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Updated results of 2OHOA study in cancer presented at ASCO 2015

Palma de Mallorca, May 30, 2015. – Lipopharma announced today that updated results of the ongoing Phase I/IIA clinical trial with 2OHOA in patients with advanced solid tumours, including malignant glioma (MIN-001-1203), have been presented in a poster discussion session at the 51st annual meeting of the American Society of Clinical Oncology (ASCO), held in Chicago from the 29th of May to the 2nd of June, 2015.

In this event, the latest findings from cancer clinical trials, including new drug studies that could change patient care, are announced to more than 25.000 worldwide physicians, researchers and representatives of pharmaceutical and biotechnology companies.

The results of the first 6 cohorts of the MIN-001-1203 study were presented in an abstract and poster discussion session that raised significant interest among the ASCO community. 22 evaluable patients (10 with glioblastoma) have been recruited in the first 6 cohorts in 3 sites located in the UK and in Spain. The study drug is given as a PO suspension, 2 or 3 times daily, in 21-day cycles in order to determine the safety profile and the maximum tolerated dose (MTD). Dose escalation in the trial continues as 2OHOA has hitherto been well tolerated, even in very high doses (12 mg/day) with no drug-related serious **adverse events** reported. In addition to the safety results, Lipopharma presented data on secondary endpoints for the trial, including pharmacokinetics (PK) and early indications of efficacy. The **PK profile** was dose-proportional with no accumulation up to 4g/day and no food interactions were observed. At doses up to 4g/day the t1/2 ranged from 1,5 to 3,8 hr, while at the highest dose (12 gr/day) t1/2 was 10,8h.

Furthermore, **clinical benefit** has been reported in **4 patients**, 3 of them with glioblastoma (GBM), including one GBM patient (ongoing) that has achieved a **sustained partial response (PR)** on RANO criteria (tumour shrinkage >91%) lasting now for more than **20 months**. Two other GBM patients (ongoing) have Stable Disease (SD) after 4 and 6 months of treatment respectively. A fourth patient with progressive mesothelioma had SD lasting up to cycle 15 (10 months).

MIN-001-1203 Phase I/IIa 2OHOA trial background: The Phase I/IIA trial of 2OHOA is an open label, non-randomized, safety, pharmacokinetics, pharmacodynamics and efficacy study for adult patients with advanced solid tumors including malignant glioma. Patients must have tumor progression after first or second line standard-of-care treatment. The study will be performed in two phases - a dose escalation phase following a standard "3+3" design to establish dose-limiting toxicity (DLT) and a safe dose of 2OHOA followed by two expanded safety cohorts (10 malignant glioma and 10 other advanced solid tumours suitable for biopsy) treated at the maximum tolerated dose (MTD). If the MTD is well tolerated in the expanded safety cohorts, that dose becomes the recommended Phase 2 dose (RP2D). Primary endpoints are to determine the safety and tolerability of 2OHOA administered orally using a continuous dosing schedule and to identify the RP2D of 2OHOA. Secondary endpoints include to characterize the single-and steady-state pharmacokinetic (PK) profiles of 2OHOA; with a continuous daily dosing schedule, to evaluate the effect of 2-OHOA on sphingomyelin (SM) and dihydrofolate reductase (DHFR) in non-glioma patients (patients with lesions suitable for biopsy -dose escalation phase and all patients-expanded safety cohort) and to assess the preliminary anti-tumor efficacy of 2OHOA. Radiological progression of disease will be assessed every two cycles (6 weeks) starting after the first two cycles have completed (after 6 weeks treatment) up to the end of Cycle 6 (thereafter every 3-4 cycles, at the Investigator's discretion). Tumors will be measured by CT or MRI scan. Changes will be scored according to RANO criteria (glioma) or Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 (other solid tumor).

Contact:

Lipopharma
Ctra. Valldemossa, Km. 7,4. ParcBIT. Edif. 17. 2nd. C-8. E07121 – Palma de Mallorca. Spain.
Tel. (+34) 971 439 886 :: Email: info@lipopharma.com :: lipopharma.com

ADDITIONAL INFORMATION

About 2OHOA

2OHOA (2-hydroxyoleic acid) is an orally bioavailable synthetic analog of the fatty acid oleic acid that selectively activates **sphingomyelin synthase (SMS)**, thereby increasing the concentration of sphingomyelin (**SM**), ceramide (**Cer**) and diacylglycerol (**DAG**) in the tumor cell membrane and decreasing membrane levels of phosphatidylethanolamine (PE), phosphatidylcholine (PC) and phosphatidylserine (PS). This restores the normal, healthy levels and ratios of membrane lipids, inhibiting membrane-protein associated signalling and the aberrant activity of signalling pathways in tumor cells, including the Ras/MAPK and PI3K/AKt pathways, stopping tumor cell proliferation, inducing tumor cell differentiation, and eventually causing selective cancer cell death by autophagy/apoptosis.

In pre-clinical studies this compound has demonstrated high efficacy (with no apparent toxicity) against some of the most lethal forms of cancer. Positive "proof of concept" studies of 2OHOA in animal models of human tumours of Glioma, NSCLC, Pancreas or Prostate are already available.

2OHOA has obtained the **Orphan Drug** designation by the EMA for the treatment of glioma in October 2011. A PI/IIa **clinical study** in glioma and other solid tumors (**MIN-001-1203**) is currently on-going since May 2013, so far with very positive results.

About MLT

Membrane-Lipid Therapy (MLT) derives from a highly specialized scientific knowledge developed by Lipopharma's scientists and consists on the design of molecules that regulate the structure and functions of the membrane lipids, instead of targeting cellular proteins. This innovative know-how is Lipopharma's main expertise and lays on new discoveries made by Lipopharma's scientists related to the role of membrane lipids and membrane lipid structure on the regulation of localization and activity of membrane signalling proteins.

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