

*For Immediate Release*

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## **HRV Phase IIb Study Achieves Primary Endpoint**

- ***Oral Treatment for Human Rhinovirus Infection Results in Statistically Significant Reduction of Symptoms in Asthmatics***

Biota Holdings Limited (ASX:BTA) today announced that the Phase II clinical study of its oral antiviral BTA798 (WHO assigned non-proprietary name vapendavir) for the treatment of naturally acquired human rhinovirus (HRV) infection in asthmatics resulted in a statistically significant reduction in cold symptoms compared to a placebo.

The successful completion of the Phase II study delivers a major milestone in the development of BTA798 and establishes the basis for the further development of the product. Work will now commence on the design of appropriate Phase III studies and detailed findings will be provided to potential commercial partners over the next few months.

Biota CEO Peter Cook said that the outcome of the Phase II study was extremely positive.

"This trial not only represents a valuable step in the successful delivery of one of Biota's key programs but it is also a unique accomplishment in the field of antiviral development. While the clinical link between HRV infection and loss of asthma control is now widely accepted, Biota is the first company to evaluate the use of an antiviral to treat the infection in asthmatics," he said. "This has the potential to be of considerable benefit to sufferers through better control of their asthma."

The study was delivered at a significantly lower cost than originally budgeted.

## **Study design and conduct**

The Phase II multicenter, randomized, double-blind, placebo controlled study in asthmatic adults with symptomatic, naturally acquired human rhinovirus infection was conducted over two consecutive seasons in 48 centres in the United States. Subjects received 400 mg of BTA798 or placebo twice daily for six (6) days. The study enrolled 300 subjects, 93 were confirmed HRV A, B or C infected by PCR and of these 85 (~90%) fully complied with the study protocol.

The trial's primary efficacy endpoint used WURSS-21 (Wisconsin Upper Respiratory Symptom Survey-21) to assess the severity of cold symptoms for fourteen (14) days after the onset of illness. High WURSS scores have previously been shown to predict subsequent deterioration in asthma control.\*

Other exploratory measures of efficacy included lung function, asthma control and virology.

Safety was monitored throughout the study.

## **Efficacy**

### **Primary end point**

The primary efficacy parameter was the mean daily difference in WURSS-21 severity score over days two (2) through four (4), the anticipated peak of the infection. BTA798 treatment resulted in a statistically significant reduction in the severity score of cold symptoms when compared to placebo ( $p=0.028$ ).

### **Other WURSS conclusions**

The WURSS scores also showed a statistically significant improvement in mean daily difference over the longer period of days two (2) through fourteen (14) ( $p=0.001$ ). Although sample sizes were small, BTA798 appeared to be effective in all HRV species.

In addition, BTA798 treated subjects improved earlier with peak symptoms occurring at 1.7 days compared to 2.5 days with placebo ( $p=0.036$ ).

### **Other efficacy measures**

#### **Lung Function**

Evening peak expiratory flow (PEF) was significantly higher in the treated group on day 5 ( $p=0.023$ ) and the PEF difference was clinically significant (LSMD of 29.4 L/min compared to a clinically significant threshold of 20.0 L/min).

#### **Asthma Control**

Reduction in the use of asthma reliever medication (short acting  $\beta_2$ -agonists – such as Ventolin<sup>®</sup>) showed a positive trend toward improvement in the BTA798 group as early as day 3 of treatment and reached statistical significance on day 13 ( $p=0.045$ ). On day 13 BTA798 treated subjects used approximately half that of placebo recipients (1.22 puffs/day for the placebo group to 0.67 puffs/day for the BTA798 group).

#### **Virology**

Protocol compliant BTA798 treated subjects showed a statistically significant lower incidence of virus infection (74.4%) compared to placebo (91.4%) on day 3, as measured by PCR of nasal swabs ( $p=0.025$ ).

### **Safety**

There were no serious adverse events and generally BTA798 was well tolerated.

## **Additional information**

### **About human rhinovirus (HRV) and its association with Asthma & COPD**

HRV is the frequent cause of the common cold which in otherwise healthy people is a minor infection of limited duration. However HRV infection is a major cause of hospitalisation for patients with underlying respiratory conditions, such as asthma, chronic obstructive pulmonary disease (COPD) and cystic fibrosis, where HRV can aggravate the underlying existing disease. Estimates suggest that HRV is linked to about 70% of all asthma exacerbations and more than 50% of the hospitalised cases. Studies also suggest that more than 35% of acute COPD patients requiring hospitalisation are associated with respiratory viruses, including rhinovirus.

HRV can be a serious problem for other segments of the population such as infants and the frail elderly. For example, in the United States, 75% of common colds in children under five years are medically attended and HRV has been linked with roughly one third of children with middle ear infections (acute otitis media). HRV is the second most frequently recognized infection associated with pneumonia and bronchiolitis in infants. There is also growing evidence for HRV as the causative agent for severe lower respiratory tract illness in older adults. In transplant patients who are highly immunocompromised, such as lung or bone marrow transplant recipients, HRV infection can be fatal.

There is currently no effective treatment for HRV. Therefore, if successful, Biota's HRV antiviral will address a number of important, unmet medical needs.

\* Walter, M J et al (2008) Eur. Respir. J. 32(6) 1548-1554

## About Biota

Biota is a leading anti-infective drug development company based in Melbourne Australia, with key expertise in respiratory diseases, particularly influenza. Biota developed the first-in-class neuraminidase inhibitor, zanamivir, subsequently marketed by GlaxoSmithKline as Relenza. Biota research breakthroughs include a series of candidate drugs aimed at treatment of respiratory syncytial virus (RSV) disease and Hepatitis C (HCV) virus infections. Biota has clinical trials underway with its lead compound for human rhinovirus (HRV) infection in patients with compromised respiration or immune systems.

In addition, Biota and Daiichi Sankyo co-own a range of second generation influenza antivirals, of which the lead product Inavir<sup>®</sup>, is marketed in Japan. Biota holds a contract from the US Office of Biomedical Advanced Research and Development Authority (BARDA) for the advanced development of laninamivir in the USA.

Relenza<sup>™</sup> is a registered trademark of the GlaxoSmithKline group of companies.

\*Further information available at [www.biota.com.au](http://www.biota.com.au)

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