



***Biotron*** ASX:BIT

**AGM**

**16 October 2009**



# Key Highlights for 2008/2009

- Successful completion of Phase I/IIa clinical trial (BIT225-003) of BIT225 in Hep C+ subjects
- Successful rights issue, raising \$0.8 million in March 09



# BIT225-003: Proof-of-Concept Trial

***A Phase Ib/Ila, Placebo-Controlled, Randomised Study of the Safety, Pharmacokinetics and Antiviral Activity of BIT225 in Patients (Males and Females) with Hepatitis C Virus Infection.***

*Objectives:*

1. To assess the safety and tolerability of 35 and 200 mg of BIT225 twice daily compared with placebo
- 2a. To assess the pharmacokinetics of 35 and 200 mg of BIT225 in patients with chronic HCV infection
- 2b. To assess the antiviral activity of BIT225 in patients with chronic HCV infection



# BIT225-003 Shows Proof-of-Concept

- BIT225 was well tolerated with no serious adverse events reported and no discontinuations from the study.
- BIT225 reached good levels in the blood, that are within the potential therapeutic range and are consistent with the potential for once or twice-daily oral dosing.
- BIT225 reduced blood virus levels at the highest dose (200 mg), in three of the six subjects dosed.
  - Minimal effect, if any, at lower dose (35 mg)
  - ***Increasing ability to reduce virus levels as dose increases supports proof-of-concept i.e. that BIT225 can target and reduce virus levels in infected patients.***

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# Trial Reflects HCV Types in the Community

Genotype	Frequency of Specific Genotypes	
	BIT225-003 Trial	Australia
1a/b	56%	50%
2	6%	7%
3a	38%	35%

***Not all HCV genotypes respond equally to current treatment;  
Genotype 1 is particularly resistant to interferon and ribavirin***



# BIT225 – Potential New Treatment for HCV

- Preclinical studies indicated:
  - Activity against hard-to-treat genotype 1
  - Synergistic with current standard-of-care (IFN/ribavirin)
- Clinical trials have shown:
  - Good PK (half-life, bioavailability, etc) and safety profile in studies to date
  - Statistically significant reduction in viral in several subjects treated with BIT225 on its own

***Demonstrated Proof-of-Concept i.e. that BIT225, a p7 inhibitor, can target and reduce HCV replication in man***

# Further Development of BIT225

- Focused on developing products we can sell to a pharma partner
  - *Aim is to maximise value to shareholders*
- Future HCV therapies expected to be a cocktail of antiviral drugs
  - Industry focus on developing new, specific antiviral drugs to use in combination
  - P7-inhibitors are new addition to this mix
  - Biotron has the first p7-inhibitor – BIT225
- BIT225 expected to have significantly higher potency in combination with IFN/ribavirin on basis of preclinical data
- Phase II trial proposed be a combination study of BIT225 with standard of care treatment for HCV

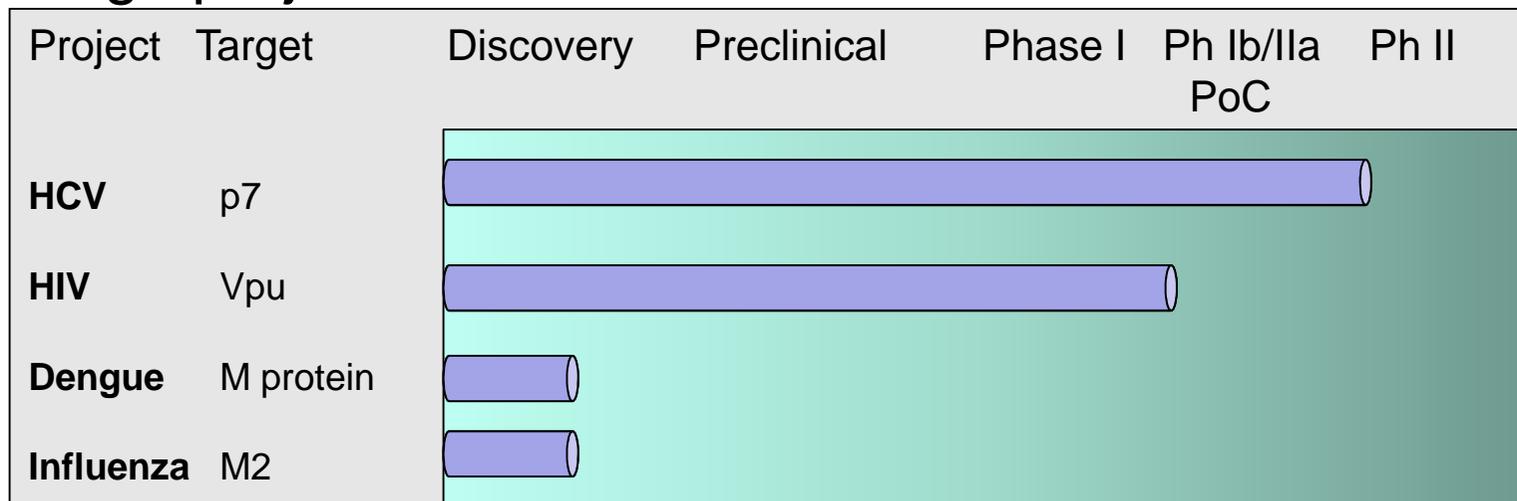


# Further Development of BIT225 (cont)

- BIT225-003 – extend to do 400 mg dose
  - Protocol amendment to existing trial
  - One more cohort (6 subjects)
  - Timeframe – submit amendment in Oct; Approvals early Nov; Conclude early Q1 2010
  - Aim to show higher dose further improves activity of BIT225
- BIT225-005 – Combination HCV trial
  - Phase IIa – 14 day, POC study in combination with current standard of care (IFN/ribavirin)
  - Finalising trial design
  - Timeframe – Submission and approvals 1Q 2010; complete 3Q 2010
  - Future treatment trends are for cocktails of drugs for HCV

# Beyond HCV - Pipeline of Antiviral Drug Programs

- Developing new generation antiviral drugs with large, expanding world markets.
- Current major focus on developing new drugs to treat Hepatitis C virus (HCV) and HIV; pipeline of earlier stage projects



# SUMMARY

- Biotron has a strong competitive position in a high profile therapeutic area
  - New mode of action drug for HCV
  - Proven activity in Phase Ib/IIa clinical trial
  - Strong patent position (applications for drug itself as well as usage)
  - New mode of action drug for HIV - Ib/IIa trial ready to go when funding is available
  - Additional early development stage projects showing promise

***Total focus on developing a commercialisable product to maximise returns to shareholders***



# *Biotron*

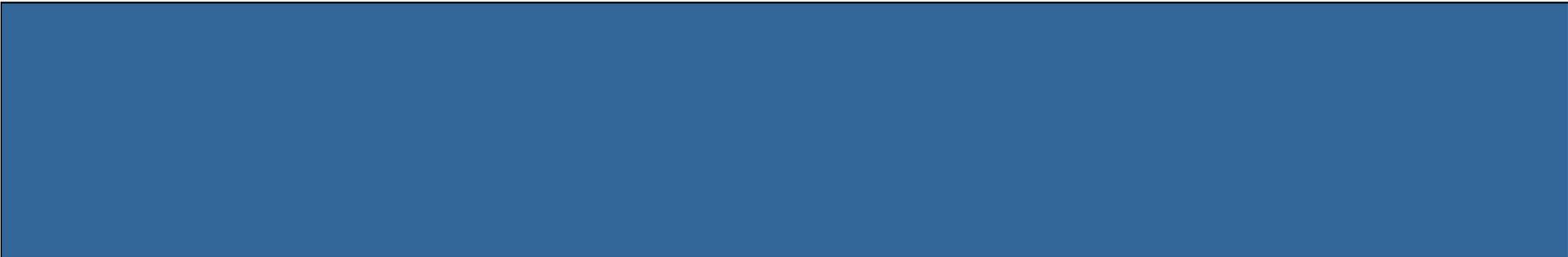
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**COMMENTARY FOR A PRESENTATION TO  
THE 2009 ANNUAL GENERAL MEETING**

**16 OCTOBER 2009**

I am pleased to be able to present this update on the Company's activities.

**Slide 1**

The last 12 months have seen significant advances on clinical progression of Biotron Limited's ('Biotron' or the 'Company') antiviral drug development program, in particular with its Hepatitis C virus program.

Biotron recently announced the successful completion of the Phase Ib/IIa trial of BIT225. This was the first trial of Biotron's lead antiviral drug in patients infected with HCV (the previous trial had been in healthy volunteers) and its completion marks a major milestone for the Company.

In March 2009 Biotron initiated and subsequently completed a Share Purchase Plan (SPP) to raise additional capital for clinical development of its antiviral programs. The company raised \$0.8 million in a very difficult financial climate, and the Director's would like to thank all those shareholders who supported the Company by participating in this capital raising.

**Slide 2**

Biotron's HCV program is developing a new way to treat this serious infection, with a new drug that works in a different way to other existing HCV treatments. To date no one has developed and clinically tested a drug of this class (HCV p7 inhibitor) – BIT225 is a world first. While we had previously shown that the drug works in cell-based models of infection, we needed to show that the drug can lower the level of HCV in the blood of infected people to show proof-of-concept i.e. that this new class of drug has the potential to be used to treat HCV infection.

During the trial, 18 HCV-infected people were randomly assigned to receive either 35 mg or 200 mg of BIT225, or placebo; they took the drug twice daily for 7 days. Before, during and after the trial blood samples were taken and analysed to see how much virus was in their bodies.

The trial was designed primarily to test the safety of BIT225 but also to provide this proof-of-concept.

**Slide 3**

The assessment of safety was the prime concern in this trial as this was the first time that any humans had received more than one dose of the drug – at this stage of development of a new drug, regulatory authorities and human ethics committees that oversee and approve such trials are more concerned about safety aspects of new drugs than whether they work. We recognise that this is not the key concern for shareholders who want to know if the drug works, but it should be noted that the HCV drug graveyard is littered with drugs that "worked" but had unacceptable safety profiles, and that clinical trials and their endpoints are dictated by external authorities to ensure patient safety. There are always heightened safety concerns with HCV-infected patients as toxicity problems can be amplified if they have liver damage. During Biotron's trial patients were closely monitored to determine if the drug passed stringent safety guidelines. During the trial there were no reported serious adverse events and no discontinuations from the trial, which was an excellent outcome.

Results from the trial were only available after the end of the study, at which time they were unblinded and analysed. It was important to take the necessary time to perform a complete analysis of all the data. This is not something that can be rushed and the fact that Biotron completed its analysis, with full review of all safety data by an external Data Safety Monitoring Committee, within 2 months of the end of the trial is an excellent achievement.

Results from the trial indicate that at the lower dose of drug (35 mg) there was no effect on virus levels. However, at the higher dose (200 mg) half of the subjects had a significant reduction in virus levels. This is an excellent finding in a small, first-in-patient trial, and shows that increasing the dose of drug improves the result. We would expect, therefore, that if we further increased the dose then virus levels may drop further.

#### **Slide 4**

There are different forms, known as genotypes, of HCV. The prevalence of different genotypes varies around the world, and genotypes can differ in how they respond to different drug treatments. The major genotype in Australia is genotype 1, and this type is particularly difficult to treat with current treatment i.e. Interferon (IFN) and ribavirin. In this trial we did not exclude any genotype. It is interesting to note that the trial participants very closely reflected the range and proportion of genotypes present in Australia.

#### **Slide 5**

Preclinical studies (i.e. in cell cultures in a laboratory) with BIT225 suggested that the drug may have activity against genotype 1 – the hardest to treat form of HCV. These laboratory studies also showed that BIT225 was much more potent when used together with interferon and ribavirin against the virus. In the trial just completed we had to test BIT225 on its own to look at its safety profile, but its likely use in the clinic would be in combination with interferon and ribavirin. Clinical studies so far have reflected what the preclinical studies predicted, as indicated by safety results and the proven ability of BIT225 to reduce virus levels, so we are keen to test BIT225 in combination with interferon and ribavirin in man to see if we can further improve results. The outcome of the current trial, however, is very important as it shows proof-of-concept i.e. that BIT225 can target and reduce virus levels in a clinical setting.

#### **Slide 6**

Biotron's development of BIT225 is being undertaken with one very clear, focused aim – to secure a suitable partner for the HCV program, thus ensuring a commercial outcome and financial return to shareholders. Biotron's business strategy is to develop BIT225 to a stage suitable for partnering with an international pharmaceutical company for further clinical development. During the year, ongoing discussions were held with potential partners. New drugs such as BIT225, which are first-in-class, provide challenges in that they are forging new territory, but traditionally have shown better returns than "me-too" drugs. We continue to engage with potential partners, but believe it is important to proceed with the next stage of development of BIT225 to ensure we keep increasing the value of the program.

#### **Slide 7**

Now that we have demonstrated that BIT225 can reduce virus levels in patients at 200 mg, with no serious adverse events, the next step is to see if a higher dose can have a greater effect. This can

most easily be done by extending the recently completed trial to include another group of patients to receive a higher dose of drug. We also know from preclinical cell culture assays that the potency of BIT225 appears to be significantly increased in combination with the current drugs used to treat HCV infection, interferon/ribavirin, so we are currently preparing protocols for a combination study of BIT225 with interferon and ribavirin, which is how BIT225 would be most likely to be used in a clinical setting – antiviral drugs cannot be used on their own to treat chronic infections due to development of drug resistance.

#### **Slide 8**

BIT225 is not a one off drug. Biotron has an impressive portfolio of clinical and preclinical antiviral programs developing antiviral drugs. In addition to its clinical programs for HCV and HIV, the Company has earlier stage drug programs for influenza, dengue and other viral diseases, generating an on-going pipeline of candidates to progress to clinical trials. These early stage programs currently receive minimal funding as the Company focuses on current clinical programs for HCV and HIV.

#### **Slide 9**

We believe that Biotron has a very strong competitive position, with world-class clinical programs targeting diseases with unmet medical need. In the last year we have further progressed the HCV program, proving that BIT225 is able to reduce virus levels in HCV-infected patients, showing for the first time that a drug targeting the p7 protein of HCV has clinical potential. Under the HIV program we have a Phase Ib/IIa proof-of-concept clinical trial ready to go as soon as funding becomes available; BIT225 has the potential to treat both of these serious diseases. We will continue to advance these programs in a rational, cost-effective manner to maximise their value and potential returns to shareholders.