parallel with continuing development of its early stage programs, the Company is currently undertaking a detailed review of all programs as it continues to investigate pathways to a commercial outcome to benefit shareholders.

Expenditures

As disclosed in the Company's Quarterly Cash Flow Report, expenditure on these research and development activities during the quarter totaled $289,000 and $166,000 of related staff costs. As disclosed in the Company's Quarterly Cash Flow Report, payments to related parties and their associates during the quarter totaled $103,000 for director fees, salaries and superannuation payments.

Subsequent to the end of quarter the Company received an R&D Tax Incentive rebate of $1,814,495 for the 2023/24 financial year.

By order of the Board

Peter J. Nightingale
Company Secretary

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