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Pharmaxis, Boehringer PXS4728A Meets Phase I Endpoints

Pharmaxis says that the Boehringer Ingelheim acquired PXS4728A has met all its primary and secondary endpoints in its phase I trial for inflammatory diseases.

Pharmaxis said that Boehringer Ingelheim acquired PXS4728A to develop it as a treatment for cardio-metabolic diseases such as non-alcoholic steato-hepatitis or NASH.

Pharmaxis chief executive officer Gary Phillips told Biotech Daily that although there were no milestone payments attached to completing the phase I trial, there would be at the start of the phase II trial process.

In January, Pharmaxis began a two-part phase I trial of with an the initial single ascending dose study in 48 subjects, to be followed by a multiple ascending dose study in a separate group of 24 subjects (BD: Jan 21, Apr 7, 2015).

In May, Pharmaxis said that the Ingelheim, Germany-based Boehringer Ingelheim would pay an upfront fee of $39.2 million and potentially more than $750 million for PXS4728A for non-alcoholic steato hepatitis (BD: May 18, 2015).

Pharmaxis said at that time that PXS4728A which was a semicarbazide-sensitive amine oxidase vascular adhesion protein-1 (SSAO/VAP-1) inhibitor that worked by blocking leucocyte adhesion and tissue infiltration in inflammatory processes.

Today, the company said that following the April phase Ia single ascending dose positive results, the phase Ib multiple ascending dose trialled three oral daily doses ranging from 3mg to 10mg of PXS4728A over 14 days, which “was found to be safe and well tolerated”.

Pharmaxis said the data “confirmed the high oral bioavailability of PXS4728A and most importantly, showed these low doses are efficacious in inhibiting the enzyme and cause a long lasting inhibition suggesting PXS4728A can be dosed once a day”.

The company said that the positive phase I results enabled Boehringer Ingelheim to proceed with further development of the program.

Mr Phillips said that NASH was “becoming more prevalent and there is a clear need for more effective therapies”.

“PXS4728A inhibits an enzyme which has been highlighted in independent peer-reviewed publications as an excellent target to treat NASH and this first human trial of the drug confirms its strong pre-clinical profile translates into human studies,” Mr Phillips said.

“It is rare to be able to demonstrate effective target engagement in a phase I study so the fact that the long lasting enzyme inhibition seen in the phase Ia study was reinforced when given once a day for 14 days adds to our confidence in PXS4728A,” Mr Phillips said.

“We now look forward to the next value appreciating steps as the clinical development program proceeds with Boehringer,” Mr Phillips said.

Mr Phillips told an investor meeting in Melbourne today that the company had moved its focus to drug discovery for fibrosis and inflammation and had more products coming from its amine oxidase chemistry platform.

Mr Phillips said Bronchitol for cystic fibrosis was being marketed by commercial partners and the company would concentrate on taking drug candidates to phase II for partnering.

The University of Sydney’s Prof Jacob George said that about 30 percent of the world’s population apart, from sub-Saharan Africa and rural India, had fatty liver disease and the simplest intervention of diet and exercise was not being adopted.

Prof George said that obesity had led to liver fat and fibrosis in people aged over 60 years, but today children were obese and developing type 2 diabetes, implying that in 10 years there would be a significant increase in non-alcoholic steato-hepatitis and fibrosis.

Pharmaxis head of drug discovery Dr Wolfgang Jarolimek told the meeting that PXS4728A had a fast uptake, a half-life of less than two hours and was a long-lasting inhibitor of enzyme activity of more than 24 hours, and had no negative safety signals.

Pharmaxis was up two cents or 9.8 percent to 22.5 cents.