Press Release

Boehringer Ingelheim is initiating Phase IIa study for the development of a new treatment for diabetic retinopathy – a leading cause of vision-loss

- Diabetic retinopathy (DR) is the second severe metabolic complication on top of non-alcoholic steatohepatitis (NASH) to be investigated for BI 1467335, which was acquired from Pharmaxis
- Pharmaxis will receive €10 million milestone payment when the first patient is dosed in this 2nd indication Phase IIa study.
- Boehringer Ingelheim's holistic cardio metabolism R&D strategy reaches from risk factors, like obesity to complications, like NASH and DR

INGELHEIM, Germany and SYDNEY, Australia – 7 September 2017 – Boehringer Ingelheim and pharmaceutical research company Pharmaxis (ASX: PXS) announce that Boehringer Ingelheim is initiating the Phase IIa study ROBIN (Randomized study of Orally administered BI 1467335 in patients with Non-proliferative diabetic retinopathy without center-involved diabetic macular edema). This marks the beginning of the clinical development program for BI 1467335 in a second indication targeting a severe diabetes complication. An already ongoing Phase II clinical study program is investigating the compound in NASH. BI 1467335 is an oral inhibitor of amine oxidase, copper containing 3 (AOC3)[1].

Diabetic retinopathy (DR) is the leading cause of vision-loss in adults aged 20-74. It progresses from mild nonproliferative diabetic retinopathy to moderate and severe nonproliferative diabetic retinopathy (NPDR), characterized by retinal hemorrhages and vascular changes in the retina, to proliferative diabetic retinopathy (PDR), characterized by the growth of new blood vessels on the retina. Diabetic Macular Edema (DME), characterized by retinal thickening from leaky blood vessels, can develop at all stages of retinopathy. Of an estimated 285 million people with diabetes mellitus worldwide, approximately one third have signs of DR and of these, a further one third of DR is vision-threatening DR (severe NPDR, PDR and DME).[2]

The ROBIN trial is a Phase IIa multi-centre, double-masked design in 100 patients with moderately severe to severe non-proliferative diabetic retinopathy (NPDR) without center-involved diabetic macular edema (CI-DME). The primary objectives are to establish proof of clinical principle and to evaluate the safety and tolerability of BI 1467335. Patients will be randomized to either BI 1467335 or to placebo for a 12-week treatment period with an additional 12-week follow-up period afterwards. A subsequent Phase IIb study will seek to confirm and extend these findings.[3]

Dr. Christopher Corsico, Chief Medical Officer Boehringer Ingelheim said, "We are delighted to advance BI 1467335 into Phase II clinical research for a second indication, targeting a severe complication of diabetes. This is important news for the millions of patients threatened by losing their vision. Boehringer Ingelheim is committed to developing novel treatments designed to address unmet medical need and improve public health and looks forward to studying this novel compound in NPDR patients".

Gary Phillips, Pharmaxis CEO said, "I'm delighted that our partner Boehringer Ingelheim has decided to pursue a second indication for the drug acquired from Pharmaxis in 2015. It will be very rewarding for the

[1] Also known as vascular adhesion protein-1 (VAP-1) or semicarbazide-sensitive amine oxidase (SSAO)
[2] Lee R, Wong TY, Sabanayagam C. Epidemiology of diabetic retinopathy, diabetic macular edema and related vision loss. Eye Vis (Lond) 2015;2:17
[3] https://clinicaltrials.gov/ct2/show/NCT03238963

Pharmaxis team to see another group of patients benefit from our initial work. The deal structure negotiated with BI recognised the potential that the drug had in multiple indications so expanding the development plan to include diabetic retinopathy as well as NASH means that we will receive a €10m milestone payment when the first patient is dosed in the DR Phase IIa study and that all the potential development milestones in the deal (€418.5m /A$625m), would be payable to Pharmaxis should both indications be approved. Our belief that Boehringer Ingelheim would be a company that sought to maximize the potential of the drug was central to our choice of partner and this latest development reaffirms that view."

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About Boehringer Ingelheim
Innovative medicines for people and animals have for more than 130 years been what the research-driven pharmaceutical company Boehringer Ingelheim stands for. Boehringer Ingelheim is one of the pharmaceutical industry's top 20 companies and to this day remains family-owned. Day by day, some 50,000 employees create value through innovation for the three business areas human pharmaceuticals, animal health and biopharmaceutical contract manufacturing. In 2016, Boehringer Ingelheim achieved net sales of around 15.9 billion euros. With more than three billion euros, R&D expenditure corresponds to 19.6 per cent of net sales.

Social responsibility comes naturally to Boehringer Ingelheim. That is why the company is involved in social projects such as the "Making More Health" initiative. Boehringer Ingelheim also actively promotes workforce diversity and benefits from its employees' different experiences and skills. Furthermore, the focus is on environmental protection and sustainability in everything the company does.

More information about Boehringer Ingelheim can be found on www.boehringer-ingelheim.com or in our annual report: http://annualreport.boehringer-ingelheim.com.

About Pharmaxis
Pharmaxis (ACN 082 811 630) is an Australian pharmaceutical research company focused on inflammation and fibrosis with a portfolio of products at various stages of development and approval. Its product Bronchitol® for cystic fibrosis is marketed in Europe, Russia and Australia. 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 a series of Lysyl Oxidase Inhibitors that will enter clinical development in 2017 targeting fibrotic diseases of the heart, kidney, liver and lung. In May 2015, Boehringer Ingelheim acquired the Pharmaxis investigational drug PXS-4728A, a potent inhibitor of Semicarbazide-Sensitive Amine Oxidase (SSAO), to develop it for the treatment of the liver-related condition Non-alcoholic Steatohepatitis (NASH) and other inflammatory diseases. 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.