Media Release

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BRONCHITOL PAEDIATRIC CYSTIC FIBROSIS CLINICAL TRIAL REPORTS POSITIVE RESULTS

Pharmaceutical research company Pharmaxis (ASX: PXS) is pleased to announce positive results of its recently completed Phase II trial of Bronchitol® (mannitol) in children and adolescents with cystic fibrosis (CF). The trial, conducted across 39 global centres, met its primary endpoint and confirms that Bronchitol is efficacious in young patients, regardless of concomitant dornase alfa use.

The trial (CF204) was a crossover design with patients aged 6 to 17 years receiving either 400mg of Bronchitol or a placebo twice a day for eight weeks on top of standard of care before a washout period of eight weeks followed by a further eight week treatment period on the alternate treatment.

During the Bronchitol treatment period patients had a statistically significant improvement in lung function compared to placebo showing an absolute improvement of 3.42% (p=0.004) in FEV_1 (% predicted) which equates to a relative change in FEV_1 (% predicted) of 4.97% (p=0.005). This treatment improvement in the primary endpoint occurred irrespective of whether patients were taking dornase alfa.

Secondary endpoints in the trial included absolute change in FEF_{25-75} (% predicted) which is thought to have particular significance in younger patients. Bronchitol produced an absolute improvement of 5.75% (p=0.005) in FEF_{25-75} equating to a relative improvement of 10.5%. In other secondary endpoints, treatment induced sputum weight was significantly increased (p=0.012) and a positive trend was seen in FVC. Although not recorded as an endpoint, patients on Bronchitol experienced approximately 25% fewer lung infections and exacerbations of CF which is supportive of the improvements seen in earlier studies despite the short duration of this study.

Gary Phillips, Pharmaxis Chief Executive Officer said: "These clinical trial results are very pleasing. The positive results were seen in a group of patients with a range of genetic subtypes and reinforce the view that Bronchitol has a clear place in the treatment of CF.

"The trial utilised a number of different design features to overcome some of the issues seen in this age group in the earlier phase 3 studies; in particular the European Medicines Agency (EMEA) agreed to the use of large particle size non-respirable mannitol as the placebo in this study rather than a smaller dose of the active drug as used in the phase 3 trials. As a result the placebo effect seen in this study is minimal and it has therefore not only provided important and reassuring additional evidence on the benefit of Bronchitol in the paediatric and adolescent population but also highlighted that the results of the earlier phase 3 studies where a control effect was seen in younger patients may have been understated."

The 92 subjects randomized and treated had a mean age of 12 years. The mean lung function on entry to the trial was 72.2% of the predicted normal FEV_1, and 60% of the population were female. 69% of the patients were taking dornase alfa and 70% were on antibiotics.

In the trial subjects, Bronchitol was well-tolerated overall and had a favourable safety profile. There was no difference in the rate of adverse events or serious adverse events between the treatment groups. The most common adverse event was cough, which was mild to moderate in most cases and similar between the treatment arms. Three patients experienced haemoptysis on Bronchitol and two on placebo. All haemoptysis events were categorised as either scant or mild and the overall level is below background rates reported in other comparable studies.

Mr. Phillips said: “The young patients entered into this study were already receiving high levels of concomitant medication and had moderately impaired lung function so the improvements shown with Bronchitol on top of this standard of care are very welcome. Cross over studies of this type are challenging and I would like to thank everyone involved in the study for their valuable contribution.”

The trial was conducted in centres in Belgium, Canada, France, Germany, Italy, Netherlands, Switzerland, and the United Kingdom. It was designed in consultation with the EMEA as a condition of the marketing authorisation granted for Bronchitol for treating adult cystic fibrosis patients in Europe. To meet the condition in full Pharmaxis will submit a detailed study report to the EMEA in 2016. Based on the positive trial results Pharmaxis will consider an application to extend the European Union marketing authorisation to include children and adolescents but it is not yet known if the trial results alone will be sufficient to gain an approval.

The first scientific presentation of the results will be made at the European Cystic Fibrosis Society meeting in Switzerland in June 2016.

Bronchitol is a precision spray-dried form of mannitol, delivered to the lungs by a specially designed, portable inhaler. The product is approved for marketing for patients aged over six years in Australia and for patients aged 18 years and over throughout the European Union. Marketing authorisation approvals are expected in Russia and Brazil in 2016.

Name of trial	DPM-CF-204: A multicentre, randomised, double-blind, crossover, placebo-controlled study determining the efficacy of dry powder mannitol in improving lung function in subjects with cystic fibrosis aged six to seventeen years	
Trial design	Randomised, multicentre, double-blind, placebo-controlled, crossover. 8 weeks on drug/placebo; 8 weeks washout; 8 weeks on placebo/drug	
Blinding status	Double blind	
Placebo controlled	Yes	
Ratio – mannitol: placebo	1:1	
Placebo	Non-respirable mannitol	
Treatment route	Inhalation	
Treatment frequency	Twice daily	
Dose level	400mg mannitol (or placebo)	
Number of subjects	92	
Subject demographics	Mean age: 12.0 Female: 59.8% FEV_1 mean % predicted : 72.2%	
Study withdrawal rate	Study withdrawals: 8 (mannitol 4; placebo 4) Study withdrawals due to adverse events: 3 (mannitol 2; placebo 1)	
Subject selection criteria	• Confirmed diagnosis of cystic fibrosis • Be aged ≥ 6 years and < 18 years, male and female • Predicted FEV1 of ≥ 30% and ≤ 90% • Pass mannitol tolerance test • rhDNase and maintenance antibiotic use allowed but treatment must have been established at least 3 months prior to screening. No hypertonic saline allowed	
Trial locations	Belgium, Canada, France, Germany, Italy, Netherlands, Switzerland, UK	
Commercial partners involved	No commercial partner	
Trial results		
Primary endpoint	Absolute change from baseline to week 8 in percentage of predicted FEV_1 Relative change in FEV_1 (% predicted)	3.42% (1.12, 5.71) p=0.004 4.97% (1.53, 8.42) p=0.005
Key secondary endpoints	Absolute change in FVC (% predicted)	1.80% (-0.71, 4.32) p=0.158
	Absolute change in FEF_{25-75} (%) (exploratory endpoint)	5.75% (1.82, 9.69) p=0.005
	Treatment induced sputum weight difference (gms)	1.33 (0.30, 2.37) p=0.012
Safety	• No treatment emergent deaths. Number of adverse events and serious adverse events similar between treatment groups • Respiratory adverse events similar between mannitol and placebo: o Cough (16.1% vs 16.1%) o Haemoptysis (3.4% vs 2.3%) • Pulmonary exacerbation and lung infection incidence lower on mannitol than placebo (11.5% vs 16.1% and 2.3% vs 5.7%)	
Results Summary	• Study CF-204 confirms that Bronchitol (inhaled mannitol) is efficacious in children and adolescents, regardless of concomitant rhDNase use. • No safety signals apparent from this study; no difference in haemoptysis between groups. Pulmonary exacerbations were lower in the Bronchitol group	

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About Pharmaxis

Pharmaxis (ACN 082 811 630) is an Australian research pharmaceutical company with a portfolio of products at various stages of development and approval. Its product Bronchitol® for cystic fibrosis is marketed in Europe and Australia and a phase 3 trial to enable completion of an NDA for the US market is underway. Its product Aridol® for the assessment of asthma is sold in Europe, Australia and Asia. The company's development pipeline is centred on its expertise in amine oxidase chemistry and includes Semicarbazide-Sensitive Amine Oxidase Inhibitors (SSAO) for Non-alcoholic Steatohepatitis (NASH) and inflammatory diseases including Chronic Obstructive Pulmonary Disease (COPD), and Lysyl Oxidase Inhibitors (LOX) targeting fibrotic diseases including pulmonary fibrosis and some cancers. In May 2015, Boehringer Ingelheim acquired the Pharmaxis investigational drug PXS4728A, to develop it for the treatment of the liver-related condition NASH. Pharmaxis is listed on the Australian Securities Exchange (symbol PXS). The company's head office, manufacturing and research facilities are located in Sydney, Australia. For more information about Pharmaxis, please see www.pharmaxis.com.au.

Forward-Looking Statements

Forward-looking statements in this media release include statements regarding our expectations, beliefs, hopes, goals, intentions, initiatives or strategies, including statements regarding the potential of products and drug candidates. All forward-looking statements included in this media release are based upon information available to us as of the date hereof. Actual results, performance or achievements could be significantly different from those expressed in, or implied by, these forward-looking statements. These forward-looking statements are not guarantees or predictions of future results, levels of performance, and involve known and unknown risks, uncertainties and other factors, many of which are beyond our control, and which may cause actual results to differ materially from those expressed in the statements contained in this document. Except as required by law we undertake no obligation to update these forward-looking statements as a result of new information, future events or otherwise.