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IN THE CLINIC

Hutchison-discovered fruquintinib moves into phase III CRC trial

By Cornelia Zou, Staff Writer

HONG KONG – The R&D arm of a China-based health care group owned by the multinational conglomerate Hutchison Whampoa Ltd. (HK:13) has moved its leading oncology candidate into phase III.

Hutchison Medipharma Ltd. (HMP), the majority-owned R&D company of Hutchison China Meditech Ltd. (Chi-Med), said it initiated the phase III registration study in colorectal cancer (CRC) patients in China for its investigational small-molecule fruquintinib (HMPL-013), which selectively inhibits vascular endothelial growth factor receptors (VEGFR).

"Fruquintinib's main point of differentiation is its very high selectivity of VEGFR1, 2 and 3 as compared to other therapies in this area," Christian Hogg, CEO of Hutchison Medipharma,

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told *BioWorld Today*.

At an advanced stage, tumors secrete large amounts of vascular endothelial growth factor to stimulate the formation of excessive vasculature to provide greater blood flow, oxygen and nutrients to the tumor. The drug works by blocking the development of new blood vessels tumors need to grow and invade.

The first patient in the trial was dosed Dec. 12 when preparations and site selection began in June this year.

"CRC, lung and gastric cancer in aggregate represent 48.4 percent of all new cancer cases in men in China and 34 percent of all new cancer cases in women in China," Hogg said. "Therefore, the potential for fruquintinib is significant."

CRC is the third most commonly diagnosed cancer and the fifth most common cause of cancer death in China after lung, liver, stomach and esophagus cancers. In 2012, there were an estimated 390,000 cases of CRC diagnosed in China, representing 10 percent of the total cancer incidence in the country.

The randomized, double-blind, placebo-controlled, multicenter, phase III study is targeted at treating patients with locally advanced or metastatic CRC, who have failed at least two prior systemic antineoplastic therapies, including fluoropyrimidine, oxaliplatin and irinotecan. Patients will be randomized at a 2-to-1 ratio to receive either 5 mg of fruquintinib orally once per day, on a three-weeks-on, one-week-off cycle, plus best supportive care (BSC) or placebo plus BSC.

The primary endpoint of the trial is overall survival, with secondary endpoints of progression-free survival, objective response rate, disease control rate and duration of response. The company said more than 400 patients will be enrolled in about 25 centers, with top-line results expected in 2016.

Fruquintinib was discovered by HMP in China and at this time is undergoing clinical trials only in China.

HMP conducted the first-in-human phase I trial in 2011, in which 40 CRC patients were treated with fruquintinib. The company released positive results in April 2013. Based on those data, a phase Ib study was initiated later with 62 more CRC patients involved. Clinical trials for solid tumors are ongoing at different phases in China, testing fruquintinib as single-agent therapy or in combinatopm with chemotherapy.

"Fruquintinib is in a phase II study in third-line non-small-cell lung cancer as well as a phase Ib study in second-line gastric cancer," Hogg said.

In October 2013, HMP and big pharma firm Eli Lilly and Co. entered a licensing agreement that allows the two parties to co-develop and commercialize fruquintinib in China. Under the terms of that agreement, HMP will be responsible for all future development of fruquintinib in China. The two parties will share costs.

HMP will receive up-front payments as well as development and regulatory approval milestone payments from Lilly, which could add up to $86.5 million, plus tiered royalties starting in the midteens on net sales upon fruquintinib's successful commercialization in China.

"The collaboration with Lilly will allow for fruquintinib to be developed across various tumor types in China and at a far greater speed than if we went alone," Hogg said.

HMP focuses on discovering novel therapeutics in oncology and autoimmune diseases. The company's other leading oncology drug candidate is volitinib, a c-Met inhibitor that has shown strong results in patients with papillary renal cell carcinoma (PRCC). With positive phase I data, volitinib is potentially the breakthrough therapy for the rare form of cancer. (See *BioWorld Today*, May 29, 2014.)

Just a few months ago, HMP terminated the phase III trials for its lead candidate, HMPL-004, a botanical treatment for ulcerative colitis, citing a high placebo effect. But the company has grown a robust small-molecule pipeline, partnered with Lilly, Astrazeneca plc and Johnson & Johnson unit Janssen. (See *BioWorld Asia*, Aug. 27, 2014.) //

OTHER NEWS TO NOTE

Ossianix Inc., of Philadelphia, said it expanded and extended its collaboration with **H. Lundbeck A/S**, of Valby, Denmark, which follows a previous equity investment in 2012 and prior research collaboration in 2013. The deal involves the use of Ossianix's single domain antibody platform based on the shark VNAR structure to deliver next-generation central nervous system biotherapeutics. Ossianix will work with Lundbeck on multiple targets aligned with the big pharma's therapeutic goals, and the collaboration will continue to work on the ligand-gated P2X3 ion channel expressed on sensory neurons for the treatment of neuropathic pain. Lundbeck will fund the research plan with development and regulatory milestones, and a joint research committee will manage the projects. A third component of the agreement provides an additional equity investment for Ossianix to advance its own therapeutic programs. Specific financial details were not disclosed.

Portage Biotech Inc., of Toronto, said subsidiary Portage Pharmaceuticals Ltd. (PPL) successfully validated a new cell permeable peptide platform technology derived from human genes that has been shown to efficiently deliver an active pharmacological agent or cargo into a cell without disrupting the cell membrane. PPL said it converted its previously filed provisional patent application for the system to an international patent application that includes a variety of structures utilizing cargos that address important areas of medical need.

Prothena Corp. plc, of Dublin, gained an FDA fast track designation for NEOD001, a monoclonal antibody for the potential treatment of amyloid light-chain amyloidosis. The company said it is the first investigational immunotherapy specifically targeting the disease-causing protein in AL amyloidosis to receive fast track status. It recently initiated a phase III global registration study of the therapy.