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Cuban-discovered lung cancer vaccine heading to U.S. phase III; Bioven lands marketing option

By Nuala Moran, Staff Writer

LONDON – Bioven Europe Ltd. has taken an option on U.S. marketing rights to the Cuban-discovered lung cancer vaccine EGF-PTI, as it moves to extend the pivotal phase III trial to the U.S.

"We have not got approval, but we are well into the process. We expect a response on the IND [soon]," said Steve Drew, CEO.

Despite a warming relationship, the U.S. trade embargo against Cuba remains in place. However, the agreement to license U.S. rights is not contingent on the ban being lifted, because at this stage Bioven is seeking to include the U.S. in the phase III trial, rather than to commercialize the product.

The company is talking to the Office of Foreign Assets Control to get approval for the importation of EGF-PTI into the U.S. for the clinical trial. The phase III open-label study is due to recruit 418 patients, of which it is expected around 40 will be in the U.S. arm.

The rights to EGF-PTI were granted by Cimab SA, of Havana, the commercialization arm of the country's Center for Molecular Immunology, where the vaccine was discovered and developed. Bioven paid an undisclosed fee for the option.

Elsewhere, phase III development of the treatment for wild-type non-small-cell lung cancer (NSCLC) recently recommenced, following a halt for non-medical reasons.

The study is actively recruiting in Malaysia, the Philippines, Thailand and the U.K.

Bioven began phase III development of EGF-PTI (then BV-NSCLC-001) in 2012, but the trial was stopped when it became evident that the product was being overtaken by advances in cancer immunotherapy.

Drew said that by 2013 immunotherapy had become a hot topic, reaching the top of the agenda at the annual American Society of Clinical Oncology meeting. The following year, biomarkers were the talk of the conference. "We were stuck with an immunotherapy with no biomarker – we weren't keeping pace with the market. On the advice of clinicians we decided to stop the trial," he told *BioWorld Today*.

"We clearly needed to identify a biomarker, and in collaboration with our partner in Cuba, we looked at Cuban data, and data from Malaysia," said Drew. The research found that a high level of circulating epidermal growth factor at initial screening correlates to longer overall survival. Bioven subsequently got approval to recommence phase III development on the basis that patients would be tested to select likely responders.

Bioven was formed in 2002 by a group of investors from Malaysia – a country that remained on good terms with Cuba during the cold war with the U.S. and its allies – to commercialize vaccines discovered and developed at Cuba's Center for Molecular Immunology.

The consortium had put in sufficient funding to complete phase III development of EGF-PTI; however, the pause to develop the biomarker increased costs and, in April last year, Bioven raised $29 million from a Malaysian government fund to cover the shortfall.

To further boost the coffers, Bioven is planning to list on the Alternative Investment Market in London later this year, with the ambition of raising about $30 million.

Phase III development of EGF-PTI first recommenced in Malaysia in May 2015, with the other centers starting recruitment in January 2016. As with the stopped phase III, the new study is not placebo-controlled. "The FDA has accepted this as an open-label pivotal trial and [pending approval of the IND] will join the international study," Drew said.

Patients with advanced, nonresectable lung cancer will be vaccinated before, during and after chemotherapy, with vaccination continuing for as long as there is no disease progression.

EGF-PTI, which consists of recombinant EGF with a carrier and an adjuvant, stimulates the immune system to generate anti-EGF antibodies that neutralize EGF at a systemic level, preventing it from binding to its receptor.

That blocks the cascade of cellular events that otherwise results in uncontrolled tumor growth. The systemic neutralization of EGF distinguishes EGF-PTI from drugs that target overexpression of EGF at a tumor level, and in that

sense, Bioven said the product is a true vaccine. The acronym PTI stands for pathway targeted immunization.

STILL AN UNMET MEDICAL NEED

In parallel with the clamor for biomarkers, the NSCLC market is fragmenting around specific subtypes of the disease, with products aimed at specific EGF mutations. However, Drew noted that, as yet, there is no targeted therapy for the 60 percent of cases of wild-type lung cancer in which there is no underlying EGF mutation.

Indeed, the latest research indicates patients with wild-type NSCLC do better on standard chemotherapy than when treated with epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors.

A meta-analysis of clinical trials, carried out by June-Koo Lee, of Seoul National University Hospital, South Korea, and published in the *Journal of the American Medical Association* in April, found there was improvement in progression-free survival, but not in overall survival, in patients receiving conventional chemotherapy vs. patients treated with EGFR tyrosine kinase inhibitors.

"We are very confident about the science and there is still unmet medical need for wild-type NSCLC," said Drew.

Bioven is awaiting the imminent publication of overall survival data from the Cuban phase III trial of EGF-PTI (the product is known as Cimvax-EGF in Cuba).

Interim data from the study reported survival of 50 percent at 12 months in the treated group, compared to 30 percent for standard of care.

Cimvax-EGF was approved in Cuba on the basis of five phase I/II studies and one 80-patient phase II controlled trial.

The improving relationship between the U.S. and Cuba has not as yet had much practical impact on Bioven, according to Drew. "Diplomacy and changing rules between countries takes time to have an effect, but it helps to have a more positive climate," he said.

Speaking in Havana in March, U.S. President Barack Obama called on Congress to end the trade embargo, but there is little prospect of that happening before Obama steps down next year.