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FDA BRONCHITOL APPROVAL TO GENERATE CASH FLOWS FOR PHARMAXIS

It is the gold standard of success in biotech, but not many Australian companies can boast it – approval from the United States Food & Drug Administration (FDA) of a medicine you have researched and developed.

Sydney based Pharmaxis has reached the top biotech echelon with the US agency's approval of its cystic fibrosis treatment Bronchitol® (mannitol).

Bronchitol is now cleared for sale in the US as an add-on maintenance therapy to improve pulmonary function in cystic fibrosis (CF) patients 18 years of age and older. The product – an inhaled dry powder – is already sold in Europe, Russia and Australia, and now will be available to patients in one of the world's largest markets.

Pharmaxis will manufacture, package and export the product to the USA from its purpose-built Sydney factory where high tech equipment transforms a powder into tiny particles that can be inhaled via a hand-held device.

FDA approval is a "transformational step" for Pharmaxis, says Gary Phillips, chief executive officer of Pharmaxis. "We're very pleased that Bronchitol, an Australian drug discovery, will now be available for patients in the USA. FDA approval is a testament to the capability of our team, who conducted the three large-scale Phase 3 clinical trials that established Bronchitol's safety and efficacy."

Bronchitol joins Pharmaxis' first commercial product from its mannitol platform, Aridol, as being FDA-approved. Aridol is a lung function test designed to help doctors diagnose and manage asthma by detecting active airway inflammation through measuring airway hyper-responsiveness. Patients inhale increasing doses of Aridol through a simple hand-held device: respiratory clinicians administering the test measure the patient's lung function to identify airway inflammation, which can help doctors in providing appropriate asthma treatment.

What makes Bronchitol's FDA approval so transformational for the company and its shareholders, says Phillips, is that it triggers cash flows that bankroll the company to take its PXS-5505 drug candidate, aimed at myelofibrosis in adults, through its planned Phase 1c/2 trials. The ultimate aim of the transformation, he says, is to make Pharmaxis a global leader in myelofibrosis, and flowing from that, to develop PXS-5505's potential in several other cancers, including liver and pancreatic cancers.

"With the two mannitol products in the marketplace and generating revenue, we can shift the focus to our pipeline of small-molecule drugs for big diseases. It's already enabling us to put the most promising of those, PXS-5505 into Phase 1c/2 trials," he says.

PXS-5505 inhibits all the lysyl oxidase (LOX) family of enzymes, which play a crucial role in the development of severe fibrosis, as well as cancers to which fibrosis contributes. The drug is being aimed in the first instance at myelofibrosis, a rare cancer in which normal bone marrow tissue is gradually replaced with a fibrous scar-like material; over time, this leads to progressive bone marrow

failure preventing the production of adequate numbers of red cells, white cells and platelets. Myelofibrosis has a poor prognosis and limited therapeutic options.

Because there is no effective treatment, earlier this year the FDA granted Pharmaxis "orphan drug" designation for PXS-5505 for treatment of myelofibrosis. This is a special status granted to a drug to treat a rare disease or condition; the designation means that PXS-5505 can potentially be fast-tracked, and receive tax and other concessions to help it get to market. The FDA has also given Pharmaxis Investigational New Drug (IND) approval to proceed to Phase 1c/2 trials with PXS-5505.

"All the building blocks are in place now for the Phase 2 trial, and we expect to start recruiting for the study in the first quarter of 2021, and conclude it by the end of 2022," says Phillips. "The aim is to show that our drug is disease-modifying, and will make a real difference to patients with myelofibrosis. That is an attractive market, at more than US$1 billion ($1.4 billion) a year.

"While our primary focus is the development of PXS-5505 for myelofibrosis, the drug also has potential in several other cancers including liver and pancreatic cancers, where it aims to breakdown the fibrotic tissue in the tumour and enhance the effect of existing chemotherapy," adds Phillips. "We already have a lot of interest in the drug from other clinicians, and they're proposing to do studies of the drug in other cancers. Naturally, we're very keen to supply the drug to any such trials."

Importantly, Bronchitol's approval by the FDA gives Pharmaxis the financial runway to see PXS-5505 fully through the clinical trial process, starting with milestone payments from development and commercialisation partner Chiesi USA, the American affiliate of Italian global pharmaceutical company Chiesi Farmaceutici S.p.A, which is responsible for the regulatory approval and commercialisation of Bronchitol. With FDA approval, Chiesi will now pay a US$7 million ($9.9 million) milestone to Pharmaxis, with a further US$3 million ($4.2 million) payable on shipment by Pharmaxis of commercial launch stock, scheduled for the first quarter of 2021.

"With the milestone payments that we will get from Chiesi, plus the existing cash in the company, plus ongoing sales revenue from Bronchitol and Aridol, our funding situation for PXS-5505 is assured," says Phillips. "Our long term supply contracts with Bronchitol and Aridol distribution partners minimises our exposure to the commercial risks and secures a steady revenue stream. The focus for investors becomes PXS-5505 and the rest of our anti-fibrotic LOX program.

"PXS-5505 has a unique mechanism of action that has the potential for disease modification, and we're looking forward to seeing the effect of this drug in clinical trials," adds Phillips.

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SOURCE: Pharmaxis Ltd, Sydney, Australia

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About Pharmaxis

Pharmaxis Ltd is an Australian pharmaceutical research company developing drugs for inflammatory and fibrotic diseases, with a focus on myelofibrosis. The company has a highly productive drug discovery engine built on its expertise in the chemistry of amine oxidase inhibitors, with drug candidates in clinical trials. Pharmaxis has also developed two respiratory products which are approved and supplied in global markets, generating ongoing revenue.

Pharmaxis is developing its drug PXS-5505 for the bone marrow cancer myelofibrosis which causes a build up of scar tissue that leads to loss of production of red and white blood cells and platelets. The US Food and Drug Administration has granted Orphan Drug Designation to PXS-5055 for the treatment of myelofibrosis and permission under an Investigational Drug Application (IND) to progress a phase 1c/2 clinical trial that is scheduled to begin recruitment in Q1 2021. PXS-5505 is also being investigated as a potential treatment for other cancers such as liver and pancreatic cancer.

Other drug candidates being developed from Pharmaxis' amine oxidase chemistry platform are targeting fibrotic diseases such as kidney fibrosis, NASH, pulmonary fibrosis and cardiac fibrosis; fibrotic scarring from burns and other trauma; and inflammatory diseases such as Duchenne Muscular Dystrophy.

Pharmaxis has developed two products from its proprietary spray drying technology that are manufactured and exported from its Sydney facility; Bronchitol® for cystic fibrosis, which is approved and marketed in the United States, Europe, Russia and Australia; and Aridol® for the assessment of asthma, which is approved and marketed in the United States, Europe, Australia and Asia.

Pharmaxis is listed on the Australian Securities Exchange (PXS). Its head office, manufacturing and research facilities are in Sydney, Australia. www.pharmaxis.com.au

About Bronchitol

Bronchitol is a precision spray-dried form of mannitol, delivered to the lungs by a specially designed, portable inhaler. Bronchitol works by rehydrating the airway/lung surface and promoting a productive cough. The product is approved for marketing for the treatment of cystic fibrosis patients aged over six years in Australia and Russia and for patients aged 18 years and over throughout the European Union and the United States. In all markets, patients are required to have a tolerance test prior to being prescribed Bronchitol to ensure that they are not hyper responsive to mannitol.

What is myelofibrosis?

Myelofibrosis is a disorder in which normal bone marrow tissue is gradually replaced with a fibrous scar-like material. Over time, this leads to progressive bone marrow failure. Under normal conditions, the bone marrow provides a fine network of fibres on which the stem cells can divide and grow. Specialised cells in the bone marrow known as fibroblasts make these fibres.
In myelofibrosis, chemicals released by high numbers of platelets and abnormal megakaryocytes (platelet forming cells) over-stimulate the fibroblasts. This results in the overgrowth of thick coarse fibres in the bone marrow, which gradually replace normal bone marrow tissue. Over time this destroys the normal bone marrow environment, preventing the production of adequate numbers of red cells, white cells and platelets. This results in anaemia, low platelet counts and the production of blood cells in areas outside the bone marrow for example in the spleen and liver, which become enlarged as a result.

Myelofibrosis can occur at any age but is usually diagnosed later in life, between the ages of 60 and 70 years. The cause of myelofibrosis remains largely unknown. It can be classified as either JAK2 mutation positive (having the JAK2 mutation) or negative (not having the JAK2 mutation).

Source: Australian Leukemia Foundation: https://www.leukaemia.org.au/disease-information/myeloproliferative-disorders/types-of-mpn/primary-myelofibrosis/

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. For example, despite our efforts there is no certainty that we will be successful in partnering our LOXL2 program or any of the other products in our pipeline on commercially acceptable terms, in a timely fashion or at all. 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.