

## New studies confirm anti-CD160 antibodies are potential therapeutics for ophthalmic diseases

- Efficacy and safety are consistently demonstrated in several *in vivo* preclinical models
- Anti-CD160 is a potent inhibitor of ocular vascularization, alone and in combination with anti-VEGF treatment
- Anti-CD160 could be a good alternative for poor responders to anti-VEGF treatments

Lyon, FRANCE, 2 July 2018, ELSALYS BIOTECH, a new player in immuno-oncology, announces the publication of two studies validating the potential of its first-in-class anti-CD160 antibodies for the treatment of neovascular diseases of the eye. The first study reveals that in patients, CD160 endothelial expression in retinal vessels is higher and correlates with a wide range of ocular neovascular diseases, while the second reports the safety of the antibody and demonstrates, in relevant animal models, its therapeutic benefit alone and in combination with anti-VEGF agents, the current standards of care for retinal vascular pathologies. Published in *Investigative Ophthalmology & Visual Science*, the results of these two studies confirm ELSALYS BIOTECH's preclinical data in ophthalmology: CD160 antibodies could be used (i) for its additive or synergistic effect with the current standard of care, or (ii) as alternative therapies in patients with anti-VEGF-resistant or refractory neovascular diseases.

- Henry A, Boulagnon-Rombi C, Menguy T, Giustiniani J, Garbar C, Mascaux C, Labrousse M, Milas C, Barbe C, Bensussan A, Durlach V, & Arndt C. [CD160 Expression in Retinal Vessels Is Associated With Retinal Neovascular Diseases. \*Invest Ophthalmol Vis Sci.\* 2018 Jun 1.](#)
- Menguy T, Briaux A, Jeunesse E, Giustiniani J, Calcei A, Guyon T, Mizrahi J, Haegel H, Duong V, Soler V, Brousset P, Bensussan A, Raymond Letron I, Le Bouteiller P. [Anti-CD160, Alone or in Combination With Bevacizumab, Is a Potent Inhibitor of Ocular Neovascularization in Rabbit and Monkey Models. \*Invest Ophthalmol Vis Sci.\* 2018 Jun 1.](#)

Neovascularization is a process by which new blood vessels form abnormally. It is responsible for a number of corneal/retinal diseases such as ischemic retinopathies (IRs) or choroidal retinopathies, which include exudative or “wet” age-related macular degeneration (wAMD). These diseases are the primary cause of moderate to severe vision loss in developed countries and are essentially treated with agents that target the VEGF (a growth factor that stimulates blood vessel). These standards of care are effective and safe, but present however variable responses between patients and are often associated with the development of treatment-resistance. Approximately 30% of wAMD patients treated with anti-VEGF therapies are considered treatment-resistant or having refractory neovascular AMD<sup>1</sup>. For these patients as well as for those that respond incompletely to anti-VEGF therapy, there is a pressing need to

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<sup>1</sup> Yang S et al. *Drug Des Devel Ther.* 2016

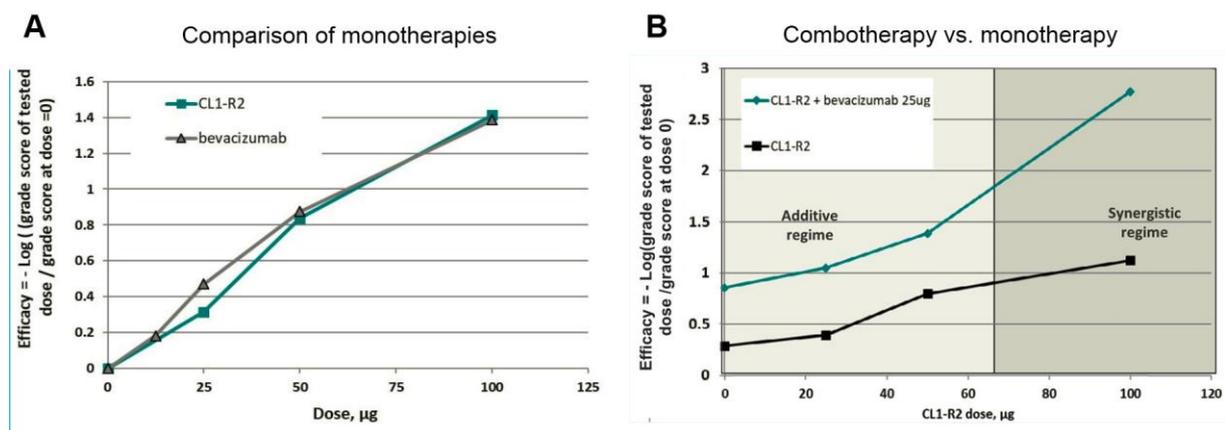
develop VEGF-independent complementary and synergistic therapies that inhibit pathological neovascularization while having little or no effect on normal mature tissue vasculature.

### CD160: a first-in-class target for the treatment of retinal neovascular diseases

CD160 was already known to be a marker of activated endothelial cells that surround newly formed blood vessels, and as such is considered a potential target for the treatment of diseases associated with neovascularization<sup>2</sup>. Henry *et al.* have now studied CD160 expression in the human eye and find that it is actually expressed mainly in endothelial cells and across some other cell types. Importantly, they reveal that its levels of expression are significantly higher in the retina of patients suffering from a range of ocular neovascular diseases, **strongly supporting that CD160 could well represent an interesting target for novel anti-angiogenic therapies for these patients.**

### Anti-CD160 is a potent inhibitor of ocular vascularization, both alone and in combination with anti-VEGF treatment

Previous studies had shown that the engagement of CD160 by an activating antibody induces cell death of endothelial cells that surround newly formed blood vessels, thereby blocking their formation, both *in vitro* and *in vivo*<sup>2,3</sup>. In the second publication, Menguy *et al.* **assessed the efficacy of this antibody as a monotherapy or as a combination therapy with bevacizumab, a monoclonal antibody that targets the VEGF.** They show that administration of an anti-CD160 has an antiangiogenic effect *in vivo* in a relevant model of corneal neovascularization. This effect is equivalent to that seen with bevacizumab (Figure 1A) or with aflibercept, a drug that also inhibits the VEGF pathway.



**Figure 1.** Efficacy of anti-CD160 treatment compares to (A) and additively combines with an anti-VEGF treatment (B). *CL1-R2: anti-CD160 antibody.*

<sup>2</sup> Chabot et al. J Exp Med. 2011

<sup>3</sup> Fons et al., Blood 2006

Strikingly, the antiangiogenic effect of the combination treatment (anti-CD160 and bevacizumab) was significantly higher than either antibody alone (Figure 1B), strongly arguing that the anti-CD160 (i) may act independently of the VEGF pathway and (ii) could be a good alternative for patients that poorly respond to an anti-VEGF treatment.

Interestingly, the additive effect observed upon treatment with CL1-R2 in combination with bevacizumab in the CNV rabbit model suggests that both CD160 and VEGF pathways contribute to the efficacy observed, and that the two mAbs probably act via different pathways. This could result in new therapeutic opportunities for co-targeted or combination therapies alongside anti-VEGFs.

### Anti-CD160 is safe and efficacious in primate

Efficacy of anti CD160 was then confirmed on choroidal neovascularisation in the most relevant primate model. Beyond the efficacy data, the CD160 antibody causes **no treatment-related adverse effects in the most relevant animal model of wAMD, (a primate model of laser-induced choroidal neovascularisation)**, confirming the safety of targeting CD160 when treating retinal neovascular diseases.

*“These results demonstrate that a combination with anti-CD160 provides a tangible alternative to patients suffering from neovascular diseases of the eye.”*, explains **Christine Guillen, CEO and Co-founder, ELSALYS BIOTECH**. *“With these positive results in hand, we are excited to move forward towards a first clinical trial with CD160 antibody in ophthalmology and confident in the continuation of the program with our partner THEA laboratories that could exercise the option taken in February 2018 on ELB011 before end of 2018<sup>4</sup>.”*

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### About ELB011 – anti-CD160 antibody in ophthalmology

ELB011 is a first-in-class anti-angiogenic antibody with an innovative mechanism of action that inhibits anarchical neovascularization resulting in the normalization of vascularization in retinal vascular pathologies. The innovative mechanism of action of ELB011 makes it possible to consider its development in monotherapy or in combination with anti-VEGF agents, the current standard of care for these pathologies, whose efficacy can diminish with time of treatment.

In February 2018, ELSALYS BIOTECH has signed a license option agreement with THEA for the development of its ELB011 program in ophthalmology. The option concerns the clinical development (expected from 2020) and the commercialization of ELB011 in the treatment of wAMD and other retinal vascular pathologies.

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<sup>4</sup> See [press release](#) of February 22, 2018, on the agreement with THEA Laboratoires

### About ELSALYS BIOTECH

ELSALYS BIOTECH is a clinical stage immuno-oncology company targeting tumors and their immune and/or vascular microenvironment.

To convert these novel targets into drug candidates, the Company is currently conducting 5 proprietary development programs including LEUKOTAC<sup>®</sup> (inolimomab), an immunotherapy antibody that has recently demonstrated its clinical superiority in Phase 3 and that is closed to market approval in an orphan “post-cancer” disease with very poor prognosis: steroid-resistant acute Graft-versus-Host Disease.

Founded in 2013, ELSALYS BIOTECH is located in the heart of the European cluster LYON BIOPOLE. Its shareholders are TRANSGENE, SOFIMAC INNOVATION, IM EUROPE, a subsidiary of INSTITUT MERIEUX, and CREDIT AGRICOLE CREATION.

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### Contacts

#### ELSALYS BIOTECH

**Dr. Christine GUILLEN**

CEO and Co-founder

+33 (0)4 37 28 73 00

[guillen@elsalysbiotech.com](mailto:guillen@elsalysbiotech.com)

#### PRESSE

**ATCG PARTNERS**

**Marie PUVIEUX (France)**

+33 (0)6 10 54 36 72

**Céline VOISIN (UK/US)**

+33 (0)6 62 12 53 39

[presse@atcg-partners.com](mailto:presse@atcg-partners.com)