PRESS RELEASE

OPM reports final results of its phase 1 study with RIPK2 inhibitor OPM-101, with strong safety data and no cardiac toxicity, paving the way for the launch of phase 1b/2a

- **Finalization of the study report on the double-blind, placebo-controlled Phase 1 trial of OPM-101 in 104 healthy volunteers (HV) who received OPM-101**
- **24-hour ECG analysis reveals no toxic effect of OPM-101 on cardiac parameters**
- **In an ex vivo whole blood study, OPM-101 rapidly and completely inhibited the stimulated release of TNFα, a downstream marker of RIPK2 pathway activation, indicating a strong pharmacological immunomodulatory effect**
- **PK/PD modeling predicts that a concentration of OPM-101 between 100 and 300 ng/mL would achieve target inhibition of at least 80% over the entire treatment period**
- **The favorable safety, pharmacokinetics and pharmacodynamics of OPM-101 support the pursuit of its clinical development for the treatment of diseases caused by deregulation of the pathway involving its therapeutic target, the RIPK2 kinase**
- **Phase 1b/2a clinical trial protocol to be filed in the fourth quarter of 2024 for launch in early 2025**

Dijon (France), October 22, 2024, at 6:00pm CEST– Oncodesign Precision Medicine (OPM) (ISIN: FR001400CM63; Mnemonic: ALOPM), a biopharmaceutical company specializing in precision medicine for the treatment of resistant and metastatic cancers, today confirms and details the final results of its Phase 1 clinical trial with OPM-101, its RIPK2 inhibitor and drug candidate administered orally to healthy volunteers, first reported on July 16, 2024. This clinical trial began in February 2023, the database was frozen in June 2024, and the full results and final study report became available, as scheduled in the study timetable, in October 2024.

OPM-101 is an experimental, powerful and selective small molecule inhibitor of the RIPK2 kinase. OPM-101 is designed to modulate the pro-inflammatory signal transmission pathway of this kinase, which is responsible for the development of inflammatory diseases, and has the potential to treat diseases in the fields of IBD (Chronic Inflammatory Bowel Disease) and immuno-oncology.

This randomized, double-blind, placebo-controlled phase 1 study was designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of OPM-101 (EudraCT: 2022-003122-50) in 104 healthy volunteers:

- In the SAD part of the trial, 72 HV (mean age = 34 years) received a single oral dose of placebo or 5, 20, 60, 150, 300, 600 or 1,000 mg of OPM-101, with one cohort dedicated to the high-fat meal effect and another to the gender effect, also receiving 150mg.

- In the MAD part of the trial, 32 HV (mean age = 36 years) received an oral dose of 75, 150 or 300 mg of OPM-101 or placebo twice daily for 14 consecutive days, including a cohort dedicated to the gender effect, receiving 150mg twice a day.

Safety assessments (physical examination, vital signs, blood tests, ECGs, holters) were performed regularly throughout the trial. In addition, blood samples were collected to measure circulating concentrations of OPM-101 and engagement of RIPK2, the pharmacological target of OPM-101 (measured by inhibition of stimulated TNFα production).

Robust safety data, no toxicity on cardiac parameters

OPM-101 was very well tolerated after administration in SAD and MAD. No severe or serious adverse events were reported, and no volunteer discontinued the study. All treatment-emergent adverse events considered to be at least possibly drug- and study-related were mild to moderate. Fourteen healthy volunteers (13.5%) reported a total of 18 adverse events considered related to study treatment (OPM-101 or placebo). Among them, 12 healthy volunteers (15%) reported a total of 15 adverse events considered to be related to OPM-101, the majority of which were headaches. 80% of these events were mild and 20% moderate. There were no clinically significant changes in safety-related laboratory tests reported during the treatment periods for all OPM-101 dose cohorts included in the analysis, with the exception of one volunteer who received a dose of 150mg twice daily and experienced a moderate (3x normal) increase in ALT (liver enzyme) during MAD, leading to discontinuation of her treatment on the morning of study day 12. In this volunteer, further increases in liver proteins were not observed.

Cardiac function was monitored in detail with daily 12-lead ECGs, particularly at the time of peak circulating concentrations. 24-hour ECG recordings (holters) and cardiac ultrasound were also performed. All these examinations showed normal results, without any relation to circulating OPM-101 concentrations, and without any clinically significant changes. This type of monitoring is common at this stage of development, particularly for kinase inhibitors. The results obtained make OPM-101 a first-rate molecule in this field.

Promising pharmacokinetic and pharmacodynamic results

OPM-101 significantly inhibits the RIPK2 pathway. Target engagement kinetics and pharmacodynamic results showed a fast and marked onset of inhibitory effect, already observed 2-6h after first administration, with maximal inhibition of 90-100%, and minimal inhibition of 65%-85% maintained over 14 days of dose-dependent administration. Inhibition remained marked (50% to 80%) 24 hours after the last administration on day 14 in the MAD part.

The pharmacokinetic parameters of OPM-101 showed consistent results between the SAD and MAD parts, and characteristics suitable for use in patients. OPM-101 is rapidly absorbed, with a Tmax observed between 2-4h, a terminal half-life of around 12h, steady-state reached after 3-4 days and dose-dependent exposure with repeated administration.

On the basis of the PK/PD relationship determined from the results of the MAD part of the study, we anticipate that a very significant target commitment (≥80%) can be achieved and maintained with a residual OPM-101 plasma concentration (Cmin) in the range 150-300 ng/mL. In addition, population pharmacokinetic modelling has enabled us to simulate different dose regimes for a future clinical study, and the target dose could be 150mg twice daily.

OPM and Professor Peyrin-Biroulet, presented the phase 1 results at the United European Gastroenterology Week (UEGW) 2024 held from October 12 to 15, 2024 in Vienna, Austria.

Based on the results presented today, OPM plans to submit a protocol for a phase 1b/2a clinical study in the fourth quarter of 2024.

"We are very pleased with the progress and results of this clinical trial with OPM-101, which provided convincing results for all primary, secondary and exploratory endpoints included in this study," said **Philippe Genne, Chief Executive Officer of OPM**. *"We are pleased to demonstrate the safety of our candidate and the strong pharmacodynamic correlation that exists. High target engagement is demonstrated at tolerated doses of OPM-101 throughout the treatment period. The modulation of TNFα production ex vivo can be considered as a key biomarker of target engagement for future clinical trials. The clinical results reported today not only highlight the consistency with the immunomodulatory effect of OPM-101 observed in preclinical studies, but also validate OPM-101 as a safe and effective inhibitor of the RIPK2 pathway. We are currently in the process of identifying with our scientists and clinicians' experts the first clinical indication that we will explore in a phase 1b/2a study before the end of the year in order to provide a first clinical proof of concept in a patient population capable of generating significant added value for our asset".*

"These complete Phase 1 results confirm and validate OPM-101 as a highly specific, effective and well-tolerated inhibitor of the RIPK2 immune pathway," added **Jan Hoflack, Deputy CEO and Chief Scientific Officer of OPM**. *"The field related to this therapeutic approach is currently booming with new high quality preclinical and clinical scientific publications mentioning a potential role for an inhibitor like OPM-101 in multiple immuno-oncology indications, in addition to the already well-established rational for the treatment of IBD and other inflammatory diseases. Our team is currently working to validate the different therapeutic options available for OPM-101, with the aim of launching a proof-of-concept clinical trial in relevant patients rapidly and efficiently before the end of the year. The current idea of a safe and effective RIPK2 inhibitor like OPM-101 suggests significant potential in both IBD and immuno-oncology, two of today's largest pharmaceutical markets with significant unmet needs".*

About Oncodesign Precision Medicine (OPM)

Oncodesign Precision Medicine (OPM), founded in 2022, is a biopharmaceutical company specializing in precision medicine, dedicated to the discovery of treatments for resistant and metastatic cancers.

OPM currently has two kinase inhibitors in clinical trials: OPM-101, for the treatment of chronic immuno-inflammatory digestive diseases and immuno-oncology, demonstrated high target engagement and absence of toxicity in its phase I trial in healthy volunteers. Phase Ib/IIa is scheduled to start at the beginning of 2025. OPM-201, licensed to Servier for the treatment of Parkinson's disease, completed its Phase I trial in healthy volunteers this year, with Phase II scheduled to start in 2025. Finally, a third kinase inhibitor, OPM-102, targeting oncology, is in preclinical development.

These three molecules come from the Nanocyclix® technology platform, which enables the design and selection of small macrocyclic kinase inhibitors that are highly effective and selective. Today, we have 12,000 molecules in our library, providing a unique, annotated database on a multitude of parameters essential to the development of this type of product. We use AI approaches to accelerate the discovery of drug candidates while reducing the cost of this phase.

OPM's two other technology platforms are:

(i) OncoSNIPER, for the selection of therapeutic targets using artificial intelligence, in partnership with Servier for the search of targets in pancreatic cancer,

(ii) PROMETHE® for the design and selection of radiolabeled biological molecules for systemic radiotherapy, for which we have signed a partnership agreement with Navigo and are currently discussing partnerships with other vectorization companies.

OPM, co-founded by Philippe Genne, Jan Hoflack and Karine Lignel, is based in Dijon, in the heart of the university and hospital cluster, and has 20 employees.

Further information: oncodesign.com

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