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Lipopharma closes patient recruitment in its first clinical study with 2OHOA in cancer

54 patients with advanced solid tumours have participated in the Phase I/IIa clinical study with 2OHOA, half of them with malignant glioma. Results show an excellent safety profile, with no drug-related relevant toxicity effects associated with the investigational product reported, even at doses well above the expected therapeutic range. Very encouraging clinical activity has been observed in nine patients with refractory advanced solid tumours, six of them with malignant glioma.

Palma de Mallorca, August 1st 2016– Lipopharma announces the closure of patient recruitment in its first clinical study with 2OHOA (**MIN-001-1203)**, a Phase I/IIa open label, non-randomized, safety, pharmacokinetics, pharmacodynamics and preliminary efficacy study of 2OHOA in adult patients with advanced solid tumors including malignant glioma. Five centres have participated in the study, three in Spain and two in the UK.

The study comprised two parts: 1) a **dose-escalation phase** where 32 patients have been treated with different doses and in which the Maximum Tolerated Dose (MTD) was defined as 12 g/day (4 g three times daily) and 2) an **expanded safety part** with two cohorts, one with malignant glioma patients (n=12) and another with other advanced solid tumors (n=10), in both cases treated at the MTD (12 g/day)

7 cohorts were completed in the dose escalation phase, with doses ranging from 0.5 g/day to 16 g/day. 32 patients (15 of them with glioma) have been treated in these first 7 cohorts, 28 of which have completed at least one cycle of treatment and are evaluable for safety assessment. 2OHOA, administered as an oral suspension two or three times daily, has been generally well tolerated up to 12 g/day, while patients have had difficulties to handle the large volume of liquid intake required for the 16g/day (8 g twice daily) dose, experiencing frequent gastrointestinal effects that in some cases were difficult to manage. No drug-related serious adverse events or other relevant toxicity effects associated to the investigational product have been reported in any of the 32 patients treated, other than the tolerability issues experienced at the highest dose levels (gastrointestinal effects). In the safety expansion phase, 22 patients have been treated with the MTD (12 g/day, 4g three times daily) in two cohorts, 18 of them being eligible for safety assessment. The results of these two expansion cohorts confirm the excellent safety profile of 2OHOA, with no drug-related relevant adverse effects reported.

Overall the **54 patients have received 2OHOA treatment for more than 125 months (182 cycles)**, 46 of them being eligible for the safety assessment. 22 patients have been dosed with 2OHOA at the Maximum Tolerated Dose (12 g/day) over a total period of more than 63 months (>90 cycles), **confirming an excellent safety and tolerability profile**.

Promising anti-cancer activity of 2OHOA as single agent has been confirmed in several patients with advanced refractory solid tumours. Five patients in the dose escalation part and **four** in the expanded safety phase have shown objective clinical benefit according to RANO (for glioma) or RECIST (for other solid tumors) criteria. **6 patients** with **refractory malignant glioma** have experienced clinical benefit, including one GBM patient that has had a marked shrinkage (>91% over baseline) of the target lesion for almost 3 years. Other four refractory malignant glioma patients have shown stable disease (SD) for at least 6 months, two of them still ongoing with SD in cycles 11 (7 months) and 10 (6 months) respectively. All available data of the study is currently being evaluated and the patient samples collected for biomarker and genetic evaluation are being analyzed at different labs in order to complete the official report of the clinical study.

The positive results of this first MIN-001-1203 trial warrants further clinical development of 2OHOA and Lipopharma is now planning a next Phase IIb study in order to evaluate the therapeutic potential and safety of this product in combination with the Standard of Care (SoC, radiotherapy plus Temozolomide), compared with the SoC alone, in subjects with newly-diagnosed malignant glioma. If results of the Phase IIb study are positive, Lipopharma will seek conditional approval as a first line treatment, in combination with current SoC) for glioblastoma in Europe.

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ADDITIONAL INFORMATION

About 2OHOA

2OHOA is an orally bioavailable synthetic derivative of oleic acid that activates **sphingomyelin synthase 1 (SMS1),** 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, 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. Robust 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. Results of this study have confirmed an excellent safety and tolerability profile of the product, while encouraging anti-cancer activity has also been observed in nine patients with advanced refractory tumours, including six patients with malignant 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 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

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