

*Biotron*

AGM

5 October 2007



# BIOTRON LIMITED

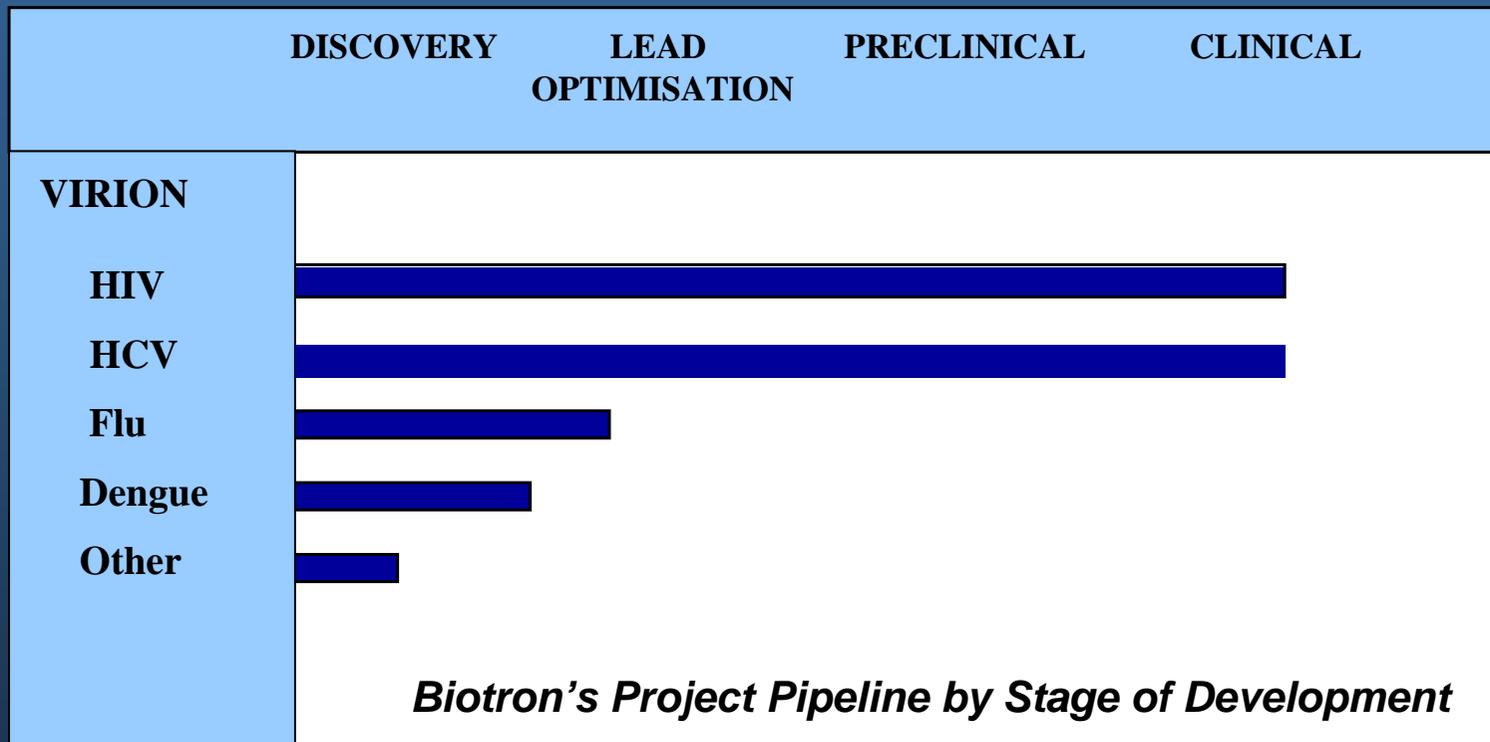
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- Developing new generation antiviral drugs with large, expanding world markets.
- Current major focus on drugs to treat HIV-1 and Hepatitis C virus.

# RECENT KEY HIGHLIGHTS

- Completed a Phase I human clinical trial of BIT225
  - No dose-limiting toxicities
  - Excellent safety profile with good blood levels of the drug
    - Achieved estimated therapeutic levels of drug
- Hepatitis C virus (HCV)
  - BIT225 demonstrated excellent activity in models of HCV infection & highly synergistic with current leading HCV therapies
  - Can be progressed into clinical trial in HCV patients
- Renegotiated agreement with ANU to Biotron's  
2 advantage

# BIT – PIPELINE OF ANTIVIRAL PRODUCTS



# BIT 225 – A NOVEL APPROACH TO HIV THERAPY

- First-in-class new anti-HIV drug
  - New mode of action
  - Targets HIV in viral reservoirs *in vivo*
  - No existing drugs target this source of HIV in the body

# HIV – HIGH GROWTH MARKET

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- 39.5 million people with HIV/AIDS at end of 2006
- 4.3 million people were newly infected with HIV in 2006
- In 2006 2.9 million people died of HIV/AIDS-related causes
- US market alone worth >US\$3.3 billion p.a.

# NEW TREATMENTS NEEDED

- Resistance is a main cause of antiretroviral therapy failure
  - ~ 26% newly diagnosed patients have resistant strains of virus
  - ~ 78% of late-stage patients develop resistance to existing therapies
- Unmet need for new drugs suitable for HAART\* therapy that attack the virus in new ways

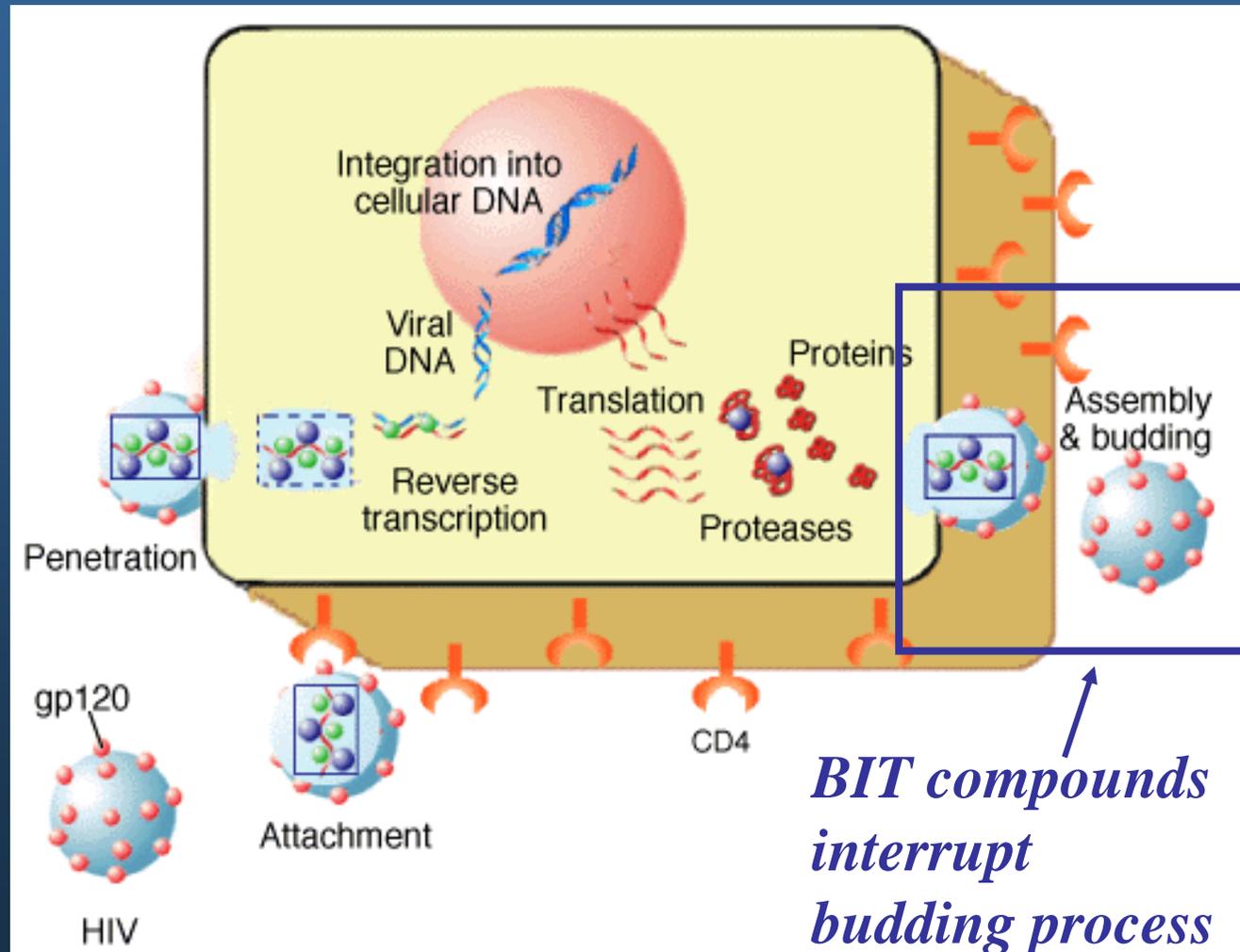
\* Highly Active Anti-Retroviral Therapy

# BIT 225 – A NOVEL APPROACH

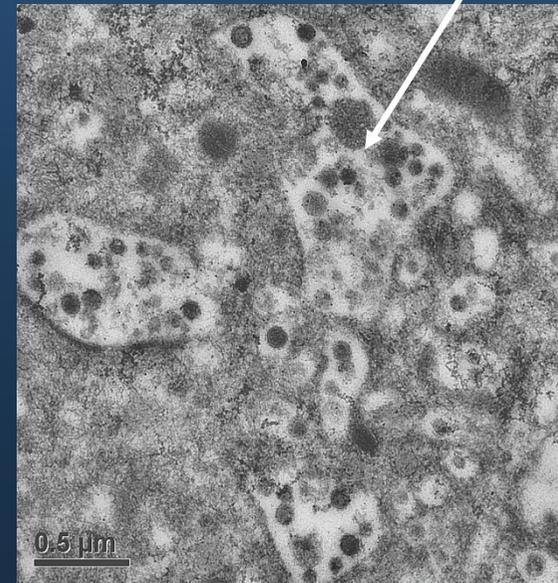
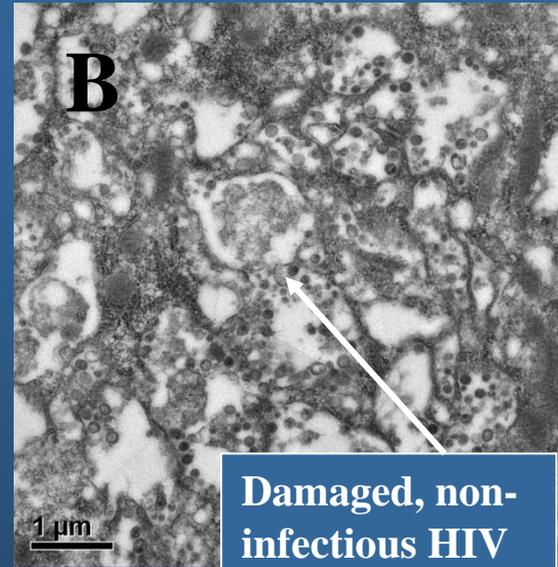
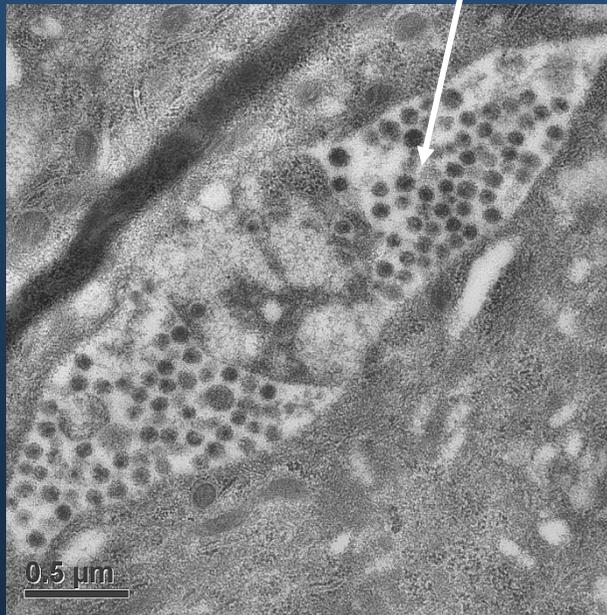
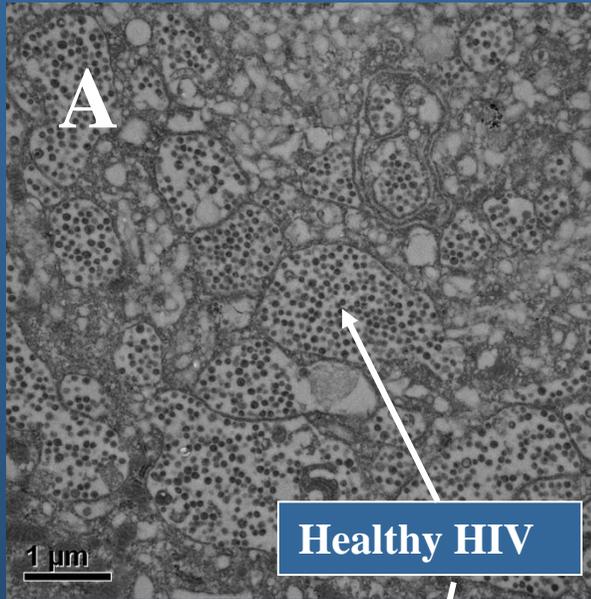
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- BIT-225 is a Viral Protein U (Vpu) inhibitor
- No existing drugs target HIV Vpu protein – novel mode of action
- Disturbs formation of new virus particles through budding process
- Reduces infectivity of virus produced by infected cells

# BIT – 225 TARGETS DIFFERENT STAGE OF HIV LIFE CYCLE

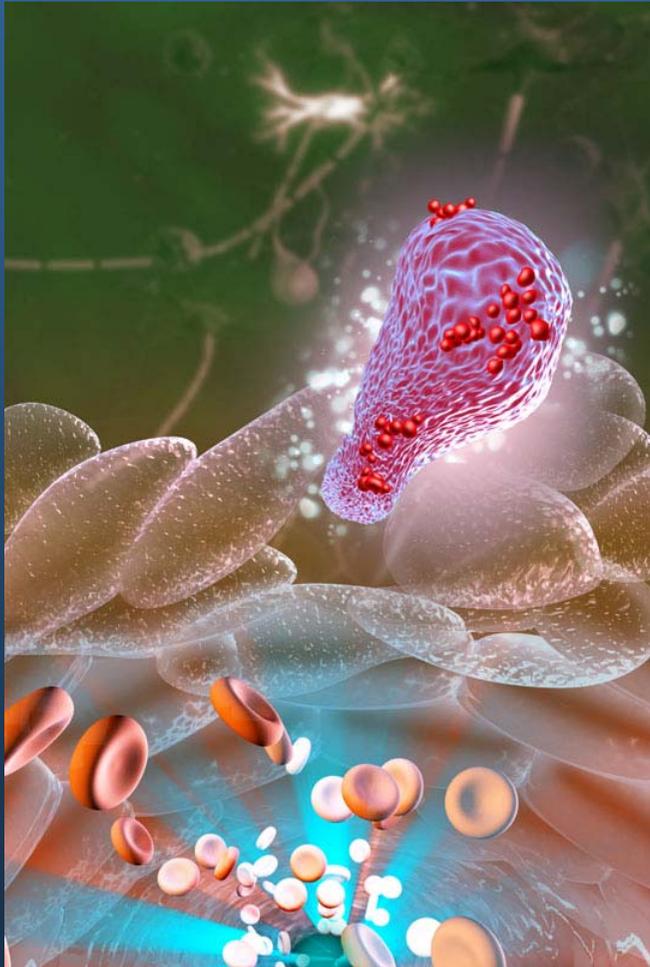


# Human cells infected with HIV – Untreated (A) and Treated with BIT225 (B)



# BIT- 225 ACTIVE IN VIRAL RESERVOIR CELLS

- Eradication of HIV from reservoirs is essential to prevent development of AIDS
- Current HIV drugs cannot eradicate the underlying seat of infection (termed the viral reservoir)



# BIT – 225 PROFILE

- ✓ • Good stability and half-life *in vivo*
- ✓ • Excellent safety profile in animals & humans in studies to date
- ✓ • Active against resistant strains of HIV
- ✓ • Synergistic with leading current HIV therapies
- ✓ • Simple chemistry for manufacture
- ✓ • Novel compound - new mechanism of action
- ✓ • Recently completed Phase I clinical trial in healthy volunteers

# BIT225 – HCV PROGRAM

- During last 12 months BIT225 shown to have good antiviral activity in preclinical surrogate models of HCV infection
- BIT225 highly synergistic with current leading HCV therapies
  - Triple combination of BIT225 with existing drugs resulted in significantly higher activity than current drugs alone
- The Phase I study completed under the HIV program can be used to support an efficacy study of BIT225 in HCV+ patients

# HEPATITIS C VIRUS (HCV) MARKET

- 4x more prevalent than HIV
- 4m patients in US (2.7m chronic infection); 170m worldwide
- Worldwide market ~US\$2.8 billion currently predicted to expand to >US\$10b
- US surgeon general considers hepatitis C is one of the most significant public health threats facing US.
- Existing therapies ineffective and toxic

# CLINICAL DEVELOPMENT PROGRAM FOR BIT225 IN 07/08

Program for rest of 07/08 FY:

1. Phase Ib/IIa clinical trial in HCV+ patients
  - Dose-range finding and efficacy study
  
2. Phase Ib clinical trial in HIV+ patients
  - Repeat-dose study
  - Aim to generate data to lead on to Phase II study

Will be major value-adding milestones

- Set up for licensing to major pharmaceutical company
- Acquiring funding for Phase II and beyond

# ANTICIPATED MILESTONES 2007/08

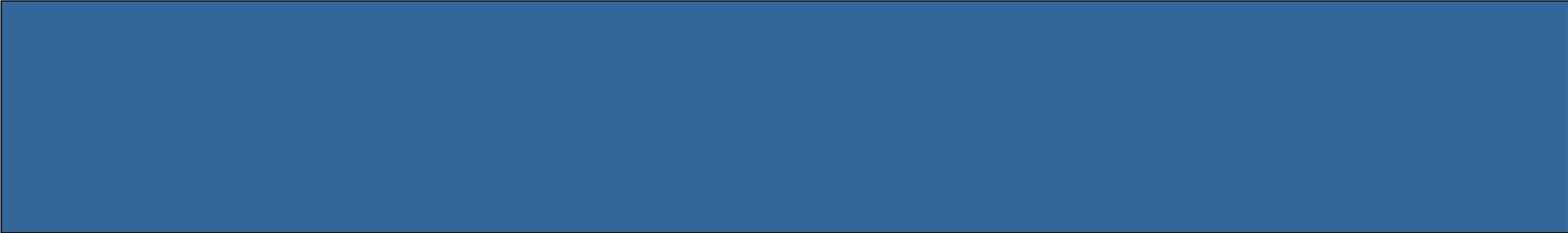
## BIT225 HIV & HCV Programs:

- Submission of protocols to ethics and regulatory authorities Q4 07
- Commencement of Phase Ib/IIa clinical trial in HCV+ patients Q1 08
- Commencement of Phase Ib clinical trial in HIV+ patients Q1 08
- Results of these two trials mid-2008

# FINANCIAL SUMMARY

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- \$ 1.38 million cash at 30 June 2007
- Expect to receive additional grant funding from AusIndustry

# *Biotron*

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**COMMENTARY FOR A PRESENTATION TO  
THE 2007 ANNUAL GENERAL MEETING**

**5 OCTOBER 2007**

I am pleased to be able to present this update on the Company's activities. The last 12 months have seen major advances in progression of the Company's projects – particularly the Virion antiviral drug development program. Biotron's prime focus is on development of small molecule drugs that target HIV and Hepatitis C virus (HCV).

**Slide 2**

This program has made excellent progress – during the last 12 months we have completed a formal preclinical safety and toxicology program, done to international regulatory standards; prepared and submitted a clinical trial protocol to human ethics committee; received approval for the proposed trial; and successfully completed the Phase I clinical trial of BIT225. This first human trial of this new drug was a major milestone for Biotron, and marks the transition of the Company to a clinical stage antiviral drug development company. The trial was a single dose, dose escalation study in healthy volunteers in the fasted and fed state. No dose-limiting toxicities were observed during the trial, and good blood levels of the drug were achieved.

During the last 12 months the HCV program was significantly advanced through the finding that BIT225 has very good antiviral activity in various models of HCV infection, and by the discovery that BIT225 is highly synergistic with the two leading approved HCV therapies (interferon-alpha and ribavirin). The addition of BIT225 to interferon-alpha and ribavirin increased the level of inhibition of viral replication from 70% with the two other drugs to 100% when BIT225 was added to the mix. The potency of BIT225 was increased tenfold in this triple combination, compared to its activity on its own. These results are significant as they indicate that BIT225 has the potential to be used in combination therapy to achieve a higher level of antiviral activity against HCV than is currently possible, while improving the potency of each of the drugs in the combination. The data is also significant as it means we can progress more rapidly to trials in HCV-infected patients.

The third significant event was the renegotiation of the head agreement with the ANU. Under the new terms, intellectual property held by the ANU, and to which Biotron had a worldwide exclusive licence, has been transferred to outright ownership by Biotron. Further, Biotron received \$442,703 for relinquishing rights to possible future intellectual property from certain ANU research programs which were primarily basic, non-commercial research and not relevant to Biotron's antiviral drug development program. Biotron will also receive a royalty from the commercialisation by the ANU of certain existing research projects at the ANU. The development of these projects will not require any funding by Biotron. These new arrangements with the ANU are a reflection of the maturing of Biotron from a research based company to a mature antiviral drug development company with an exciting portfolio of clinical development programs.

**Slide 3**

Biotron has an impressive portfolio of clinical and preclinical antiviral programs developing drugs targeting HIV, Hepatitis C virus (HCV), Dengue virus and Influenza virus. BIT225 is in clinical trials for treatment of HIV and HCV. In addition, 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. During the last 12 months a number of Biotron's proprietary antiviral compounds have been independently tested in the USA against HBV in *in vitro* cell culture assays. Several compounds had high levels of potency and specificity activity against HBV. Further tests are in progress.

**Slide 4**

BIT225 represents a new, first-in-class drug for treatment of HIV. The drug has a new mode of action, targeting HIV in reservoirs of infection - a source of virus not targeted with current approved therapies.

**Slide 5**

HIV is considered to be a high growth market. In 2006 39.5 million people world-wide were infected with AIDS, with 4.3 million new cases. Over 2.9 million people died of HIV/AIDS related causes that year. The global market is worth US\$6.6 billion per annum, with the USA accounting for 70% of these sales.

**Slide 6**

Despite the relatively large number of HIV drugs on the market, infected patients are still progressing to development of AIDS with subsequent death. Development of resistance to antiviral drugs by the HIV virus is the main cause of therapy failure. At the time of initial diagnosis 26% of patients have drug resistant virus in their body, and this increases to 78% of late-stage patients. There is an unmet need to develop drugs that attack the virus in new ways.

**Slide 7**

BIT225 targets the Vpu protein of HIV – no other drugs target this protein. BIT225 disturbs the formation of new virus particles, reducing the infectivity of resulting virus.

**Slide 8**

BIT225 works at a different stage of the HIV life cycle compared to existing classes of HIV drugs. Existing drugs target one of three HIV proteins while BIT225 targets Vpu, a new drug target in the fight against HIV. BIT225 disrupts the budding, or the production and release of infectious virus, stage of the life cycle, which is a later stage in the virus life cycle than the other drugs. BIT225 has the potential to be used in combination with existing therapies to prevent development of drug resistance, and also has the potential to be used in patients who have failed existing therapies.

**Slide 9**

Electron microscopes are very powerful microscopes that have allowed us to look directly inside human cell infected with HIV. Panel A shows untreated HIV-infected cells, where uniform, healthy HIV virus particles are clearly visible inside pockets within the cells. The lower panel shows this at higher magnification. Panel B shows HIV-infected cells that have been treated with BIT225. The virus no longer has regular, uniform shape, and when this deformed virus is tested, it is not able to infect other cells.

**Slide 10**

Critically, BIT225 specifically targets HIV in reservoir cells, in contrast to current therapies that work by reducing the levels of HIV in the blood to undetectable levels. However, these drugs have no effect on the underlying reservoir of infected cells where the HIV hides from the immune system. Over the lifetime of a patient virus from these reservoir cells rebounds into the blood, necessitating on-going treatment with antiretroviral drugs. Currently, no therapies are active in these latent cells and elimination of this reservoir of HIV is essential if the virus is to be completely eliminated from the body. BIT225 is specifically active in these reservoir cells and represents an opportunity to attack HIV at its source. BIT225 could be used in combination with existing antiretroviral therapies to achieve the dual effect of arresting viral replication and eliminating the viral reservoir to achieve total elimination of HIV in the body.

**Slide 11**

BIT225 has excellent activity and drug profiles. It has good oral bioavailability, which means it can be given in tablet form, and has shown good stability and half-life *in vivo*. It has good activity against a range of different subtypes of HIV in *in vitro* assays. Importantly, BIT225 has been shown to have good activity against strains of HIV that are resistant to other HIV drugs. *In vitro* studies have demonstrated that BIT225 is able to improve the activity of current HIV therapies, further supporting its use with existing HIV drugs. It has a relatively short synthetic process for manufacture. And most importantly, it is a novel compound with a new mechanism of action. It recently successfully passed through a Phase I clinical trial in healthy volunteers, leading the way open to progress the drug into trials in HIV+ patients.

**Slide 12**

During the last 12 months BIT225 has shown good antiviral activity in preclinical surrogate models of HCV infection. The drug was highly synergistic with current leading HCV therapies in these models of infection, with triple combination of BIT225 with existing drugs resulting in significantly higher activity than current drugs alone. The Phase I clinical trial of BIT225, recently completed under the HIV program, can be used to support an efficacy study of BIT225 in HCV+ patients.

**Slide 13**

HCV is a very attractive target for Biotron. It is estimated that in the US alone some 4 million people have been infected with Hepatitis C, with 2.7 million suffering from chronic infection. Worldwide, 170 million people are infected. Existing drugs for HCV are ineffective and toxic, leaving an unmet need for new therapies. The worldwide market is currently almost US\$3 billion, but is estimated that this market will expand to over US\$10 billion as safe, effective therapies enter the market.

**Slide 14**

Program for rest of the 2007/2008 financial year includes the following:

1. Phase Ib/IIa human clinical trial in HCV+ patients
2. Phase Ib human clinical trial in HIV+ patients

These will be major value-adding milestones, setting the HIV and HCV programs up for licensing to major pharmaceutical companies, or alternatively, will enable Biotron to acquire funding for Phase II and beyond.

**Slide 15**

We expect to submit protocols for approval to human ethics committees before end of 2007, with trials in HIV and HCV patient populations expected to commence early in 2008. The trials are expected to conclude mid-2008.

**Slide 16**

Cash balance at 30 June 2007 was \$1.3 million.

During 2007/08, Biotron looks forward to reaping the benefit of these key advances in Virion to maximise returns to shareholders.