letter to the shareholders

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Editorial

Hope keeps you going

Is there a glimmer of hope that might lift the world out of its chaos and reckless forward rush—guiding humanity toward greater wisdom and a genuine desire to live together?

It seems impossible not to place humanity at the heart of the answer, for it belongs to us. To make this world better for all of humankind—not just for a few. Are we merely living through another cycle that will ultimately bring us there, or are we losing our way?

I invite you to join me in the search for this glimmer of hope.

Today, all nuclear powers on Earth are either at war or preparing for it. The world is fragmenting in favor of the strongest, to the detriment of peace. Where will this path—so familiar from past history—lead us this time? Once again, men, women, and innocent children are paying the ultimate price with their lives, every day. In this collective madness, is humanity heading for its own self-destruction in a great radioactive flash?

Will collective intelligence finally rise above this loud background noise and allow us to make the vital leap forward—the one that could bring us out of this paradox where peace is supposedly cemented by nuclear weapons, and humanity, at last, steps from shadow into light?

Behind the scenes of the great Trumpist spectacle, Peter Thiel, Palantir, and its AI appear to be building the digital infrastructure of the U.S. government—an unprecedented machine. The underlying vision is fundamentally neoreactionary: how to disconnect social progress from technological progress. In other words, they argue that without technological progress, the future holds no alternative—stagnation would follow, and social progress becomes a brake on human evolution. In this vision, AI eliminates all randomness and silences alternative futures. These strange ideas are championed by the most powerful figures in Trumpist circles, who dream of a post-human future, as if they were gods.

Already, ChatGPT is more widely used than Wikipedia in the United States. A team from MIT recently published a scientific study on the impact of repeated ChatGPT use on the human brain. The findings are unequivocal: neurological, linguistic, and behavioral data reveal that users of ChatGPT consistently underperform compared to those performing the same tasks without AI. Working with AI language models appears to impair cognitive control and substantially alter behavior. This kind of cerebral atrophy could lead to a loss of personal autonomy, turning us into content, harmless vegetables living blissfully in our virtual bubbles.

Under these conditions, what could still be the foundation for hope in a better world?

Perhaps it's time to revisit Jacques Monod's 1970 book "Chance and Necessity", which explores scientific advancement and its philosophical consequences. The title is drawn from a quote by Democritus: "Everything that exists in the universe is the result of chance and necessity."

On a universal scale, life emerged by chance. Every living being, including humans, is the product of natural selection. Denying the role of chance is to deny life itself—its adaptability, its diversity, and, by extension, its intelligence—of which we are merely a fleeting expression, destined to disappear, with or without AI.

In living organisms, there is constant interaction between healthy and diseased cells, not unlike societal exchanges. Cancer represents the ultimate form of internal disorder: cells lose their function and aim only at eternal survival, at the expense of the organism that gave them life. No life is possible without harmonious growth, whether within a body or an ecosystem. The parallels with the state of the world today are all too clear. It's time we reactivate our societal immune system, and with it, our political autonomy, to rid ourselves of the cancer that is consuming this world. If chance brought us here through mutations, perhaps chance—through new mutations—can also lead us out. And we must act fast.

At OPM, our hope for survival is closely tied to our ability to secure funding. Our main assets lie in our two molecules: OPM-101 and OPM-201, both highly promising in their respective therapeutic areas—immuno-oncology and Parkinson's disease. In this financial environment, where both public and private investment markets are at a standstill, we've focused on partnering these two molecules with a pharmaceutical or biotech company—or a dedicated investor. If salvation is to come, it will come from there.

OPM-101 is entering its Phase 1b/2a trial in patients with melanoma resistant to anti-PD1 therapies. This trial represents real hope for patients currently without options. We are their hope—and this clinical trial is ours as well.

The note of hope I'll leave you with is that of the man who danced alone, arms wide open, in front of the church after the funeral of his murdered wife. Life is stronger than death.

Philippe GENNE

OPM wishes you a happy summer!

Karine Lignel – Chief Operating Officer, Co-founder
Philippe Genne – Chairman and CEO, Co-founder
Jan Hoflack – Chief Scientific Officer, Co-founder

Focus on the submission of the Phase 1b/2a REVERT clinical study

The REVERT study is evaluating OPM-101 in a Phase 1b/2a clinical trial in combination with pembrolizumab, a monoclonal antibody targeting the PD-1 protein, in patients with advanced melanoma who have developed resistance to anti-PD-1 therapy.

March 2025

Finalization of the REVERT study protocol and submission of the clinical trial authorization application to Swissmedic and Swissethics

Next steps

July 2025

Obtaining authorisation to conduct the Phase 1b/2a clinical trial

September 2025

Initiation of the clinical trial in the centres and inclusion of the first patient

À propos d'OPM-101

NANOCYCLIX®

OPM-101 is a macrocyclic molecule from OPM's proprietary Nanocyclix® platform. It is a highly potent selective and orally bioavailable Type 1 inhibitor (kinase active site binding inhibitor). In pharmacology, OPM-101 has demonstrated good efficacy in several preclinical models of colitis and immuno-oncology. Its safety profile, characterized in preclinical studies, meets a quality standard recognized by the pharmaceutical industry, and is compatible with chronic administration to treat pathologies such as IBD and immuno-oncology. OPM's intellectual property strategy effectively protects the value of this asset and its use in a wide range of therapeutic indications.

Key figures from the study

45 patients : minimum 6 in phase 1b and approximately 35 in phase 2a

10 - 13 clinical sites in Europe

2027 Phase 1b/2a results expected by the end of 2027

The OPM team, in consultation with Prof. Michielin, the Geneva-based study coordinator, and Swiss investigators, has finalized the protocol for the REVERT clinical study.

The application for clinical trial authorization was submitted in parallel to the Swiss regulatory authority (Swissmedic) and the ethics committees (Swissethics) on 24 March 2025. OPM received requests for clarification and information and was able to respond to these questions in early June 2025. The review process is ongoing with both authorities, and their feedback is expected in summer 2025.

The REVERT study aims to determine the safety profile and efficacy of OPM-101 in combination with pembrolizumab (an approved and widely used anti-PD-1 antibody) in patients with advanced melanoma who are becoming resistant to anti-PD-1-based therapy (alone or in combination, except with anti-LAG-3).

An abstract on the design and methodology of the REVERT study has been submitted to the ESMO Congress, which will take place from 17 to 21 October 2025 in Berlin.

Testimonial from Prof. Olivier Michielin, principal coordinator of the REVERT study

Presented during the REVERT study webinar - April 2025

Professor Olivier Michielin

Head Physician of the Oncology Department and Head Physician of the Precision Oncology Service at Geneva University Hospitals, Co-Director of the Swiss Cancer Centre Léman (Agora, Lausanne), Member of the Executive Committee of the European Society for Medical Oncology (ESMO)

During a webinar organized by OPM to present the design of the REVERT study (Phase 1b/2a) evaluating OPM-101 in oncology, Professor Michielin, the study's lead investigator and an internationally renowned expert in oncology, provided a detailed overview of the current state of treatment for metastatic melanoma.

Professor Michielin first highlighted the significant advances achieved through immunotherapy, particularly immune checkpoint inhibitors such as anti-PD-1 antibodies (Pembrolizumab, Nivolumab), whether used alone or in combination with the anti-CTLA-4 antibody Ipilimumab. Despite these advances, he pointed out that nearly 40% of patients experience rapid disease progression within the first six months of treatment, reflecting primary resistance. In the longer term, approximately two-thirds of patients develop secondary resistance, underscoring a major unmet medical need.

He went on to explain that while approaches such as dual immunotherapy or cell-based treatments (e.g., TIL therapy) can provide some benefit, their overall effectiveness remains limited and their accessibility is constrained, particularly due to logistical complexity and the fact that even in the best studies, they achieve durable response rates of only 20–30%.

In this context, Professor Michielin presented the REVERT study in detail, led by OPM. He emphasized the innovative nature of the protocol, which combines OPM-101 with the anti-PD-1 antibody Pembrolizumab, aiming to restore or enhance immune response in patients who have failed one or more prior lines of immunotherapy, including the Ipilimumab + Nivolumab combination. This positions REVERT as one of the very few clinical studies specifically targeting patients who have become resistant to existing treatments, a population for which therapeutic options are currently almost nonexistent.

Professor Michielin stressed the importance of this approach in a therapeutic landscape crowded with inconclusive single-arm trials. REVERT stands out through its rigorous design, highly relevant patient population, and the strong mechanistic potential of OPM-101, which is designed to bypass tumor resistance mechanisms.

He concluded by stating that this study represents a concrete opportunity to offer an innovative and differentiated solution in a critical segment of oncology, and that it could pave the way for new therapeutic combinations in other cancers that are refractory to standard immunotherapies.

Inhibition of RIPK2: a new immunotherapy approach for advanced cancers (1/2)

Our mission, our driving force

At OPM, our mission is to develop innovative strategies to treat therapeutic resistance and the emergence of metastases in cancer patients. This mission drives all of our research and development activities for new drugs.

Our work on RIPK2 inhibitors began several years ago in the context of chronic inflammatory diseases such as ulcerative colitis and Crohn's disease.

However, over the past two years, the promising preclinical results we have achieved in oncology with these inhibitors have led us to refocus our efforts. This shift was reinforced by a small but growing number of publications highlighting the role of the RIPK2 signaling pathway in cancer progression.

Our work thus paves the way for a novel therapeutic strategy for advanced tumours that have developed resistance to immune checkpoint inhibitors (ICIs), a medical need that remains largely unmet.

Cancer is a dynamic disease that evolves over time. In this process, chronic inflammation within the tumour microenvironment (TME) acts as a major selective force. It promotes immune escape, metastasis formation and therapeutic resistance by inducing an immunosuppressive environment.

At the heart of this inflammatory machinery is RIPK2, a central regulator of the NOD1/2 innate signaling pathway. Activation of RIPK2 triggers NF-κB signaling, leading to the release of pro-inflammatory cytokines that help tumours evade immune detection and grow.

OPM's strategy is clear and ambitious: neutralize RIPK2 activation, interrupt chronic inflammation, restore immune surveillance and re-sensitize tumours to immunotherapy.

Our reasons for believing in it: Key preclinical data from OPM

In an internal colon carcinoma model mimicking secondary resistance to anti-PD-1 treatment, OPM-101 demonstrated robust antitumour activity and significantly prolonged long-term survival — both as monotherapy and in combination with anti-PD-1.

This model replicates the clinical profile of patients targeted in our upcoming Phase 1b/2a clinical trial, which will evaluate patients with advanced melanoma and acquired resistance to ICIs.

The efficacy of OPM-101 is based on its ability to remodel the tumour microenvironment and restore tumour recognition by the immune system.

Direct effects on tumour cells: OPM-101 'unmasks' tumours by increasing the expression of HLA proteins and genes involved in antigen presentation.

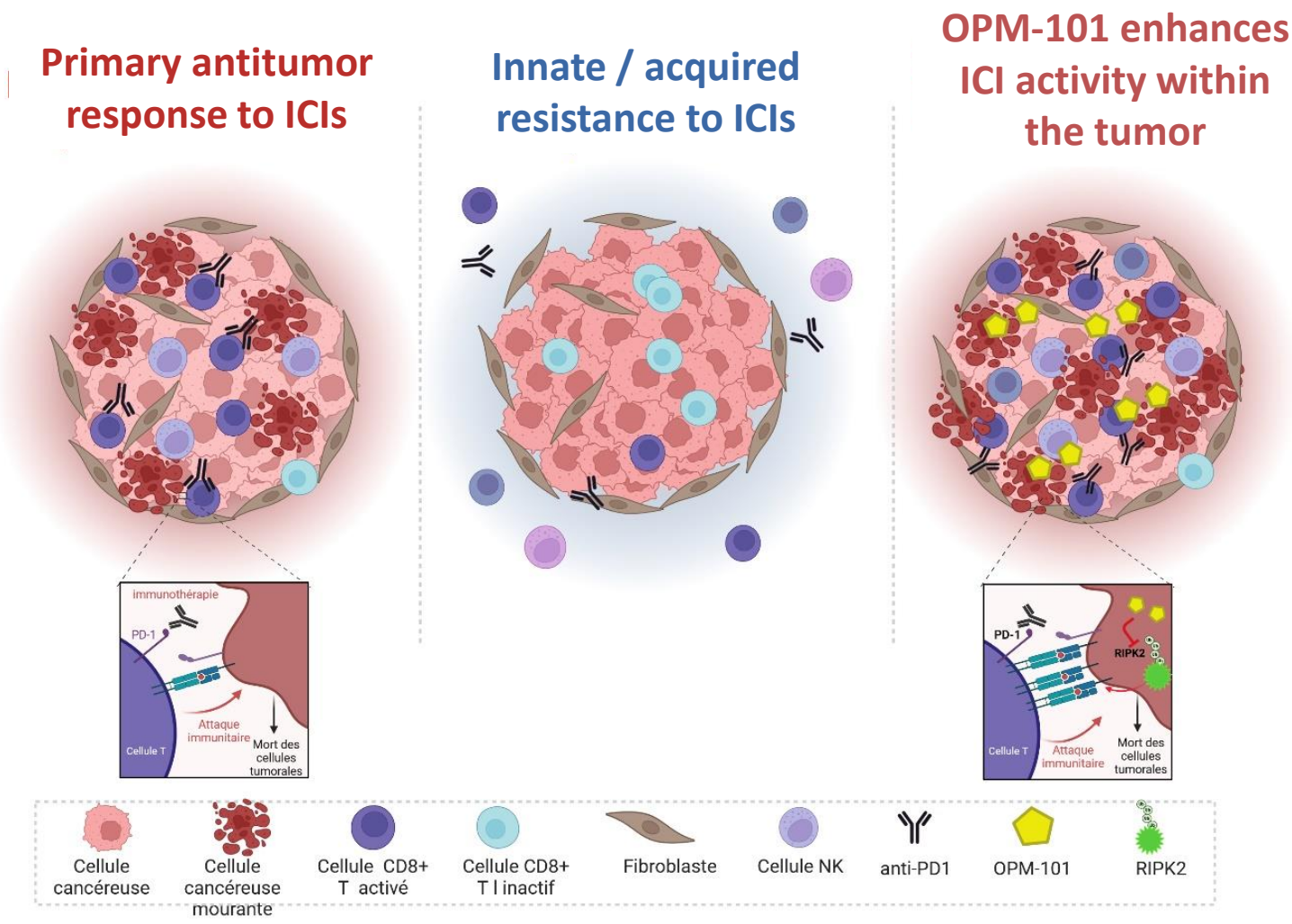
Inhibition of RIPK2: a new immunotherapy approach for advanced cancers (2/2)

An inflammatory and immunologically active tumour microenvironment

- OPM-101 increases the number of activated CD8+ T lymphocytes
- OPM-101 modulates macrophage activity
- OPM-101 stimulates key immune signals, including essential cytokines and chemokines

The result? Less resistance, more response.

By disrupting the inflammatory shield that protects tumours, OPM-101 restores immune function and enhances the efficacy of ICIs in resistant patients.



At OPM, we believe that the future of immuno-oncology lies in directly targeting the mechanisms responsible for resistance. OPM-101 could open a new chapter in cancer treatment, one in which immune escape is no longer an insurmountable barrier for patients with advanced cancer, but a challenge we are now able to overcome.

Creation of the PROMETHE association (1/2)

About the PROMETHE association

Since the 2000s, treatment options for cancer patients have seen remarkable progress with the arrival of targeted therapies. In 2025, however, cancer remains the leading cause of death in France. The availability of new, more effective treatments with acceptable tolerance is still essential to improve patient survival. Radiotheranostics is now recognized as one of the most promising approaches for cancer treatment and represents a real therapeutic revolution.

Historically, pharmacoimaging projects have been developed in Dijon through Pharm'image, bringing together laboratories active in the field of nuclear medicine.

It is in this general context that the PROMETHE association is positioned. It is governed by the law of 1 July 1901 and the decree of 16 August 1901, and is entitled: **Association for the development of nuclear medicine applied to the development of radiotheranostic molecules for the treatment of cancer, or PROMETHE (PRecision Oncology MEdicine THEranostics).**

The purpose of this association is to improve public health, in particular by bringing effective treatments to patients more quickly in the field of nuclear medicine, and more specifically, radiotheranostics (radiotherapy and its diagnostic companion).

The association was founded by Oncodesign Precision Medicine (OPM) and the Georges-Francois Leclerc Cancer Centre (CGFL). Philippe Genne, CEO of OPM, is the association's president, and Charles Coutant, CEO of CGFL, is the association's secretary.

31 March 2025

First Radiotheranostics Awareness Day

On 31 March 2025, the PROMETHE association organized the first radiotheranostics awareness day in Dijon, with the aim of raising awareness of radiotheranostics among as many people as possible (patients, patients' family members, doctors, politicians, scientists, etc.). This therapy is relatively new and therefore not well known, yet it plays an important role in the therapeutic arsenal and is gradually moving up the treatment ladder.

An additional objective is to educate young and future healthcare professionals in order to inspire them to pursue careers in this field. The radiotheranostics sector is currently experiencing a shortage of trained professionals (radiographers, nurses, doctors, radiopharmacists).

Around 100 participants registered for the day, including patients, students, scientists (from industry and academia) and administrators (representatives from the Bourgogne Franche Comté region, the Directorate for Entrepreneurship and Business Creation, Santenov and the Regional Economic Agency).

Creation of the PROMETHE association (2/2)

PROMETHE
PRecision Oncology MEdicine THEranostics

31 March 2025

First Radiotheranostics Awareness Day

The day began with a short presentation of the association and a few words from Prof. Charles Coutant and Dr Philippe Genne.

Prof. Pierre Fumoleau and Prof. Alexandre Cochet then presented precision medicine in oncology, going into detail about nuclear medicine and radiotheranostics.

The morning concluded with a session dedicated to patients, beginning with a presentation of the Fondation Oncidium and its work in France, followed by a round table discussion with several patients who shared their experiences with radiotheranostics, some of whom are still undergoing treatment. This initiative inspires other patients, gives them hope and 'de-dramatises' the term 'nuclear', which can be frightening.

The afternoon focused on more technical presentations on the subject, including:

- A presentation on the supply of radioactive isotopes for medical use in France by Dr Marion Libessart, who works at the CEA in Cadarache on the Jules Horowitz reactor project.
- A presentation by Dr Céline Mirjolet (CGFL, Dijon) on the combination of radiotheranostics and external radiotherapy.
- A presentation by Dr Sophie Poty (ICMUB, Dijon) on the promising technique of pre-targeting and its future in clinical practice.

The day ended with the PROMETHE 2025 General Meeting.

News from the first half of 2025

March 2025

Submission of the protocol for the Phase 1b/2a REVERT clinical study to evaluate OPM-101 in combination with pembrolizumab in patients with advanced melanoma who are resistant to anti-PD-1 therapy

March 2025

Appointment of Christophe Thurieau as independent director of the OPM Board of Directors

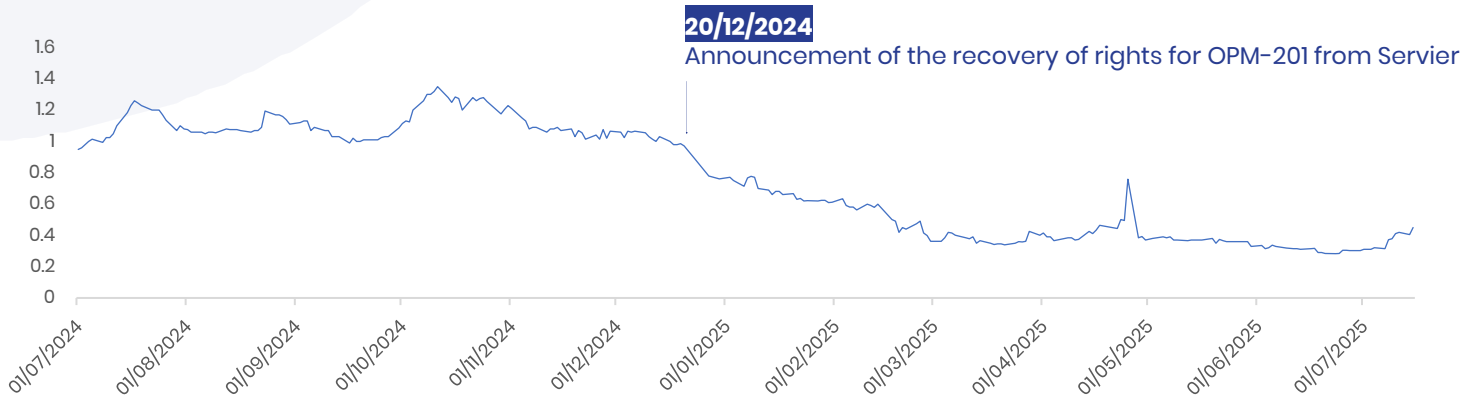
A Corporate Social Responsibility (CSR) approach embedded in OPM's culture

Consistent with its vision, values and the expectations of its stakeholders, OPM has made CSR a cornerstone of its business since its creation and is committed to demonstrating this commitment in all its activities. OPM has therefore joined the Club RSE BFC to be able to exchange experiences with other companies in our region on this topic. In 2024, OPM implemented several initiatives to further its CSR approach:

A team of OPM employees participated in Odyssea Dijon, an event supporting breast cancer research. OPM included Alexis Miellet, a Dijon athlete supported by OPM in his preparation for the 2024 Paris Olympics, in its team.

In July 2024, all employees took part in a CSR workshop designed as an escape game called 'Code Climat'. This fun and educational experience aimed to raise awareness among our employees about climate issues, identify concrete ecological actions and strengthen environmental responsibility within the company. Thanks to this collective immersion, everyone was able to reflect on the impact of our industry on the climate and consider sustainable solutions.

OPM share price evolution over one year



Stock market information

ISIN Code	FR001400CM63
Number of shares	18 190 878
Market capitalization*	8.2 M€
Share price*	0.45€

ELIGIBLE PEA PME

data as of 15/07/2025 after market close

To receive all the latest news from Oncodesign Precision Medicine in real time, and to subscribe to our newsletter, send us your e-mail address at oncodesign@newcap.eu.

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