

PharmaMar presents positive results with its conjugated antibody MI130110 in CD13-expressing tumor-cells

Madrid, December 1st, 2016. PharmaMar (MSE:PHM), a world leader in the discovery, development and commercialization of new antitumor compounds of a marine origin, has announced that its antibody-drug conjugate (ADC) has demonstrated a remarkable *in vitro* antitumoral activity in a CD13, fibrosarcoma positive animal model. CD13 is an aminopeptidase, involved in the modulation of several vasoactive peptides and is known to influence major biological events, such as cell proliferation, invasion and angiogenesis. MI130110 is formed by a compound of marine origin (PM050489) that has been conjugated to a monoclonal anti-CD13 antibody through a non-hydrolysable linker. The results of this study have been presented today during the EORTC-NCI-AACR international meeting on “Molecular Targets and Cancer Therapeutics” that is taking place in Munich (Germany) from November 29th to December 2nd.

Juan Manuel Dominguez, Screening and Biochemistry Departmental Manager of PharmaMar’s Oncology Business Unit, has presented the data on the study entitled “MI130110, a new ADC combining an anti-CD13 antibody and a payload of marine origin shows remarkable *in vivo* activity” (abstract #397), and carried out in collaboration with both Prof. Francisco Sánchez Madrid’s and Dr Juan Manuel Zapata’s research groups from the Madrid Autónoma University, within the framework of the “Marinmab” project, financed by the Ministry of Economy.

MI130110 showed a high potency and good selectivity in *in vivo* in tumor cells that expressed CD13, namely NB-4 and HT-1080, with respect to other cell lines that do not express the protein (RPMI-8226 and Raji). The authors found that MI130110 impaired tubulin polymerization and disrupted the microtubule network, impairing its function during cell division, this, leading to mitotic aberrations in tumor cells that express CD13. These findings are consistent with the mechanism of action of the antitumoral compound PM050489, present in the ADC.

CD13, fibrosarcoma positive HT-1080 tumor cells were subcutaneously implanted in immunosuppressed mice, to develop tumors of approximately 180 mm³. After the treatment with MI130110 at different doses, once weekly for two weeks, the mice bearing HT-1080 tumors that received the highest dose showed an important reduction in tumor size, with complete remission and a significant increase in

median survival time. As expected, MI130110 treatment didn't produce any antitumoral effect on animals that didn't express CD13, as those in subcutaneously implanted RPMI-8226 multiple myeloma cell lines.

The effect of MI130110 in CD13 positive tumors was confirmed 24 hours after the treatment, through the appearance of alterations in the mitosis of the tumor cells, demonstrating that the antitumor activity derives from disrupting the microtubule network and impairing its function during cell division.

About PharmaMar

Headquartered in Madrid, PharmaMar is a world-leading biopharmaceutical company in the discovery and development of innovative marine-derived anticancer drugs. The company has an important pipeline of drug candidates and a robust R&D oncology program. PharmaMar develops and commercializes YONDELIS® in Europe and has three other clinical-stage programs under development for several types of solid and hematological cancers, PM1183, plitidepsin, and PM184. PharmaMar is a global biopharmaceutical company with subsidiaries in Germany, Italy, France, Switzerland, United Kingdom, Belgium, Austria and the United States. PharmaMar fully owns other companies: GENOMICA, Spain's leading molecular diagnostics company; Sylentis, dedicated to researching therapeutic applications of gene silencing (RNAi); and two other chemical enterprises, Zelnova Zeltia and Xylazel. To learn more about PharmaMar, please visit us at www.pharmamar.com.

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