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# Lipopharma initiates recruitment in expansion cohorts of clinical study with 2OHOA in cancer

***The main primary objective of the MIN-001-1203 clinical study has already been achieved with the identification of the Maximum Tolerated Dose. 2OHOA has proved to be safe and generally well tolerated up to 12g/day (4g three times daily), while at 16g/day (8g twice daily) frequent gastrointestinal effects occurred in most patients. No other toxicity effects related to the medication reported in any of the patients treated with doses ranging from 0.5g to 16g per day. Promising clinical activity confirmed in 4 patients (3 with glioblastoma, GBM), including one GBM patient with a sustained tumour regression after 26 months of treatment.***

*Palma de Mallorca, November 23rd, 2015.* – Lipopharma announced today that in the Dose Escalation TC held this morning with all the Clinical Investigators and the Medical Monitor it has been agreed that the **Maximum Tolerated Dose (MTD)** in this study will be set as **12g per day (4g TDS, three times daily)**. As from today two additional **safety expansion cohorts** (one with 10 glioma patients and another with 10 patients with solid biopsiable tumours) will start recruiting participants at a dose of 12g/day (4g TDS) in order to evaluate the effect of 2OHOA in different biomarkers and to further explore preliminary efficacy in glioma patients.

7 cohorts of the MIN-001-1203 study have already been completed, with doses ranging from 500mg/day to 16g/day. 32 patients (12 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 2 or 3 times daily, has been generally well tolerated up to 12 g/day, while patients have had difficulties to handle the large volume of medication required for the 16g/day (8g twice daily) dose, experiencing frequent gastrointestinal effects that in some cases were difficult to manage. No drug-related **serious adverse events (SAE)**, 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). The pharmacokinetic (**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 3,8h, while at 12 gr/day t1/2 was 9,4h. Accumulation was observed at doses of 8g/day and higher.

Even though this is safety study which does not contemplate patient selection criteria with a view of exploring efficacy (particularly in the dose escalation part just completed) **relevant clinical activity** has been reported in **4 patients**, 3 of them with 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 **26 months**. Two other GBM patients have had Stable Disease (SD) for 6 months and a fourth patient with progressive mesothelioma had SD lasting for 10 months.

MIN-001-1203 is a Phase I/IIA, open label, non-randomized, safety, pharmacokinetics, pharmacodynamics and efficacy study of 2OHOA for adult patients with advanced solid tumors including malignant glioma. 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)

Lipopharma is now opening a new **fund-raising campaign** in order to conduct a **PIIb study** with 2OHOA in GBM which, if successful, could lead to a conditional approval in Europe for the treatment of newly-diagnosed GBM in combination with radiotherapy and temozolomide.

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## ADDITIONAL INFORMATION

### About 2OHOA

**2OHOA (2-hydroxyoleic acid)** is an orally bioavailable synthetic analog of oleic acid that selectively modulates **sphingomyelin synthase (SMS) activity**, 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 tumour cells, including the Ras/MAPK and PI3K/AKt pathways, stopping tumour cell proliferation, inducing tumour 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 tumours (**MIN-001-1203**) is currently ongoing 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*