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# Canbridge confirms ligand CD95 in Chinese patient biomarker study

***By Shannon Ellis, Staff Writer***

SHANGHAI – Canbridge Life Sciences Inc. has confirmed the existence of ligand CD95 in Chinese glioblastoma patients after completing the first such biomarker study of its kind on the mainland. The study demonstrated a high degree of CD95 ligand expression consistency between geographically diverse Chinese and Western glioblastoma multiforme patients.

Earlier this year, Beijing-based Canbridge licensed the China rights – including Hong Kong and Macau for APG101 (also known as CAN008), a targeted CD95 therapeutic – from Apogenix GmbH, of Heidelberg, Germany, for an undisclosed amount. (See *BioWorld Asia*, July 22, 2015.)

The deal covered glioblastoma – a relatively rare but deadly form of brain cancer – as well as other solid tumors.

CD95 is also present in several other cancers, notably pancreatic, head and neck, lung and certain blood cancers. It's an important factor in the cancer immune pathway.

APG101 is a fully human fusion protein that inhibits the CD95 ligand, a member of the tumor necrosis factor superfamily. By blocking the CD95 ligand, APG101 restores the immune response against tumors and inhibits invasive tumor cell growth. For patients with a high level of CD95 expression, APG101 has a dual function: It can activate and restore immune response to inhibit tumor growth, similar to PD-1 immune therapy, as well as directly inhibit tumor cell migration.

The Apogenix phase II trial in Europe, with the aid of a companion biomarker diagnostic, found that patients having a newly identified epigenetic biomarker associated with CD95 ligand experienced the greatest benefits. Biomarker-positive patients treated with APG101 showed a statistically significant prolongation of overall survival of 16.1 months compared to 6.5 months in patients treated with radiotherapy alone.

In developing CAN008 for the China market, the first order of business, according to James Xue, CEO of Canbridge, has been to prove the ligand exists in Chinese patients as well.

"We confirmed the expression level of CD95 among Chinese glioblastoma patients was highly consistent with what Apogenix had confirmed in the Western population," Xue told *BioWorld Today*. "This reduces the risk of phenotype differences or that the target therapy might work differently in different populations. This is a way to validate the mechanism of action in the Chinese population and de-risk the program."

## TAIWAN FIRST FOR PHASE I/II

Along with the announcement of the biomarker study, Apogenix has extended Canbridge's development, manufacturing and commercialization rights to include Taiwan. And given the biomarker results, Canbridge will kick off a phase I/II study of CAN008 in newly diagnosed glioblastoma patients in that territory. The first patient is expected to be dosed later this year.

There are a couple of reasons why branching into Taiwan makes sense. According to Xue, even though the market is relatively small, with a population of 23 million and a few hundred glioblastoma patients each year, Taiwan offers other advantages.

"It is an attractive market for us. Taiwan is a world-class health care market, if we have a successful product in Taiwan we should expect very good level of pricing and reimbursement," said Xue.

But he makes it clear the best reason for starting with Taiwan is to get the drug to market as expeditiously as possible, given the few treatment options available for glioblastoma patients and poor survival rates. Taiwan offers the chance to collect trial data quickly that could serve to speed up approvals on both sides of the Taiwan Straits.

The administrative process for getting a clinical trial approved in Taiwan is still quicker than on the mainland, even with recent moves to clear up the CFDA application backlog, and there is now the added advantage that the two governments have made moves to harmonize regulations.

Xue pointed out that Taiwan and mainland agencies will now accept data from the other side, if coming from the list of top clinical trial hospitals designated as eligible. Canbridge is hopeful that the data collected in Taiwan will be permitted when the company files for the China

investigational new drug application (IND) – expected to happen in 2017 after the CMC technology transfer is completed for local manufacturing, a necessary step to apply as a local drug.

Since there are plans to collect efficacy data in Taiwan, this opens the door to the possibility that regulators might feel comfortable bypassing phase II in China and going straight to phase III.

"This will speed things up considerably," adds Xue.

After interacting with regulators, Xue said, Canbridge received positive signals that it will receive green channel treatment given that the product candidate is a fusion protein, a targeted therapy with a companion diagnostic, and has the potential to be first in class to meet a very dire medical need.

European data collected by Apogenix, which has completed the phase II study, may also be considered a strong reference for the regulators.

The Apogenix phase II study tested APG101 as a second-line treatment, in patients who had failed first-line treatment. The highest dose, of 20 mg per kilogram of body weight was well tolerated and no anti-drug antibodies against the therapy were detected. Given the good safety profile of the treatment, Xue said the aspiration is to eventually test the candidate as a front-line treatment.

Canbridge has two other candidates in the pipeline as well.

Furthest along is Caphosol, a rinse treatment for oral mucositis that afflicts patients after cancer treatments. Canbridge plans to submit a China registration application this year.

It has also licensed the Greater China and Korea rights for ATI-1123 from Azaya Therapeutics Inc., of San Antonio, a stabilized liposomal formulation of docetaxel with the potential to be more effective than conventional docetaxel in inhibiting NSCLC tumors. Canbridge plans to submit the IND in China in 2017.