ElsaLys Biotech

PRESS RELEASE

ELSALYS BIOTECH ACQUIRES A FIRST-IN-CLASS ANTIBODY WITH A DUAL BIOLOGICAL MECHANISM OF ACTION: ANTI-ANGIOGENIC AND IMMUNO-MODULATOR

- **Developed so far by MABLIFE in ophthalmology, the anti-CD160 antibody has also a significant therapeutic potential in oncology.**
- **According to preliminary efficacy data observed in animals, ELSALYS BIOTECH has already initiated the preclinical evaluation of this antibody in neovascular eye disease.**
- **Two years after its inception, the Company hosts three proprietary antibodies and four development programs in cancer, ophthalmology and inflammation.**

Lyon and Illkirch-Graffenstaden, 2 July 2015, BIOTECH ELSALYS, a biopharmaceutical company that designs and develops "first-in-class" therapeutic antibodies against cancer and inflammatory diseases, today announced the acquisition of the development and marketing rights of the anti-CD160 antibody from the company MABLIFE. As the anti-CD160 antibody has shown its efficacy in cancer and eye disease animal models, ELSALYS BIOTECH has already initiated the preclinical evaluation of different humanised versions of this antibody in age-related macular degeneration, an eye disease associated with uncontrolled vascular proliferation. The result of this study, which should lead to the selection of a first drug candidate, is expected in the first half of 2016.

Originates from the work of Dr Armand BENSUSSAN (Centre de Recherche sur la Peau, UMR 976, University Paris Diderot, St Louis Hospital) and Dr Philippe LE BOUTEILLER (Centre de Physiopathologie Toulouse-Purpan, INSERM UMR 1043, CNRS UMR 5282, University of Toulouse III), the anti-CD160 antibody has a dual mechanism of action: it triggers the death of new blood vessels associated with tumours and certain eye diseases (anti-angiogenic effect) and stimulates the action of immune tumours killers (immunomodulatory effect). This unique dual property has lead ELSALYS BIOTECH to develop two versions of the anti-CD160 antibody: the first (anti-angiogenic effect only) is for the treatment of vascular eye diseases and the second (which combines anti-angiogenic and immunomodulator effects) target cancer.

"The anti-angiogenic effect of anti-CD160 is really new. Unlike other drugs of its class, anti-CD160 does not deprive the new blood vessels of growth factor to hinder their development, but induces their death while preserving the existing vessels", said Dr Philippe LE BOUTEILLER. *"With this antibody, we are thus able to reduce new retinal vessels in mice eyes with retinopathy".*

"By combining anti-CD160 with chemotherapy, we were also able to reduce the tumour burden and prolong the survival of mice with aggressive tumours, such as melanoma or fibrosarcoma", said Dr Armand BENSUSSAN. *"The antibody appears to starve the tumour by reducing the number of new intra-tumour vessels, facilitate the delivery of chemotherapy by stabilising existing vessels, but also stimulate the activity of NK cells and T lymphocytes".*

"The acquisition of anti-CD160 is obviously a great opportunity for a company like ours", said Dr Christine GUILLEN, CEO and co-founder of ELSALYS BIOTECH. *"With this antibody, we not only strengthen our position in antibody immunotherapy, but we reach a stage of maturity that allows us to envisage more rapid development and thus reinforce the commitment of our investors. In addition, it demonstrates once again that the expertise and experience of our team make a difference when it comes to identifying gems with very strong therapeutic potential".*

About the anti-CD160 antibody

Identified and characterised by Dr Armand BENSUSSAN and Dr Philippe LE BOUTEILLER, the CD160 receptor is highly expressed on the surface of activated endothelial cells that line the new blood vessels present in most tumours. It is also associated with vascular anarchic proliferation that is found in eye diseases, such as macular degeneration or diabetic retinopathy affecting some patients and preterm child's. In both cases, CD160 helps regulate uncontrolled vascularisation: once bound to its natural ligand (the signal recognised by the receptor, in this case the self molecule HLA-G and HVEM, the receptor which serves as an entry route for the Herpes virus), it activates and triggers the death of activated endothelial cells of new vessels. Conversely, existing vessels are stabilised since they fail to express CD160 on their surface.

To reduce vascular proliferation (anti-angiogenesis), scientists have generated and characterised an antibody against the CD160 receptor. This antibody, an agonist, reproduces and amplifies the action of the ligand to trigger the death of new vessels while stabilising existing vessels. Today, the effectiveness of this approach has already been validated in different animal models of eye diseases and cancers:

- In a retinopathy mouse model, treatment with anti-CD160 restores the vascular circulation of the diseased retina.
- In melanoma and fibrosarcoma mice models, anti-CD160 combined with chemotherapy results in a significant reduction in tumour burden and prolonged survival of animals. These benefits are associated with a decrease in the number of intratumoral blood vessels, stabilisation of existing vessels and stimulation of NK cell activity.

By selectively triggering the death of new vessels, anti-CD160 differs from existing anti-angiogenics, all aimed at counteracting the effects of pro-angiogenic growth factor VEGF. Preliminary data has already established the synergistic effect of the anti-CD160 with these antiangiogenics. Ultimately, it could also be an alternative to those treatments whose efficacy varies greatly from one cancer to another and often generate resistance among patients with eye disease.

CD160 is also expressed on the surface of circulating immune cells, such as some NK and T cells subpopulations to which it contributes to modulating the activity. Early studies have shown that anti-CD160 prevents tumour escape by activating Natural Killer cells. Combined with other inhibitors of immunity checkpoints, such as the anti-PD1 antibodies (Nivolumab / Opdivo® by Bristol-Myers Squibb, Penbrolizumab / Keytruda® by Merck), it also helps to prevent T-cell "exhaustion".

After an initial antibody format of anti-CD160 with an anti-angiogenic mechanism for ophthalmology, the dual biological action of CD160 thus offers an unprecedented opportunity to combine through a single target, two mechanisms of action that now dominate the field of oncology: anti-angiogenesis and immune-modulation of the innate and adaptive immune responses.

About ELSALYS BIOTECH

ELSALYS BIOTECH is a biopharmaceutical company that designs and develops innovative therapeutic antibodies against cancer and inflammatory diseases. These antibodies, called "first-in-class", aim for innovative targets involved in cellular events at the core of the pathological process: immune response, angiogenesis, survival, proliferation, adhesion and migration.

To drive these innovations, ELSALYS BIOTECH relies on an academic network of international standing, an R&D platform that covers validation of targets in the clinical evaluation of antibody candidates and a team of experts dedicated to developing immune-based therapies.

The company has already signed licensing option and / or collaboration agreements (Institut Curie, IGBMC-ICS, Inserm, Centre Léon Bérard, CNRS) and maturation agreements (SATT Conectus, SATT SE), and has acquired a first strategic asset. Two years after its foundation, the Company hosts three proprietary antibodies and four development programmes.

Founded in 2013 with the support of TRANSGENE and SOFIMAC Partners and led by Dr Christine GUILLEN, ELSALYS BIOTECH consists of a team of nine people. Its head office is located in the centre of the Lyon Gerland bio-district and its laboratories are based in the Illkirch Graffenstaden Science and Technology Park.

More information on www.elsalysbiotech.com

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