

*For Immediate Release*

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### **Phase III trial with CS-8958 for flu prevention underway**

Biota Holdings Limited (ASX:BTA) and Daiichi Sankyo Co., Ltd. today announced the commencement of the Phase III trial for the anti-influenza drug, CS-8958, in Japan. The goal is to gain an influenza prevention indication in Japan.

CS-8958 is a prodrug and administered by inhalation. Once inhaled it is converted to the active metabolite known as laninamivir. To date, the development of this product has focused on treatment of influenza patients and the new study examines its use in prevention.

This Phase III study is a multicenter, placebo-controlled, double-blind trial that will evaluate prevention and safety of CS-8958 for families of influenza A and B sufferers. The study measures influenza transmission among those receiving CS-8958 or a placebo. It will be conducted in Japan and subjects will be enrolled from household's with influenza infected patients. The trial is a Study of Household Influenza prophylaxis Effect of Long-acting anti-influenza Drug, with the acronym of SHIELD.

SHIELD is also intended to establish the optimum dosage of CS-8958 for this indication and provide a further evaluation of safety. Intra-group comparisons will be made with regard to the incidence of adverse events and other safety measures.

Laninamivir is a novel neuraminidase inhibitor discovered by Daiichi Sankyo for the treatment of influenza and is co-owned with Biota Holdings Limited. Daiichi Sankyo is pressing ahead with the development program of CS-8958 in Japan. An application for manufacturing and marketing approval is planned to be submitted by March 2010 for the treatment of adult and paediatric influenza utilising the results of the Phase III therapeutic trial completed in June 2009.

A copy of Questions and Answers on the trial is attached to this announcement.

### **About LANI's (Long-Acting Neuraminidase Inhibitors)**

Current neuraminidase inhibitors for influenza require daily or more frequent dosing. The ability to dose patients on a weekly, or even less frequent, basis offers numerous potential benefits. These include greater efficiency of storage and distribution for a given treatment period and/or number of patients and improved patient compliance.

### **About Daiichi Sankyo**

A global pharmaceutical innovator, Daiichi Sankyo Co., Ltd., was established in 2005 through the merger of two leading Japanese pharmaceutical companies. Daiichi Sankyo discovered laninamivir and has a key partnership with Biota for the development of the product.

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## **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 have included novel nucleoside analogues designed to treat hepatitis C virus (HCV) infections, licensed to Boehringer Ingelheim, and a series of candidate drugs aimed at treatment of respiratory syncytial virus (RSV) disease. 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 has a key partnership with Daiichi Sankyo for the development of second generation influenza anti-virals.

Relenza™ 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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## QUESTIONS & ANSWERS

### CS-8958 Phase III Influenza Prophylaxis Trial in Japan

**Q: When do you expect to file an application with the Japanese Ministry of Health and Welfare (J-MHW) seeking approval for prophylactic indications of CS-8958 and when do you expect to receive notice of approval?**

A: We aim to file the J-NDA in the first quarter of 2011 and receive approval by the end of the first quarter of 2012.

**Q: When do you anticipate receiving approval from the J-MHW for clinical therapeutic treatment indications with CS-8958?**

A: We forecast that approval for clinical therapeutic treatment indications will be granted by the end of the first quarter of 2011.

**Q: Will approval be accelerated if trial goes well?**

A: We cannot comment about the timing of manufacturing approval.

**Q: How is CS-8958 superior to Tamiflu?**

A: For treatment indications, Tamiflu is taken orally twice daily for five days. CS-8958 is administered by inhalation of a single dose. Daiichi Sankyo has confirmed in Asian clinical trials that CS-8958 is as effective as Tamiflu and is well-tolerated. CS-8958 has also been shown to be effective against Tamiflu-resistant viruses.

**Q: How is CS-8958 superior to Shionogi & Co.'s Peramivir?**

A: CS-8958 acts directly on the trachea and lungs, which influenza targets. It acts quickly and efficiently and has limited side effects on the rest of the body.

**Q: What development plans for CS-8958 do you have for the United States, Europe, or elsewhere in Asia, either in-house or through licensees?**

A: Biota Holdings Limited, our Australian licensing partner, has submitted an IND (Investigational New Drug) application in the United States. Together with Biota we are actively seeking licensees to development and market CS-8958 for the rest of the world.

**Q: What are your peak sales projections for influenza treatment and prevention with CS-8958 in Japan?**

A: We do not disclose sales projections.

**Q: Will trial patients take CS-8958 at home in this Japanese study?**

A: In principle, we plan for patients to consult medical institutions and take the treatment under instruction from doctors and pharmacists.

**Q: What is the target age group of trial patients?**

A: There are no age restrictions. Anyone able to take this medication can participate in the clinical trial.

**Q: What endpoints are you using to assess efficacy in the prophylaxis trial of CS-8958? Also, what specific protocol design are you using, and what is the schedule?**

A: We will compare influenza transmission between family members of patients with confirmed influenza infections. Over the ten day study period, patients will receive two doses of either CS-8958 or placebo with a seven day interval and transmission rates will be monitored. Trial entries should begin in early November, and we should reach the target sample size during the current flu season.

**Q: Of the patients who use Tamiflu, what proportion are for treatment or prevention use at Japanese medical institutions?**

A: Most administrations are for treatment. Among people in contact with influenza sufferers, preventive usage is restricted to high-risk subjects—such as those with chronic respiratory complaints or metabolic diseases —prophylaxis is not covered by local public insurance.

**Q: Where can interested parties apply to enroll in this trial?**

A: We cannot disclose the names of the facilities involved, although we can say that 50 medical institutions are participating.

**Q: Will people vaccinated against H1N1 influenza participate in the trial?**

A: They will be eligible for inclusion in the study.

**Q: Why are you using a placebo as the control drug?**

A: We must confirm that CS-8958 delivers better preventive efficacy than a placebo that contains no active ingredients.

**Q: Will influenza patients infected with either the 9A H1N1 pandemic influenza strains or seasonal influenza influenza strains be eligible for enrolment in the study? For which influenza strain(s) would use of CS-8958 be approved?**

A: Patients infected with either type of influenza can participate in the trial. Based on the approved label indications for Tamiflu and Relenza, we believe that approval will not be limited to a particular influenza strain.

**Q: What are your production plans for Japan?**

A: We plan to supply enough treatments for 3 to 4 million people by 2010 and for 10 million people from 2011.

**Q: A vaccination program for influenza began in Japan in October. Is CS-8958 related to that effort?**

A: CS-8958 is an anti-viral drug not a vaccine. Public health vaccinations are a useful addition to the use of anti-influenza drugs for treatment and prevention of influenza infections.