PRESS RELEASE

OPM announces positive results of its phase 1 in healthy volunteers with OPM-101: strong target engagement with excellent safety profile

- **End of double-blind, placebo-controlled phase 1 trial with OPM-101: 104 healthy volunteers (VS) participated in this trial designed to assess the safety of OPM-101 in humans**

- **Very good safety profile of OPM-101: no serious treatment-related adverse events occurred, and no discontinuation of the study was necessary**

- **Oral administration of OPM-101 demonstrated dose-related increases in systemic exposure, fast absorption with a T_{max} of 2-4 hours; the mean terminal elimination half-life was 12-13 hours, with steady state reached after 3-4 days**

- **Strong pharmacological effect: in an *ex vivo* whole blood assay to stimulate production of TNFα, OPM-101 rapidly and completely inhibited the stimulated release of TNFα, a downstream marker of activation of the RIPK2 pathway**

- **Strong semi-maximal inhibitory plasma concentration (≥80%): inhibition of TNFα release estimated at 150 ng/mL. These concentrations were reached and maintained during 14 days of administration for the 2 highest doses of MAD**

- **The favorable safety, pharmacokinetics and pharmacodynamics of OPM-101 support its further development for the treatment of diseases caused by deregulation of the RIPK2 kinase pathway, the therapeutic target of OPM-101**

- **Start of phase 1b/2a clinical trial planned for the fourth quarter of 2024**

Dijon (France), July 16, 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 announced positive results of phase 1 trial testing the drug candidate OPM-101, administered orally in single ascending doses (**SAD**) and multiple ascending doses (**MAD**), in healthy volunteers (**HV**).

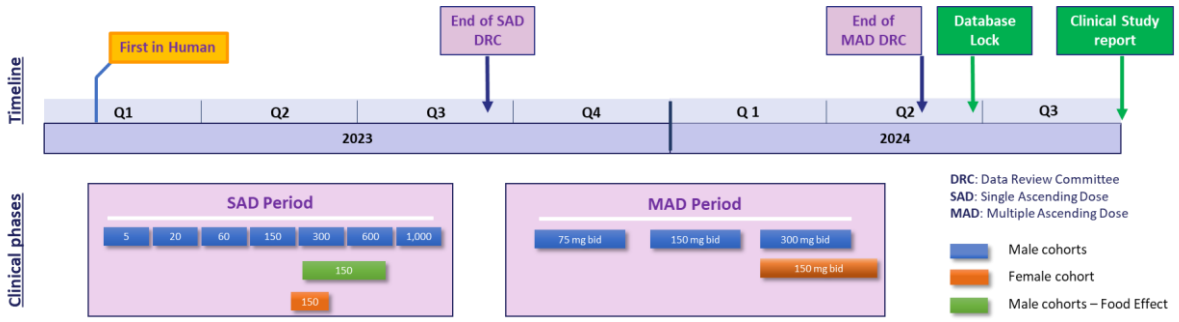
OPM-101 is an experimental, powerful and selective small molecule inhibitor of the RIPK2 kinase. OPM-101 is designed to modulate the pro-inflammatory signal transmission pathway of this kinase, which is responsible for the development of inflammatory diseases, and has the potential to treat diseases in the fields of IBD (Chronic Inflammatory Bowel Disease) and immuno-oncology. RIPK2 is a key protein in the regulation of immune responses and inflammatory processes. Recent research highlighted its potential as a therapeutic target, both in chronic inflammatory disorders and in several types of cancer.

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 (78 HV with OPM-101 and 26 with placebo):

- 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.
- 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.

This phase 1 trial, which began in February 2023, was completed on schedule in June 2024.

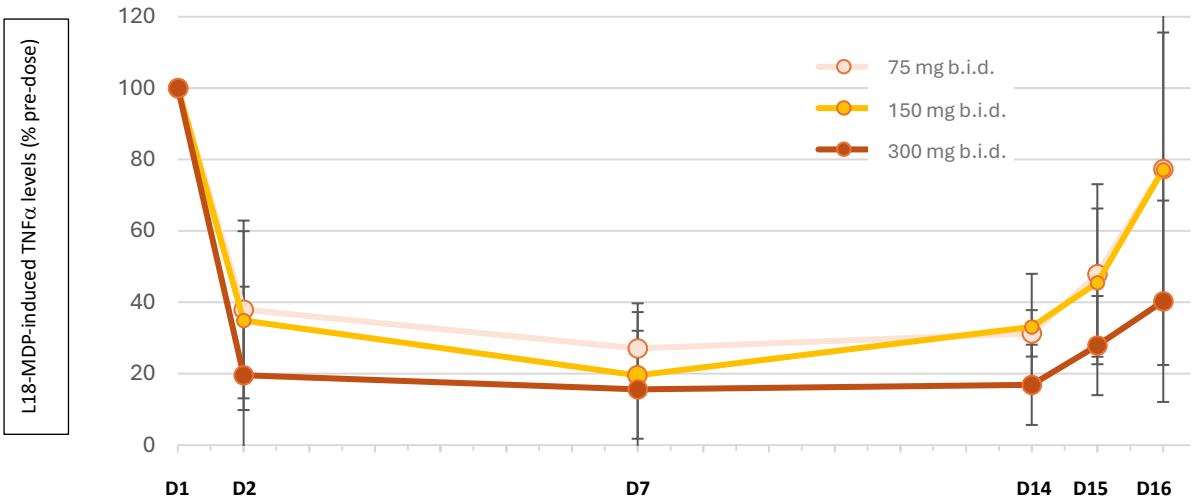
The results of the SAD and MAD administrations in the clinical trial demonstrated that OPM-101 is well tolerated and significantly inhibits the RIPK2 pathway at doses as low as 60 mg single administration and 75 mg b.i.d. (bis in die - Twice daily). Target engagement kinetics and pharmacodynamic results showed a fast development of inhibitory effect, already observed 2 to 4 hours after the first administration, and inhibition maintained for 14 days of administration. The mean level of target engagement was 65% (75 mg b.i.d), 75% (150 mg b.i.d) and 85% (300 mg b.i.d) over the 14 days of treatment.



Safety evaluations (vital signs, blood tests, ECG, holters) were carried out regularly throughout the trial. The trial also collects secondary pharmacokinetic measures, including half-life assessments. Exploratory measures to assess OPM-101 target engagement were calculated by tracking changes from baseline in L18-MDP-stimulated TNFα production *ex-vivo* in whole blood samples.

The results of the MAD cohorts demonstrated maximum target engagement by OPM-101, demonstrated by a 90 to 100% reduction in TNFα production, leading to complete inhibition of stimulated production and a return to basal levels of TNFα, thus showing immunomodulation rather than total suppression of immunity as observed with other IBD treatments. This maximum engagement of the target was observed, depending on the dose, between 2 and 6 hours after the first administration of the treatment. Residual target engagement prior to the next dose was maintained over the 14 days of administration at mean levels of 65%, 75% and 85% with the 3 dose levels tested in MAD, respectively.

Involvement of the target in the MAD part of the study (inhibition of TNFα production induced by L18-MDP, in % of predose)



In the MAD part of the study, on Day 15, i.e., 24 hours after the last administration, 50%, 55% and 80% of target engagement were still observed in the three doses of MAD tested. At 48 hours after the last administration, target engagement levels gradually decreased as expected. These results demonstrate time- and dose-dependent target engagement. These proof-of-concept results for the immunomodulatory mechanism were obtained with oral administration of OPM-101 for 14 consecutive days, which was also generally well tolerated in all SAD and MAD cohorts.

No serious adverse event was reported. All treatment-emergent adverse events considered to be at least possibly related to the drug and the study were mild to moderate in both the SAD and MAD cohorts. Twelve healthy volunteers (15%) reported a total of 15 adverse events considered to be related to OPM-101. 80% of these events were mild and 20% moderate. There was no clinically significant change in safety-related laboratory tests reported during the treatment periods for all dose cohorts of OPM-101 included in the analysis, except for one volunteer who experienced a moderate (3N) increase in ALT (liver enzyme) during MAD, resulting in discontinuation of treatment after 12 days.

The pharmacokinetic results in the MAD part are consistent with those observed in the SAD part of the study. The main pharmacokinetic characteristics of OPM-101 are: fast absorption with a T_{max} observed between
2-4h, a terminal half-life estimated at 12-13h, a steady state reached after 3-4 days and a dose-dependent exposure.

On the basis of the PK/PD correlation determined from the results of the SAD part of the study, we anticipate that a very significant target engagement (≥80%) can be achieved and maintained with a plasma concentration of OPM-101 remaining above 150 ng/mL in the interval between 2 treatment administrations. This threshold was achieved with the 2nd and 3rd dose levels in the MAD part of the study.

OPM plans to present additional results from the phase 1 cohorts at a future medical meeting in Q4 2024, subject to acceptance of the abstract by the United European Gastroenterology Week (UEGW) organizing committee.

Based on the results presented today, OPM plans to initiate enrolment in a phase 1b/2a clinical trial 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 PK/PD 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 clinical 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 results 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, which demonstrated a significant therapeutic margin and lack of toxicity in phase I trials with healthy volunteers, with a phase Ib/IIa scheduled to start at the end of 2024. 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. We now have 12,000 such molecules in our library and will be using AI 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 radioligand therapies, for which we are currently discussing partnerships with vectorization companies. The current agreement is a result of these discussions.

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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