PROFILE

Protein Alternatives ('**PROALT**') is a Spanish biotechnology company founded in 2006 by researchers of the Spanish Research Council (CSIC) and the Cancer Research Center (CNIO) focused on the development of biomarker-based assays for early diagnosis of cancer and the development of therapeutic monoclonal antibodies for the treatment of metastatic cancers. The company also offers Contract Research (CRO) and Manufacturing (CMO) services and owns a broad catalogue of research-use-only products..

SPEAKER

Dr. Juan Ignacio Imbaud, is a Biochemist (UM), Ph.D. in Molecular Biology (UAM) and PADIIT2 degree (Senior Management Program of Research, Innovation and Technology Transfer Institutions) by IESE Business School. Leads Protein Alternatives spin-off company since its creation in 2006, building up the Therapeutics, Diagnostics and CRO/CMO business units. More than 16 years of experience in biotechnology industry combining scientific with management skills.

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PRODUCT

PA-0661 monoclonal antibody for the treatment of metastatic colorectal cancer

MECHANISM OF ACTION

The candidate hPA-0661 inhibited cell adhesion, cell migration and cell proliferation in in vitro studies. In in vivo efficacy studies, hPA-661 significantly improved survival rates of all treated animals and avoided metastasis formation in 50% of the treated individuals in the metastatic CRC tumor model.

Blockade of the CDH17-$\alpha 2\beta 1$ (ligand-receptor) interaction. PROALT's founder Dr Ignacio Casal (Centro de Investigaciones Biológicas - CSIC) has discovered and demonstrated that RGD motifs in some cadherins (CDH17, VEcadherin, CDH6) are ligands capable of activating $\alpha 2\beta 1$ integrin, a cell surface protein receptor. This discovery also demonstrated the critical role of $\alpha 2\beta 1$ integrin in cancer metastasis and its capacity to be considered an RGD receptor, which was previously unknown. hPA-0661 antibody inhibits the activation of $\beta 1$ integrin, thus diminishing the activation FAK, JNK, and ERK kinases, which correlate with a decrease in cell adhesion and proliferation.

TARGET INDICATIONS

Oncology. Main therapeutic indication: liver metastasis of colorectal cancer (mCRC). Additional potential indications: lung metastasis of melanoma or breast cancer.

CURRENT STATUS

- Completion of in vitro and in vivo efficacy studies generated with the murine monoclonal antibody (mPA-0661) in metastatic colorectal and melanoma models.

- PA-0661 antibody humanization completed in collaboration with Fusion Antibodies Plc (UK) and development candidate selected for pre-clinical studies.
- Non-regulatory in vitro and in vivo efficacy results generated with the humanized selected candidate hPA-0661 in metastatic colorectal cancer (mCRC) murine models.
- Non-clinical safety studies and pre-clinical development strategy for enabling first-in-man study designed.

INNOVATIVE ASPECTS

- Data about the target and in vitro and in vivo results obtained with the humanized monoclonal antibody hPA-0661 (the selected candidate for development), demonstrating the efficacy of this biological drug in inhibiting beta-1 integrin activation, a critical cell-signaling pathway associated to metastasis.
- Different therapeutic target and mechanism of action (MOA) compared to Avastin®, Erbitux® and Vectibix®, the three monoclonal antibodies on market currently used alone, or in combination with chemotherapy, for the treatment of CRC.
- No active developments of anti-CDH17 compounds.
- Proven interest of big pharma companies in cadherin targets: CDH3 and CDH6 therapeutic mAbs developed by Pfizer, Novartis and Fujifilm are in Phase I clinical studies.
- No anti cadherins RGD specific drugs under development.

IPR

International Application No. PCT/EP2015/058527 (Filed 22 April 2015) extended to Europe (EP3286218; Intention to Grant Feb 2021), Canada (2,980,495; Filed), Australia (2015392603; Filed) and EEUU (10,829,560, Granted 10 November 2020).

Complementarity-Determining Regions (CDRs) in the heavy (VH) and light chains (VL) from the monoclonal antibody clone 6.6.1 protected. Patent of product and use.

Opportunity to create new additional IP around the humanized sequences: under evaluation.

PARTNERING OPPORTUNITIES

The completion of the regulatory preclinical stage of the therapeutic antibody hPA-0661 requires 6 M € of private capital within 2 years. The company is willing to create a new company (Joint venture) to separate hPA-0661 from the rest of its business units.