Lipopharma awarded a 6,15M€ grant by the H2020 Programme to conduct a PIIb trial with 2OHOA in patients with newly-diagnosed glioblastoma.

The European Commission (EC) has awarded a 6,15M€ grant to develop the project CLINGLIO to a multinational consortium lead by Lipopharma and integrated by 12 leading clinical research institutions, Universities and SMEs from Europe, Israel and the USA. The objective of CLINGLIO is the execution of "A Clinical Phase IIB trial with 2OHOA in patients with newly-diagnosed malignant glioma". The duration of the CLINGLIO project is 36 months and the starting date is 1st of December, 2017.

Palma de Mallorca (Spain) and Acton (MA, USA). January 21st 2018– Lipopharma, a pioneering clinical stage biopharmaceutical company developing a new generation of products modulating metabolism of membrane lipids based on the groundbreaking MLT platform, announces that the European Commission has awarded a 6,15M€ grant to the CLINGLIO consortium, lead by Lipopharma, to execute the project entitled "*A Clinical Phase IIB trial with 2OHOA in patients with newly-diagnosed malignant glioma*".

The CLINGLIO project was evaluated as a Research and Innovation Action (RIA) within the call *H2020-SC1-2017-Two-Stage-RTD, Topic SC1-PM-08-2017 (New Therapies for Rare Diseases)*, part of the Health, Demographic Change and Well-being Work Programme of the H2020. Total budget available for this H2020-SC1-2017-Two-Stage-RTD call was 173M€, of which 65M€ were for topic SC1-PM-08-2017. Overall, 668 proposals were submitted to this call, of which 37 were pre-selected for funding across the four topics of the call (5,5% of the initial proposals). In the *New Therapies for Rare Diseases* topic, the EC will select for funding up to 11 proposals with an average budget per project of around 6M€.

The grant was awarded to a multinational, well balanced consortium formed by 5 leading clinical research institutions in the UK (**Royal Marsden Hospital** and **Northern Institute for Cancer Research, University of Newcastle** upon Tyne), France (**Institut Gustave Roussy**), Italy (**Istituto Neurologico Carlo Besta**) and Israel (**Hadassah Medical Organization**), two universities in Spain (**Universitat de les Illes Balears, UIB**) and Italy (**Universita degli Studi di Salerno**) and 4 specialized SMEs from The Netherlands (**SMS Oncology**, clinical CRO), Hungary (**Lipodom Kft**, lipidomic analysis), USA (**LMBRI**, pharmacoeconomics and market access) and Spain (**Praxis Pharmaceutical**, Drug product manufacturing and commercialization, and **Lipopharma**, coordinator and sponsor of the clinical trial).

The main objective of the CLINGLIO project is to execute a randomised, double-blind, placebo-controlled adjuvant trial in primary newly diagnosed glioblastoma patients to assess the efficacy and safety of 2OHOA in combination with radiotherapy and temozolomide. This study is a phase IIB trial with interim dose selection, sample size reassessment and biomarker threshold/omics signature determination. It is anticipated that around 15 clinical research hospitals across Europe and Israel will recruit 150 patients in the first part of the study, distributed in three arms: 1) control, with Standard of Care (SoC) plus placebo, 2) SoC plus 2OHOA "low dose" and 3) SoC plus 2OHOA "high dose". An interim analysis will take place after 75 events (Disease Progression) occurs and depending on the results of this interim analysis 60 to 120 additional patients will be enrolled in the second part of the study. The primary endpoint will be Progression Free Survival, according to RANO criteria, and Overall Survival will be a key secondary endpoint.

If the results of this clinical trial are positive, Lipopharma plans to apply for a conditional approval of 2OHOA in Europe for the treatment of newly diagnosed GBM patients, in combination with radiotherapy and temozolomide.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 755179

ADDITIONAL INFORMATION

About LP561A1 (2OHOA)

LP561A1 (2-hydroxyoleic acid, 2OHOA) is an orally bioavailable synthetic derivative of oleic acid that activates **sphingomyelin synthase 1 (SMS1)**, an enzyme catalysing the reversible conversion of phosphatidylcholine (**PC**), phosphatidylethanolamine (**PE**) or ceramide (**Cer**) into sphingomyelin (**SM**) and diacylglycerol (**DAG**), which restores the normal, healthy levels and ratios of membrane lipids. This "normalization" modulates the localization and activity of important peripheral membrane proteins, such as K-Ras, which is translocated from its active domain in the cell membrane to the cytosol. Consequently, Ras-associated proliferative signalling pathways are effectively regulated, including MAP Kinases, Pi3K/AKT/MTor, PKC/Cyclin CDK or Notch pathways, which commonly exhibit an aberrant activity in different types of cancer.

In several pre-clinical studies in cellular and animal models, 2OHOA has demonstrated very high efficacy with no apparent toxicity in different types of cancer with low basal levels of SMS1. Available data, both from internal studies and from external literature references, suggest that a significant percentage (30% to 50%) of patients with aggressive cancer malignancies (such as brain, pancreas, lung, colon, prostate cancer or leukaemia) have important alterations in the SMS system.

2OHOA obtained the **Orphan Drug** designation in Europe by the EMA for the treatment of glioma in October 2011. Comprehensive safety and tolerability data has been generated in a PI/IIa clinical study (MIN-001-1203) where 54 adult patients with advanced solid tumors including malignant glioma have been treated with different doses of 2OHOA. The results of this study confirmed an excellent safety and tolerability profile of the product, while encouraging overall **clinical activity** was reported in **13 heavily pre-treated patients** with advanced recurrent solid tumours, including **eight patients with recurrent high grade glioma**.

About MLT

Membrane-Lipid Therapy (MLT) is an innovative scientific platform based on an expanding area of knowledge in today's cell biology that derives in the design of novel molecules that regulate the activity of key membrane-associated signal transduction proteins, through the modulation of the structure and organization of the membrane lipid micro-domains involved in cell signalling. This innovative approach is a paradigm-shift in drug discovery and pharmacology that can lead to the development of transformative new medicines with an exceptional safety/efficacy combination in serious pathologies with critical medical needs unmet, such as Oncology, Neurodegenerative diseases, Metabolic disorders or Inflammation. Results available of the first clinical trials with MLT-based molecules, such as MIN-001-1203 study with 2OHOA in oncology, represent a major step forward towards the clinical validation of this novel therapeutic strategy.

About Lipopharma

Lipopharma is a pioneering clinical-stage biopharmaceutical company that focuses on the discovery, design and clinical development of a new generation of medicines that act through the innovative therapeutic strategy: Membrane-Lipid Therapy (MLT). Since 2006 Lipopharma develops industrial applications of new scientific breakthroughs and discoveries patented by leading researchers at the University of the Balearic Islands (UIB).

Disclaimer

Except for historical information, this press release may contain forward-looking statements, which reflect the companies' current expectations regarding future events. These forward looking statements involve risk and uncertainties, which may cause but are not limited to, changing market conditions, the successful and timely completion of clinical studies, the establishment of corporate alliances, the impact of competitive products and pricing, new product development, uncertainties related to the regulatory approval process and other financial, technical or market risks. All forward-looking statements are qualified in their entirety by this cautionary statement and Lipopharma Therapeutics SL does not undertake any obligation to revise or update this press release to reflect events or circumstances after the date hereof.

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