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IN THE CLINIC STARTING PHASE IB

Hua Medicine tests glucokinase activator in Chinese diabetics

By Shannon Ellis, Staff Writer

SHANGHAI – Hua Medicine Ltd. has commenced a phase Ib trial for HMS5552, a glucokinase activator (GKA), in early stage type 2 diabetes patients in a multicenter, multidose study in China.

Coming off strong results in its phase Ia trials including 60 healthy volunteers, HMS5552 demonstrated glucose regulatory hormone modulation capabilities. Now it is looking to find similar results in diabetic sufferers.

According to Chen, its phase Ia results show for the first time significant effect of GKA on increasing human plasma GLP-1 levels.

"Now we have the second part. First we validated that our glucokinase activator is a blood glucose dependent activator, and significantly reduced hypoglycemic risk in the clinic. This is differentiated from some of the previous GKAs studied in clinical trials."

"In preclinical and previous clinical studies we realized that glucokinase plays a central role in blood glucose regulation, through controlling hormones, in particular insulin, glucagon and GLP-1, that are the major players in controlling blood glucose," Li Chen, CEO of Hua Medicine, told BioWorld Asia.

It is looking to push diabetes treatment further with the possibility that GKA would be affecting most of the major glucose-regulation pathways in the body including insulin secretion, postprandial glucose control, hepatic glucose production, and GLP-1 modulation.

The phase Ia study showed effects in a variety of biochemical diabetes markers, notably glucose stimulated insulin release (GSIR) – which is particularly important to Asian diabetics.

The stand out factor for HMS5552 is it consistently increased post-meal GSIR multiple-fold above the post-meal insulin levels seen in the placebo group, with very low risk for hypoglycemia. Chinese diabetics suffer earlier beta cell deterioration, and have high blood glucose levels after meals.

"Phase Ia results showing higher GSIR profiles were important in affirming that HMS5552 should be particularly beneficial in treating Chinese and Asian-dominant diabetics," said Yi Zhang, director of clinical development at Hua Medicine.

Several companies are developing GKA drugs but none have been approved. Hua sees the potential for HMS5552 to be a best-in-class candidate – and demonstrate China's ability to innovate.

Hua Medicine holds the global rights to HMS5552 after in-licensing the drug from Roche AG, of Basel, Switzerland. Chen was a former CSO at Roche China. (See BioWorld Asia, Jan. 2)

The company is trying to tackle the control of blood glucose levels at an early stage before organ function deteriorates beyond repair – which is currently not achievable with current standard of care.

In China, first-line therapies can begin with metformin or acarbose. When these fail to control blood glucose levels various therapies are added on, oral and then injectable. Chen said less than 30 percent of type 2 diabetics in China are able to control their blood glucose through these methods.

"Our approach is targeting three major organs – pancreas, liver and intestine – to allow the glucose management system to work properly and coordinate to do the job," said Chen, "rather than current therapy which only targets one particular organ to drive the drug effect."

Hua is advocating a personalized therapy approach to diabetes and has designed the phase Ib trials to determine which type of diabetic will benefit the most from HMS5552.

The hope is that a multi-pathway strategy will be especially effective for earlier stage diabetic patients everywhere but more common in China and Asia.

The phase Ib trials are being held at two sites in Nanjing with the possibilities of more sites being added. The trial will be completed by the third quarter of this year. It will be a double-blind, placebo-controlled multiple-ascending dose trial in 50 diabetic male and female adults.

Daily doses will range from 25 mg to 200 mg (and up to 400 mg if needed). The trial is set to test HMS5552's safety, tolerability and pharmacokinetics, and evaluate the hormone biomarkers and pharmacodynamics of multiple oral doses of HMS5552 over a period of two weeks.

Chen said the plan is to continue trials in China through phase II, "then validate our personal medicine concept and expand it with a clinically useful biomarker to initiate global trials. For global trials, we would like to identify partners from the U.S. or EU community to work together with Hua to deliver this medicine to the regions for those patients."

Hua Medicine is a drug development company with global rights to two novel assets and an internally developed central nervous system compound. Hua's strategy is to leverage China's cost effective drug development capabilities while in licensing promising candidates from the West.

Data from the phase Ia have been submitted to for presentation at the 74th American Diabetes Association Conference in San Francisco in June.