Oncodesign Precision Medicine

Targeted therapies for inflammation & oncology

- We initiate coverage of Oncodesign Precision Medicine (OPM), a French clinical-stage biopharmaceutical company, with a target valuation range of EUR 1.9-2.7. We consider the company a compelling investment opportunity for numerous reasons:

  1/ OPM-101: RIPK2 inhibitor for immune checkpoint inhibitor-associated colitis (ICI-AC) and inflammatory bowel diseases (IBDs)
  - **Compelling scientific rationale and (pre)clinical data**, indicating safety, preliminary efficacy, and selectivity, support RIPK2 inhibition as a mechanism of action to target both ICI-AC and IBD (ulcerative colitis & Crohn's disease).
  - **Immunomodulator** (rather than immunosuppressor), acting via a **distinct molecular pathway**, allowing for **convenient oral administration potentially in combo therapy** while preserving the immune system's ability to fight infections. Hence, differentiated enough to break into both the (crowded) IBD and ICI-AC markets.
  - We project c.EUR 400m in revenue at peak for OPM, based on an envisioned (big) pharma partnership for ICI-AC and IBD post-Ph2b.

  2/ OPM-201: lucrative partnership since 2019 with French pharma company Servier on LRRK2 kinase inhibitors for Parkinson's disease (PD)
  - Servier-launched Ph1 in healthy volunteers expected to readout in H1 2025.
  - **EUR 300m in biobucks + royalties on net sales** offering significant financial upside for OPM and external validation for its innovative technology suite.
  - **PD is a blockbuster opportunity** for which we model > EUR 3bn in peak sales translating into **> EUR 300m in royalty revenue for OPM**.

  3/ Industry-unique small molecule database offering opportunities for new pipeline additions and potential out-licensing.

  4/ Seasoned management team with a strong entrepreneurial track record.

  5/ Attractive 12-month news flow including two Ph1 readouts with OPM-101 and OPM-201 which increase our valuation range, already offering > 25% upside to the last closing price, with c.10% if successful.
- OPM's cash position end of 2023 of EUR 10m, reinforced by an additional EUR 4.85m in grants and equity financing since the start of 2024, provides runway until early 2025.

EUR	12/22a	12/23e	12/24e	12/25e	12/26e
Sales	8.0	1.1	1.1	1.1	1.1
EBITDA	-0.6	-10.1	-7.8	-8.4	-20.9
Adj. Net Profit	0.8	-8.2	-7.3	-7.8	-18.1
Adj. EPS	0.16	-0.49	-0.40	-0.43	-0.99
CF per share	0.16	-0.49	-0.36	-0.38	-0.94
Dividend ps	0.00	0.00	0.00	0.00	0.00
EV/EBITDA	-1.9	-2.7	-4.7	-5.4	-3.1
Adj. P/E	10.8	-3.1	-3.8	-3.6	-1.5
Dividend yield	-	-	-	-	-

Source: Oncodesign Precision Medicine/Degroof Petercam estimates

Share price (16/04/24)	
EUR 1.53	
Target valuation range	
EUR 1.90 – 2.70	
Risk	High
Bloomberg	ALOPM:FP
Shares number (m)	18.2
Market cap (m)	EUR 28m
Net debt 12/23 (m)	EUR 2
Net debt/EBITDA 12/24	-1.1
1 year price perf.	+35.0%
Diff. with EuroStoxx	+26.3%
Volume (sh/day)	4
L/H 1 year	EUR 1.00 -2.17
Free Float	43.0%
PCG (Holding P. Genne)	46.7%
Jan Hoflack	7.5%
Man. Committee and employees including historical	1.6%
Karine Lignel	1.2%

Company description

Oncodesign Precision Medicine (OPM) is a clinical-stage biopharma company. Using its proprietary target selection platform and medicinal chemistry technology, OPM has built a pipeline of first-in-class small molecules for a number of indications including immune checkpoint inhibitor-induced colitis, IBD, and Parkinson's disease.

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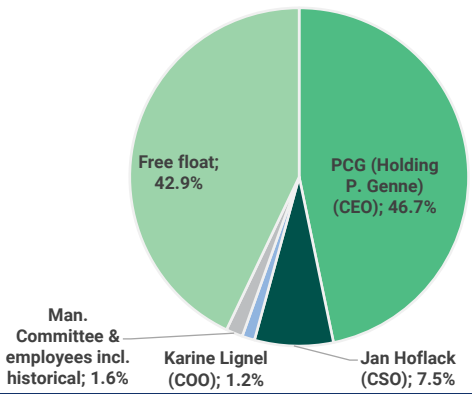
1/ Business summary

Exhibit 1 Company profile

OPM, headquartered in Dijon (France), was created in July 2022 following the separation of Oncodesign's two business lines 'Service' and 'Biotech'. OPM subsequently raised EUR 8m through an IPO on Euronext Growth Paris in Sept 2022 and financed itself with additional funding stemming from 1/ its Servier partnerships (EUR 7.5m), 2/ capital raises (EUR 2m), 3/ a bank loan (EUR 6m), 4/ ERDF and DTD grant funding (EUR 2.1m & EUR 0.8m, respectively). Using its proprietary target selection platform and medicinal chemistry technology, OPM has built a pipeline of potential first-in-class small molecules for a number indications including ICI-AC, IBDs, and PD. The company currently has runway until early 2025.

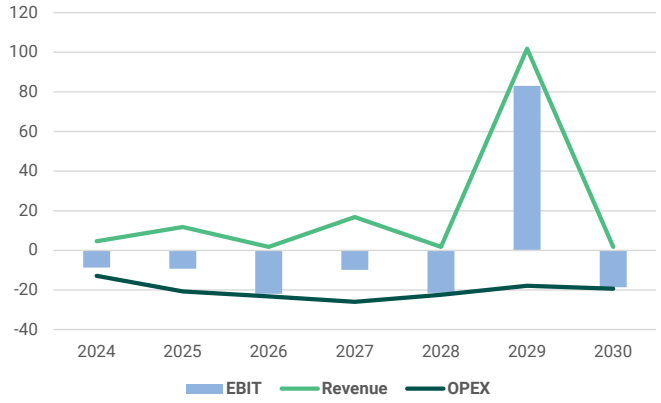
Source: OPM

Exhibit 2 Shareholding overview



Source: OPM

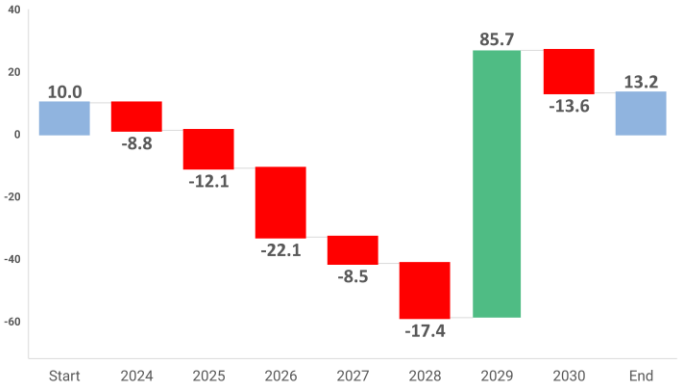
Exhibit 3 Financial projections (EUR m)



Source: Degroof Petercam estimates

We envision OPM to be profitable for the first time in 2029 as a result of an anticipated milestone payment stemming from a post-Ph2b partnership for OPM-101.

Exhibit 4 Cash (flow) projections (EUR m)



Source: Degroof Petercam estimates

Projections exclude impact of any potential debt/equity financing rounds.

Exhibit 5 SWOT analysis

STRENGHTS	WEAKNESSES
•Proprietary target selection platform and medchem technology for differentiated drug development	•ICI-AC pathogenesis still not fully elucidated
•Scientific rationale and data supporting RIPK2 inhibition as a mechanism to target ICI-AC, IBD, & cancer	•IBD and PD are crowded and highly risky indications, respectively
•OPM-101 is a small molecule immunomodulator allowing for convenient oral (vs. IV for biologics) & safe (vs. immunosuppressors) administration	•Limited clinical validation of RIPK2 and LRRK2 targets so far
•Lucrative clinical & commercial EUR 300m+royalties partnership with Servier for OPM-201 in PD	•Loss-making with profitability expected from 2029 onwards*
•Seasoned management team with strong entrepreneurial track record	•Lack of investment so far by internationally recognized life science funds
OPPORTUNITIES	**THREATS**
•Enter the ICI-AC, IBD, & PD markets with a first and/or best-in-class small molecule	•BI 706321 (BI) / DNL-151 (Denali/Biogen) being superior RIPK2 / LRRK2 inhibitors
•Combination therapies with biologics & other small molecules for ICI-AC, IBD, PD, & cancers	•Clinical development/regulatory delays and/or clinical trial failures; discontinuation of asset development
•Lucrative licensing deal for OPM-101 with big pharma for ICI-AC & IBD	•Label & reimbursement restrictions
•Early-stage programs (incl. RIPK2 inhibition) for oncology indications	•Product patent expiration resulting in loss of royalty revenue
•Macrocycle database offering opportunities for outlicensing and/or new pipeline additions	•Shareholder dilution resulting from future equity financing rounds

Source: Degroof Petercam estimates

*We envision OPM to be profitable for the first time in 2029 as a result of an anticipated milestone payment stemming from a post-Ph2b partnership for OPM-101.

2/ Brief recap on OPM's birth

In July 2022, Oncodesign announced the subsidiarization of its Biotech & AI activities to create a **pure-play clinical-stage biopharma company with a precision medicine focus**. This was realised through a partial transfer of assets to the OPM subsidiary, and the listing of this subsidiary through an exceptional distribution in kind to Oncodesign's shareholders concomitant with the admission of all OPM's shares to listing on Euronext Growth (ticker 'ALOPM').

The Service activity, dedicated to drug discovery CRO activities, named 'Oncodesign Services' was acquired by Edmond de Rothschild shortly after the separation.

An overview of OPM's current management team can be found in Exhibit 6. **In our view, the team clearly possesses the required operational, financial, and scientific experience to lead an early-stage biotech company like OPM**.

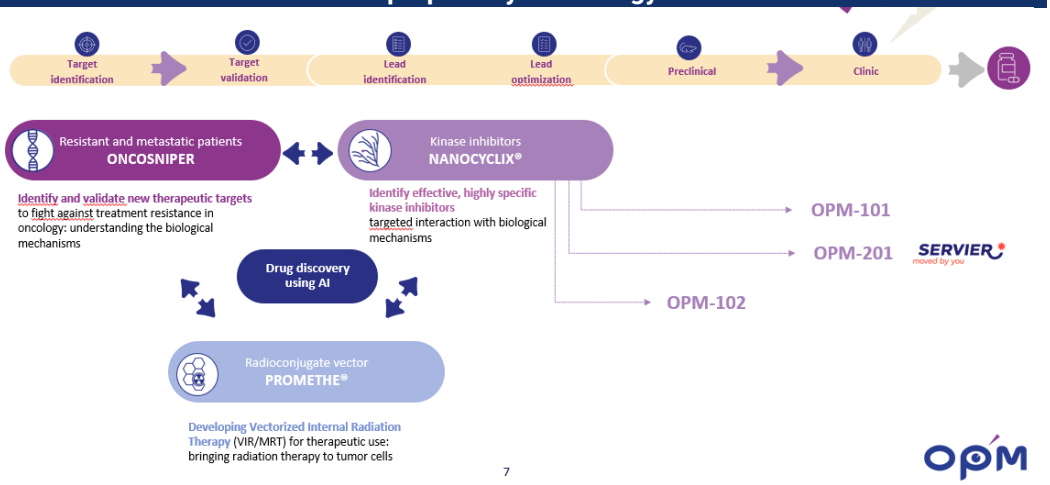
Exhibit 6 OPM management team

Source: OPM

3/ OPM's proprietary technology suite

OPM deploys a number of proprietary technologies to optimize their drug discovery and development process, being 'OncoSNIPER®', 'Promethe®', and 'Nanocyclix®' (Exhibit 7).

Exhibit 7 OPM's innovative and proprietary technology suite



Source: OPM

3.1 OncoSNIPER®: target selection platform

The OncoSNIPER® technology uses clinical information from cancer patients that are resistant to anti-cancer treatments. This allows to identify signatures enabling the stratification of different resistant patient populations. These signatures are then translated into therapeutic targets.

The OncoSNIPER® platform integrates public, private, and proprietary data sources and uses various artificial intelligence (AI) technologies (machine learning, deep learning, computer vision, natural language processing, etc.). OncoSNIPER® also integrates the knowledge of drug discovery experts into the algorithms themselves, enabling a hybrid AI approach that combines the advantages of purely data-driven and expert system approaches.

OncoSNIPER® benefits from Oncodesign Services' experimental capabilities, allowing to generate ad hoc data and validate any results identified *in silico* at the preclinical stage. OPM thus identifies and selects targets based on an *in silico* scoring process and experimentation, with OncoSNIPER® feeding both the Nanocyclix® and Promethe® platforms (see below) leading to an integrated suite of technologies.

OncoSNIPER® also allows OPM to develop partnerships to discover new targets and biomarkers and to conclude licensing agreements on pre-identified therapeutic targets with pharmaceutical and biotechnological companies. For example, in Sept 2022, **OPM and Servier entered into a collaborative research agreement, named 'STarT Pancreas', to identify and validate new therapeutic targets in Pancreatic Ductal Adenocarcinoma** (PDAC) (Exhibit 65 in addendum). The next priorities include 1/ target identification, 2/ experimental validation of AI findings, and 3/ further development until validation of the drug candidate entry into Ph1 (milestone payments to OPM expected). Subject to achieving specific objectives, OPM expects an additional EUR 0.5m milestone payment from Servier.

3.2 Promethe®: radiotheranostic approach to treat cancers

OPM's goal is to address more precisely and effectively resistant and metastatic cancers without therapeutic option. In this regard, OPM has chosen the radiotheranostic / molecular radiotherapy (MRT) approach. At a technological level, MRT is based on the administration of a labeled drug with a radioactive isotope (radiopharmaceutical) to destroy, specifically, tumor cells. Its efficiency comes from the emitted radioactivity which causes low dose rate irradiation leading to cell death. These particle-emitting radioisotopes are directed towards targets over-expressed by tumor cells, using very specific vectors, capable of recognizing and attaching to them.

The specificity of the vector for a tumor target thus makes it possible to spare healthy tissues and guarantee better effectiveness while limiting side effects, a strategy particularly well suited to disseminate diseases. Theranostics (meaning "therapy" and "diagnosis") aim to both diagnose and treat cancers as a unified approach. The advantage of MRT is precisely the potential to create a radiotheranostic agent, meaning a radiopharmaceutical which, depending on the radiation nature of the chosen isotope, allows diagnostic imaging (prediction/therapeutic monitoring) or patient therapy.

The diagnostic agent (called diagnostic companion) therefore makes it possible to understand the usefulness, effectiveness, and optimal dose of the therapeutic agent for a given patient, based on its biodistribution. This radiotheranostic approach capitalizes on the proprietary platform of recognized partners with whom they are in discussion, to jointly develop radiotheranostic molecules through one or more JV, capable of generating highly specific biological molecules for targets identified by their OncoSNIPER technology. This approach also capitalizes on Pharmimage®, the pharmaco-imaging platform from Oncodesign Services.

3.3 Nanocyclix®: proprietary medicinal chemistry technology platform

3.3.1 Progress in kinase drug development[1]

OPM has constructed a full platform of small molecule macrocyclic kinase inhibitors that is unique in the industry. Kinase inhibitors, in fact, have been around since 2001 when imatinib (Glivec®), a tyrosine kinase inhibitor, received FDA approval for the treatment of chronic myeloid leukemia. Since then > 70 other small molecule inhibitors on protein and lipid kinases have been brought to market, mainly for cancer treatment (Exhibit 64 in addendum).

Over the past 20 years the design of kinase inhibitors improved in multiple ways, principally aimed at improving selectivity and overcoming the challenges of resistance. These medicinal chemistry efforts have been facilitated by several key technical advances:

- **1st**, following the sequencing of the human genome, the comprehensive classification and annotation of the 500 plus protein kinases (the human kinome) and its subdivision into a number of subfamilies, has led to a holistic understanding of kinome relationships and facilitated a step change in the way that kinase drug discovery can be tackled.
- **2nd**, the introduction of kinase 'profiling' panels of gradually increasing size, which today encompass most of the kinome, have become less expensive owing to miniaturization, robotics and the development of novel ways to measure the activities of kinases and their interaction with small chemical entities. These developments have enabled drug developers to profile inhibitors against off-target kinases routinely, as well as the primary target, enabling promiscuous lead compounds to be discarded at early stages, and later to help guide improved selectivity within key series of compounds. Extensive kinase inhibitor profiling has also enabled new clinical opportunities to be identified and undesired side effects to be explained.
- **3rd**, increasing access to high-resolution experimental structures of kinase catalytic domains, facilitated by the Structural Genomics Consortium, has enabled routine integration of structural and computational chemistry into drug discovery, including fragment-based drug design approaches. This is providing improved information about structure–activity relationships, allowing better drug design by enabling chemical groups to be positioned more precisely.
- **4th**, mechanisms of drug resistance that have been observed in patients have helped both to identify potential resistance mechanisms that are relevant clinically and to inform the opportunities and characteristics of the next-generation inhibitors needed to overcome the effects of these mutations in patients. Therefore, the ongoing iterative cycle between bench and bedside will continue to be key to ongoing developments and their success.

3.3.2 Nanocyclix®

OPM's current platform consists of > 12,000 macrocycles, based on > 50 scaffolds and > 300 separate linkers. These type I kinase inhibitors, profiled against > 500 kinases of the human kinome, are potent, highly selective, and have good cell penetration. They also boast good developability, physicochemical properties, and ADMET[2], with a highly predictable structure-activity relationship.

This approach also makes it possible to generate molecules capable of crossing the blood-brain barrier (BBB), for applications in CNS diseases.

[1] Cohen et al. (2021). Kinase drug discovery 20 years after imatinib: progress and future directions. Nature Reviews Drug Discovery 20.
[2] Absorption, distribution, metabolism, excretion, toxicity.

Nanocyclix® molecules represent an exciting opportunity for probe-based drug discovery. In this approach, complementary to target-based drug discovery, the diversity of synthesized Nanocyclix® molecules is tested on a large number of kinases ("profiling"). This generates probes with high potency and selectivity for kinases that are little explored or difficult to target (intractable targets). This probe-based drug discovery approach thus makes it possible to identify opportunities for first-in-class therapies on kinases that are little explored, unexplored, or difficult to target, and OPM's molecular diversity screening approach for kinases of interest paves the way to potential best-in-class next-generation inhibitors.

The Nanocyclix® set of molecules is also an ideal starting point for chemical biology approaches due to its high potency, selectivity for individual kinases and cell penetration capabilities. In this approach, the molecules are tested in disease relevant phenotypic models: cell-based assays representing pathological conditions of diseases without an existing solution. Organoids generated using biopsies of cancers with unmet medical needs are a good example. The identification of Nanocyclix® molecules with high cytotoxicity in these models, with no adverse effect on normal cells, allows for both the identification of new targets and the development of new treatments.

The molecular weight of a Nanocyclix® kinase inhibitor, even after complete optimization, is generally around 350 to 450 daltons – significantly lower than a linear inhibitor with similar potency and selectivity. This generates a more drug-like profile that is still optimized using a rational and structure-based design and multi-parameter optimisation techniques from modern medicinal chemistry. Only recently, Deep Tech Development Fund has awarded EUR 745k to OPM's ANIMUS program, which main purpose is to develop proprietary technologies to improve the efficiency of the drug discovery process at OPM, based on Nanocyclix® technology. This involves the development of AI approaches enabling, first, the systematic optimization of all parameters at each DMTA[3] cycle in order to reduce the number of cycles required to identify drug candidates and, second, the use of NCX generative molecule design to assess a very large number of molecules *in silico* at the design phase.

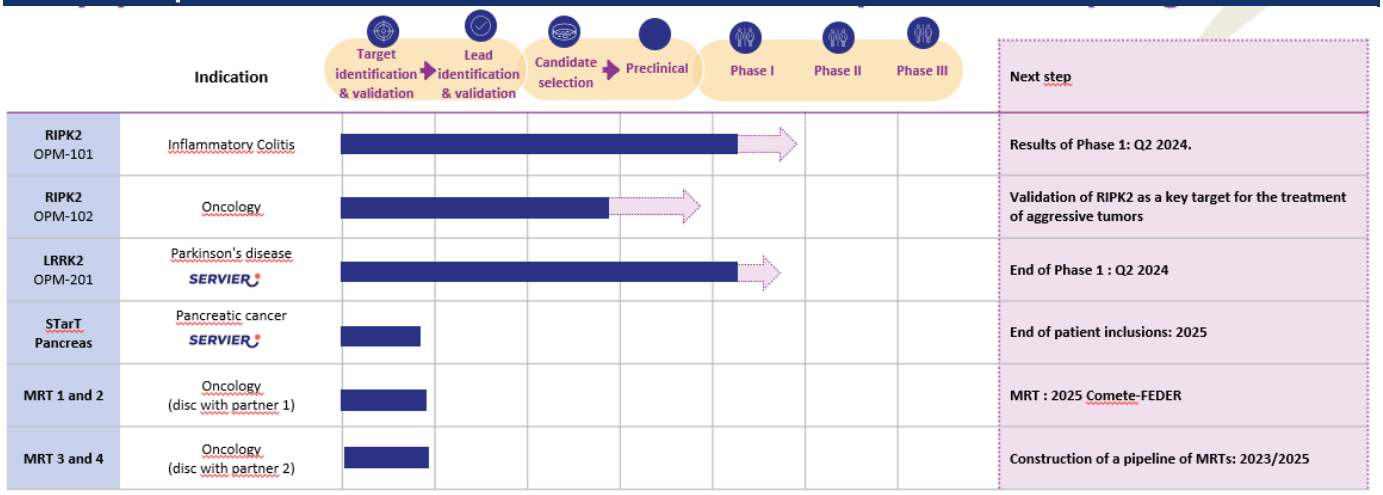
In summary, Nanocyclix® molecules can precisely target intractable and unexplored kinases in various kinase families, including lipid kinases. Due to their small size and limited conformational space, Nanocyclix® inhibitors easily cross cell membranes and even the blood-brain barrier. They can also be radiolabelled with 18F for PET-based diagnostic purposes.

3.4 Current pipeline overview

Applying its proprietary medicinal chemistry technology 'Nanocyclix®', OPM has built a diverse pipeline of small molecule kinase inhibitors for a number of indications including IBD, PD, and cancers (Exhibit 8). In this initiation report, we focus on OPM's two most advanced clinical-stage assets, being OPM-101 for ICI-AC and IBD, and OPM-201 for PD.

[3] Design-Make-Test-Analyze

Exhibit 8 Pipeline overview



Source: OPM
COMETE project: This project is supported by the FEDER grant. It focuses on the development of a portfolio of radiotheranostic molecules for the treatment of advanced digestive cancers.
MRT: revolutionary molecular radiotherapy technology, which is a radiotherapy technic used in nuclear medicine within the oncology field.

4/ OPM-101: a new opportunity for therapeutic intervention in IBD and ICI-AC

4.1 Inflammatory bowel disease

IBD is a term that describes disorders involving long-standing (chronic) inflammation of tissues in the digestive tract. Types of IBD include:

- Ulcerative colitis (UC). This condition involves inflammation and sores (ulcers) along the lining of patients' large intestine (colon) and rectum.
- Crohn's disease (CD). This type of IBD is characterized by inflammation of the lining of the digestive tract, which often can involve the deeper layers of the digestive tract. CD most commonly affects the small intestine. However, it can also affect the large intestine and uncommonly, the upper gastrointestinal tract.

IBD symptoms, which vary depending on the severity of inflammation and where it occurs, include diarrhea, rectal bleeding, abdominal pain, fatigue and weight loss. For some people, IBD is only a mild illness. For others, it's a debilitating condition that can lead to life-threatening complications (including severe bleeding/dehydration, osteoporosis, increased risk of colon cancer/blood clots).

4.1.1 Epidemiology

The exact cause of this complex disease remains unknown. The most widely accepted theory is that the cause is multifactorial, involving genetic predisposition, barrier defects of the gut, dysregulated immune responses and environmental factors. In short, IBD is the result of an inappropriate immune system response against normal gut flora in genetically predisposed individuals.

The incidence of CD has increased dramatically in recent years. This increase is evident in developing countries where Western lifestyle begins to have a significant impact. Thus, it is thought that a western lifestyle has an impact on the incidence of IBD.

An estimated 3.1m adults (1.3% of the population) in the USA have been diagnosed with IBD[4]. Although IBD is more common in white people, it can occur in any race. Cases are also increasing in other races and ethnicities.

Most people who develop IBD are diagnosed before they are 30 years old. But some people do not develop the disease until their 50s or 60s.

4.1.2 IBD treatment landscape: crowded with first-in-class potential for OPM-101

Diagnosis of both indications occurs through colonoscopy and histological findings.
While there is no cure for UC, there are several new treatments that can significantly reduce signs and symptoms of the disease and bring about long-term remission. The goal of pharmacological treatment is achieving symptom control, endoscopic/mucosal healing, limiting/eliminating corticosteroid use and most importantly clinical remission.

Pharmacotherapies for IBD include aminosalicylates (or 5-ASAs), steroids, immunosuppressants, and more advanced therapies such as biologics and small molecules. Pharmacological treatment methodology typically involves an induction therapy in order to achieve clinical remission, followed by a maintenance therapy (often at a lower drug dose) to sustain the clinical response and prevent future disease relapse. In some patients with uncontrolled disease, surgery might ultimately be required.

4.1.2.1 Anti-inflammatory agents – first line (mild disease)

The **aminosalicylate** drugs are a class of drug used in the initial management of IBD (mainly UC). Aminosalicylates are compounds that contain 5-aminosalicylic acid (5-ASA) and reduce inflammation in the lining of the intestine. According to the Crohn's & Colitis Foundation, aminosalicylates have been shown to independently induce and maintain remission in mild to moderate IBD.

There are multiple types of aminosalicylates commercially available and differentiated primarily by route of administration and formulation for delivery. Overall, **aminosalicylates are well tolerated and safe**. All 5-ASA agents may cause headache, nausea, abdominal pain and cramping, loss of appetite, vomiting, rash, or fever. In addition, 5-ASA agents may cause diarrhea (less than 1% of users), which may be difficult to distinguish from increased IBD activity. Aminosalicylates very rarely cause kidney injury. However, those with known kidney problems should not use these agents. For those taking 5-ASAs, kidney tests should be routinely performed. While few medications have been thoroughly evaluated in pregnancy, these medications are considered generally safe to use during pregnancy and breastfeeding.

In addition to the aminosalicylates, **steroids** are also prescribed in this disease setting when a patient's response is inadequate to aminosalicylates alone.

4.1.2.2 Immunosuppressants/modulators – second line (moderate disease)

Immunosuppressants (e.g. azathioprine/Imuran®) are used when treatment with steroids and 5-ASA has failed to control the inflammation associated with IBD, or when steroids cannot be stopped without the risk of causing a relapse (remember that long-term steroid use is associated with side effects including higher risk for infections, weight gain, and raised blood sugar levels).
Immunosuppressants are referred to as steroid-sparing agents as their use allows to gradually reduce or even stop taking steroids without worsening the inflammation.

[4] Centers for Disease Control and Prevention

4.1.2.3 Biologics, JAK inhibitors (JAKi) & S1P modulators – last line of therapeutic defense in IBD (severe disease)

Biologics are mechanistically comprised of anti-TNFα, integrin inhibitors and anti-IL-12/24α. While the treatment arsenal has expanded significantly in the last few years, only 40% of patients achieve remission within one year of therapy on biologic agents[5].

Anti-TNF-α (Humira®, Remicade®, Simponi®, & Cimzia®)

Tumor necrosis factor (TNF) is a protein in the body that promotes inflammation. Biologics known as anti-tumor necrosis factor (anti-TNF) agents bind and block a small protein called tumor necrosis factor alpha (TNF-alpha) that promotes inflammation in the intestine as well as other organs and tissues. In healthy individuals, excess TNF in the blood is blocked naturally, but in those who have IBD, higher levels of TNF in the blood lead to more inflammation and persistent symptoms.
All anti-TNF medications have been shown not only to reduce the IBD symptoms, but also result in healing of the inflamed intestine. While anti-TNF medications are not effective for every individual, many patients benefit from this class of medication. It may take up to eight weeks after starting an anti-TNF to notice an improvement in symptoms, though many experience more immediate improvement.
KOLs indicate that 50% of IBD patients do not have a response to anti-TNF therapies or lose response over time. The need for biologics to be administered via injection (intravenous or subcutaneous) represents an additional limiting factor, as the invasive nature of the latter impedes patient comfort and often requires hospital visits.

Integrin inhibitors/blockers/receptor antagonists (Entyvio®)

Integrin inhibitors block the action of integrin on the surface of circulating immune cells and endothelial cell adhesion molecules, thereby inhibiting the interactions between leukocytes and intestinal blood vessels. Leukocytes within the systemic circulation move to sites of inflammation and blocking this pathway could be an important treatment strategy for IBD.

Interleukin-12/23 (IL-12/23α) blockers (Stelara®, Skyrizi®, & Omvoh®)

Interleukin (IL)-12 and IL23 are two key cytokines responsible for promoting and perpetuating bowel inflammation in IBD.
While the benefits often far outweigh the risks of biologic medications in patients suffering from IBD, patients might experience side effects/intolerance, increased risk for infections, liver problems, cancer risk among others.

JAK inhibitors & S1P receptor modulators

Small molecule treatments used for adults with moderate to severe, active IBD who have had an inadequate response, loss of response, or were intolerant to either conventional therapy or a biologic medication.

JAKs (Janus kinases) are intracellular enzymes that transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. JAKi (JAK inhibitors; Rinvoq®, Xeljanz®, & Jyseleca®) are small molecule compounds that can be carried to nearly anywhere in the body through the bloodstream to work directly on the immune system. Unlike immunosuppressants, which are also taken orally but can take several weeks to control inflammation, JAK inhibitors work more quickly to achieve and maintain remission.

The class, however, has become controversial given the increased risk for major adverse cardiovascular events and thrombosis.

S1P modulators (Zeposia®, Velsipity®) bind to two subtypes of receptors, or proteins, called sphingosine 1-phosphate (S1P). S1P receptors are found on the surface membranes of the immune cells, T cells and B cells.

[5] McCormack et al. (2023). Emerging role of dual biologic therapy for the treatment of inflammatory bowel disease. World J Clin Cases. 11(12).

TL1A inhibitors

Another emerging target for inflammatory bowel disease (IBD) is TL1A as illustrated by recent Sanofi-Teva (TEV'574, Oct 2023, USD 500m upfront with USD 1bn biobucks) deal, and Merck-Prometheus Biosciences (PRA-023, June 2023, USD 10.8bn) and Roche-Telavant (RVT-3101, Dec 2023, USD 7.1bn) acquisitions. Recent studies showed that TL1A (Tumor necrosis factor-like cytokine 1A) acts as a regulator of mucosal immunity and participates in immunological pathways involved in the IBD pathogenesis.

Exhibit 9 Currently approved targeted therapies for UC

Brand	Asset	MoA	Company	UC launch in USA	UC peak sales (USD m)	UC FY28 estimate (USD m)	Patent expiration
Biologics							
Humira®	adalimumab	anti-TNFα	AbbVie	2012	1230	N/A	2023
Remicade®	infliximab	anti-TNFα	J&J	2005	N/A	N/A	2013
Simponi®	golimumab	anti-TNFα	J&J	2013	557	N/A	2021
Entyvio®	vedolizumab	anti-α4β7 integrin	Takeda	2014	2408	N/A	2032
Omvoh®	mirikizumab	anti -IL23α	Eli Lilly	2023	N/A	671	2031
Stelara®	ustekinumab	anti-IL12/23α	J&J	2019	2413	N/A	2023
Small molecules							
Rinvoq®	upadacitinib	JAK1i	AbbVie	2022	N/A	1582	2033
Xeljanz®	tofacitinib	JAK1/2/3i	Pfizer	2019	280	N/A	2025
Jyseleca®	filgotinib	JAK1i	Alfasigma	N/A	N/A	N/A	2030
Zeposia®	ozanimod	S1P1/5i	BMS	2021	N/A	936	2029
Velsipity®	etrasimod arginine	S1P1/5i	Pfizer	2023	N/A	803	2030

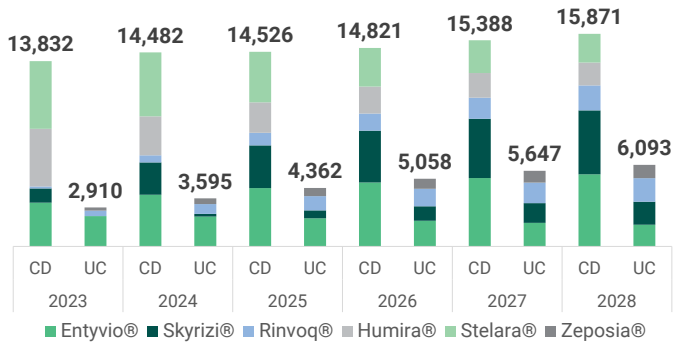
Source: Evaluate Pharma
Evaluate Pharma only indicates sales estimates until 2028.
No UC estimates could be retrieved for Remicade®.
MoA: mechanism of action

Exhibit 10 Currently approved targeted therapies for CD

Brand	Asset	MoA	Company	CD launch in USA	CD peak sales (USD m)	CD FY28 estimate (USD m)	Patent expiration
Biologics							
Humira®	adalimumab	anti-TNFα	AbbVie	2007	6306	N/A	2023
Remicade®	infliximab	anti-TNFα	J&J	1998	3496	N/A	2013
Entyvio®	vedolizumab	anti-α4β7 integrin	Takeda	2014	N/A	5385	2032
Stelara®	ustekinumab	anti-IL12/23α	J&J	2016	5051	N/A	2023
Skyrizi®	risankizumab	anti-IL23	AbbVie	2022	N/A	4775	2031
Small molecules							
Rinvoq®	upadacitinib	JAK1i	AbbVie	2023	N/A	1865	2033

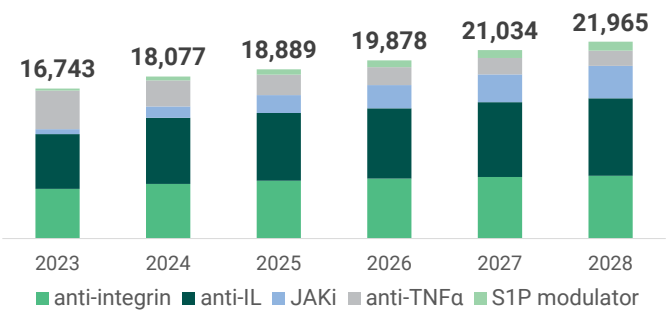
Source: Evaluate Pharma
Evaluate Pharma only indicates sales estimates until 2028.
MoA: mechanism of action

Exhibit 11 Total world-wide market value of top 10 IBD drugs 2023-2028 (USD m)



Source: Evaluate Pharma

Exhibit 12 Total world-wide market value of top 10 IBD drugs 2023-2028 by drug class (USD m)



Source: Evaluate Pharma

Exhibit 11 and Exhibit 12 provide an overview of the total world-wide market value of the top 10 IBD drugs, based on annual sales in the period 2023-2028. While Stelara® and Humira® currently dominate the CD market, Entyvio® and Skyrizi® are expected to outperform said drugs by 2028. For UC, on the other hand, Entyvio® and Stelara® generate most sales. Drugs with relatively novel mechanisms of action, including Skyrizi® (currently awaiting approval for UC), Rinvoq®, Velsipity® and Zeposia®, are expected to gain significant market share in the years to come mostly as a results of patent expirations.

4.1.2.4 Combination therapies

As described above, significant advancements in the medical management of IBD have been seen and aided by novel small molecule and biologic drugs, but **observed clinical response with monotherapy often still remains limited and sub-optimal**. Treatment strategies for IBD are therefore rapidly changing to help combat ongoing disease burden and morbidity. At present, clinician experience has guided potential novel therapy combinations with dual biologic therapy (DBT) presenting an attractive and potentially safe option for those who have failed previous biologic therapies and have refractory disease. Although current data is encouraging in terms of the use of DBT, it is still unclear which combination works best; many favour the use of an anti-TNF plus an immunomodulator such as vedolizumab (Entyvio®) or ustekinumab (Stelara®) but anti-TNF is not always an option, especially for patients in which this is contra-indicated or not tolerated. At present, one of the main limitations when evaluating the safety and efficacy of the use of DBT is the lack of further randomised controlled trials. Thus, short- and long-term safety profiles of biologic combinations in IBD is yet to be investigated in detail.

JAKi can also be used as part of a combination therapy for IBD. Unlike biologics, which are given intravenously and can have a slow onset of action, JAKi can be administered orally, with a rapid onset of action, short half-life and do not trigger an immune response. JAKi should, however, be used with caution, as they have been associated with an increased risk of developing Herpes zoster infection, thus highlighting the need to consider vaccination in high-risk patients. Additionally, JAKi are thought to also increase the risk of cardiac event, malignancy, venous thromboembolism and gastrointestinal perforation.

Summarized, while the IBD space is crowded, a significant number of patients remains inadequately controlled with existing medication ultimately leading to invasive surgery (see next section). We therefore see room for new differentiated IBD treatments in both mono and combo therapy and consider a small molecule immunomodulator, allowing for convenient oral administration while preserving the immune system's ability to fight infections, to be ideally positioned.

Prof. L. Peyrin-Biroulet (Professor of gastroenterology at Nancy University Hospital specialized and recognized as an IBD KOL):
"*IBD are rapidly increasing with millions of patients affected worldwide. These incurable and chronic disabling conditions have a major impact on their personal and professional daily life. Over the past 2 decades, new treatments, such as biologics, have emerged and clearly improved the quality of life of IBD patients. However, we are seeing a ceiling effect of efficacy with available therapeutic strategies, only 1 patient out of 5 achieving deep remission. Precision medicine treatment is a way to break this therapeutic ceiling. The IBD world is very active and I'm confident that we can succeed since innovation is a key aspect of today's research to fill the huge unmet need we're facing in the field of IBD.*
The NOD2 / RIPK2 pathway has the potential to bring real innovation to this field, and OPM-101 from OPM seems to have the right profile as a potent and safe small molecule to explore this potential. OPM-101 could be used as a standalone therapy or in combination. We very much look forward to exploring this asset in more details to ultimately bring benefit to our patients."

4.1.2.5 Surgery

Between 15-30% of patients ultimately require surgery (colectomy), most often as a consequence of a poor response to long-term medical treatment with biologics and small molecules. KOLs highlighted that this procedure also holds several risks, including post-surgical inflammation risk.

4.2 Immune checkpoint inhibitor-associated colitis[6,7,8]

4.2.1 Pathogenesis

Immune checkpoint inhibitors (ICIs) are highly effective immunotherapeutics that have transformed treatment paradigms for several cancers. Immunotherapy aims to boost natural defenses to eradicate malignant cells. Indeed, the adaptive and natural immune systems play an essential role in the surveillance and suppression of tumors. However, cancer cells and their microenvironment can evade the immune system by inducing a hypofunctional state of the immune cells, especially of the T cells, and promoting the survival of the tumor itself. One established mechanism is represented by cancer cells' activation of the immune checkpoints, proteins that usually down-regulate and limit the immune response, by maintaining the inactivated T cells, thus escaping immune surveillance.

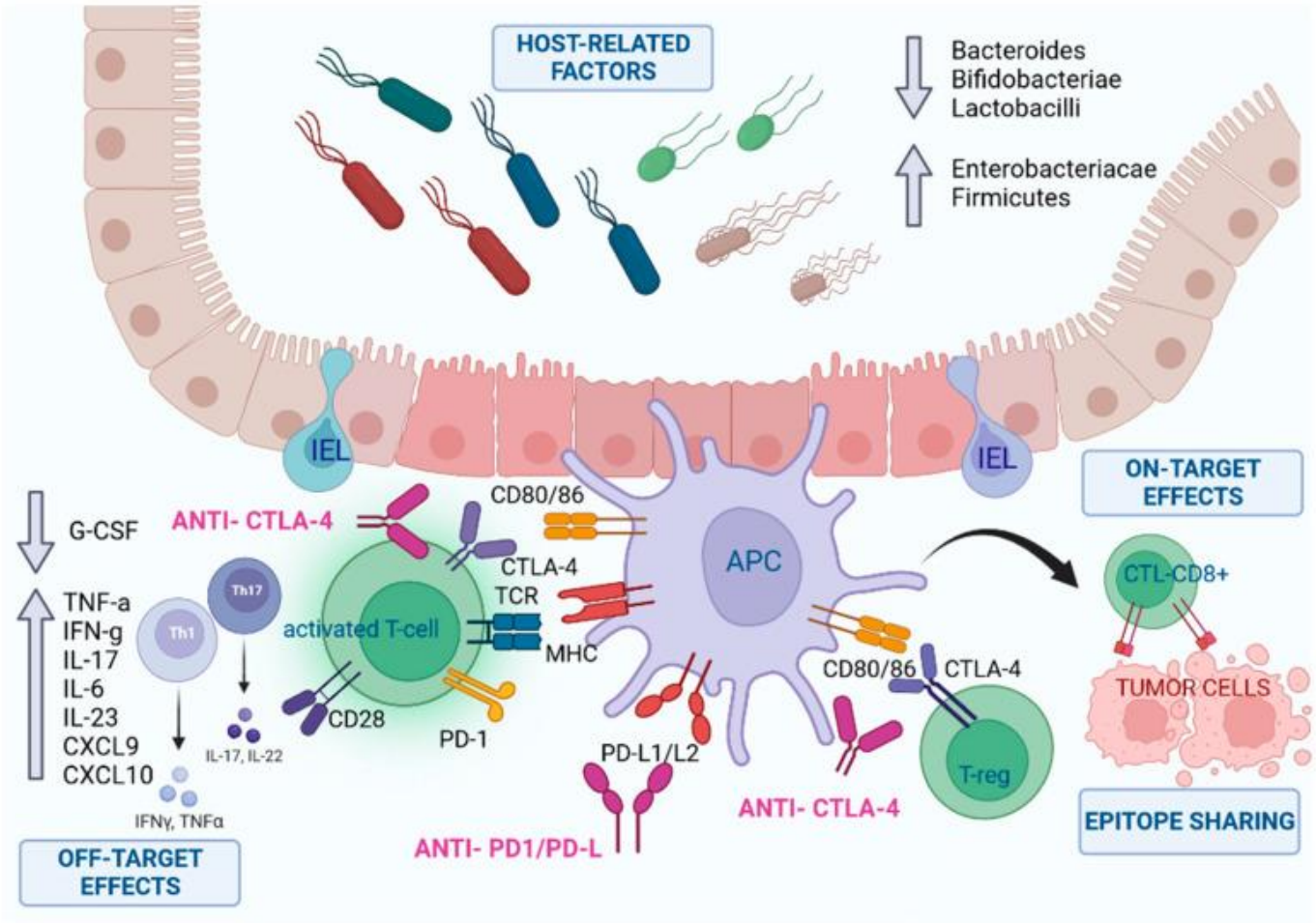
ICIs represent one of the most important categories of immunotherapy and are composed of monoclonal antibodies that aim to strengthen and reinvigorate the immune system by binding to these co-inhibitory receptors[9], inducing immune-mediated tumoral cell death. Since their first approval in 2011, they have shown promising results and have been approved by the FDA and EMA for the treatment of different neoplasms, such as melanoma, non-small cell lung carcinoma, breast cancer, gastrointestinal cancers among others.

Unfortunately, ICIs, especially in combination, can also trigger off-target immune activation in non-cancer tissues as CTLA-4 and PD-1 blockade removes autoimmunity-protection mediated by said checkpoints[9]. More specifically, CTLA and PD-1/PD-L1 inhibitors could strengthen the activation and proliferation of effector T cells, abrogate regulatory T cell function, induce inflammatory cytokines, probably boost humoral autoimmunity. This causes a range of autoimmunity-related adverse effects in multiple organs resulting in significant morbidity and mortality (see also 4.2.2).

The pathogenesis of ICI-AC has, in fact, not been fully unravelled yet and additional molecular phenomena are expected to be involved (Exhibit 13). For example, in addition to their effect on T cells, ICIs also modulate the microbiota–intestinal barrier equilibrium by inducing apoptosis of intestinal epithelial cells[10]. This results in barrier perturbation and alterations of intestinal flora [11]. Higher proportions of Enterobacteriaceae and Firmicutes have been found to be associated with ICI-AC, while higher proportions of Bacteroides, Bifidobacteriae, and Lactobacilli seem to be protective.

[6] Lo et al (2023). Immune checkpoint inhibitor-induced colitis is mediated by polyfunctional lymphocytes and is dependent on an IL23/IFNγ axis. Nature Communications 14 (6719).
[7] Terrin et al. (2023). Checkpoint Inhibitor-Induced Colitis: From Pathogenesis to Management. Int J Mol Sci. 2023 Jul; 24(14): 11504.
[8] Tang et al. (2023). Immune Checkpoint Inhibitor-Associated Colitis: From Mechanism to Management. Front. Immunol.12.
[9] PD-1 and PD-L1 are co-inhibitory proteins expressed by lymphocytes and antigen-presenting cells that induce self-tolerance and autoimmunity control, while CTLA-4 is expressed on T and B cells and functions to negatively regulate lymphocyte activation.
[10] The normal intestinal epithelial barrier is a highly organized mucosal surface that prevents microbiota from entering into the lamina propria. The epithelium is composed of a single layer of intestinal epithelial cells (IECs) covered by a mucus layer. Segmented filamentous bacteria seldom breach the barrier of mucus and contact with the IECs.
[11] The species and relative abundance of gut microbiota play an important role in the homeostasis and maintenance of the integrity of the gut epithelial barrier.

Exhibit 13 Pathogenesis of ICI-AC: complex and not yet fully unraveled



Source: Terrin et al. (2023).
APC—antigen presenting cell; IEL—intraepithelial lymphocyte; T-reg—T regulatory cell; Th—T helper cell.

4.2.2 Epidemiology

Autoimmunity-related adverse events have a wide variability of organ involvement, time of onset and association with the type of tumor and ICI. **Diarrhoea and colitis (ICI-AC) are arguably the most important adverse events and the most common cause of serious, life-threatening complications, treatment interruption and permanent discontinuation of ICI therapy.** The incidence of ICI-AC, which could occur at any time after the commencement of ICIs, depends on the type of ICI and also whether they are used in combination (Exhibit 14). So far, no study reported a statistically significant correlation between sex, tumor type and the severity of immune-mediated colitis.

Exhibit 14 Percentage ranges of all grade diarrhea & colitis events by ICI class

ICI class	Approved agents	Diarrhea (%)	Colitis (%)
Anti CTLA-4	ipilimumab, tremelimumab	31-49	7-11.6
Anti PD-1	nivolumab, pembrolizumab, dostarlimab, cemiplimab, retifanlimab, toripalimab	2.9-11.5	1.3-2.9
Anti PD-L1	atezolizumab, durvalumab, avelumab	11.6-23	0.7-19.7

Source: Som et al. (2019)

4.2.3 ICI-AC and IBD: similarities and differences in pathogenesis

Beyond the similar clinical and endoscopic manifestations, ICI-AC and IBD share some pathogenetic aspects. Both diseases exhibit upregulation of regulatory cytokines (such as IL-10, INF-γ and IL-17) at the mucosa level.

Furthermore, CTLA-4, PD-1/PD-L1 and the gut microbiome also display a key role in the intestinal immunity of both IBD and ICI-AC. Indeed, in a mouse model of IBD, PD-1 protein administration was shown to be protective against colitis. In humans affected by CD, intestinal APCs do not express PD-L1. On the other hand, some CTLA-4 polymorphisms are known to increase the susceptibility of developing both CD and UC.

A significant difference in the composition of the inflammatory infiltrate between IBD and ICI-AC involves CD20+ cells (B cells), which are common in IBD but not in ICI-AC.

A reduction in microbial diversity is typical of IBD patients compared to healthy individuals and, in particular, a significantly lower proportion of *Bacteroides* and higher proportion of *Proteobacteria phyla* are reported. As described above, higher proportions of *Enterobacteriaceae* and *Firmicutes* are associated with ICI-AC, while higher proportions of *Bacteroides*, *Bifidobacteriae* and *Lactobacil*li seem to be protective.

4.2.4 Unmet need for a safe, efficacious, and convenient treatment option permitting continued use of ICIs

ICI-AC is treated with high-dose steroids, often for prolonged periods. Unfortunately, 40% of patients fail to respond to steroids and others develop severe complications of immunosuppression, including life-threatening infection. There are important concerns that immunosuppression might impede the anti-cancer responses of ICI therapy. Two independent studies in different tumour settings, identified impaired survival in steroid exposed patients. Treatment outcomes with biological therapies, such as anti-TNF monoclonal antibodies are also heterogeneous, especially if robust outcome measures are used. Not only do many patients fail to achieve steroid-free remission, side effects, such as severe infections, frequently complicate treatment (Exhibit 15). It is therefore clear that there is a need for new safe and efficacious drug interventions to treat, but ideally also prevent, ICI-AC, allowing continued use of ICIs. Therefore, **it makes strategic sense to explore the potential of OPM-101 for this indication, keeping in mind its oral administration route and immunomodulating action (rather than immunosuppressive which suppresses the immune response)**.

Prof. O. Michielin (Head of precision oncology department and the Head of oncology department at the University hospital in Geneva (Switzerland)):

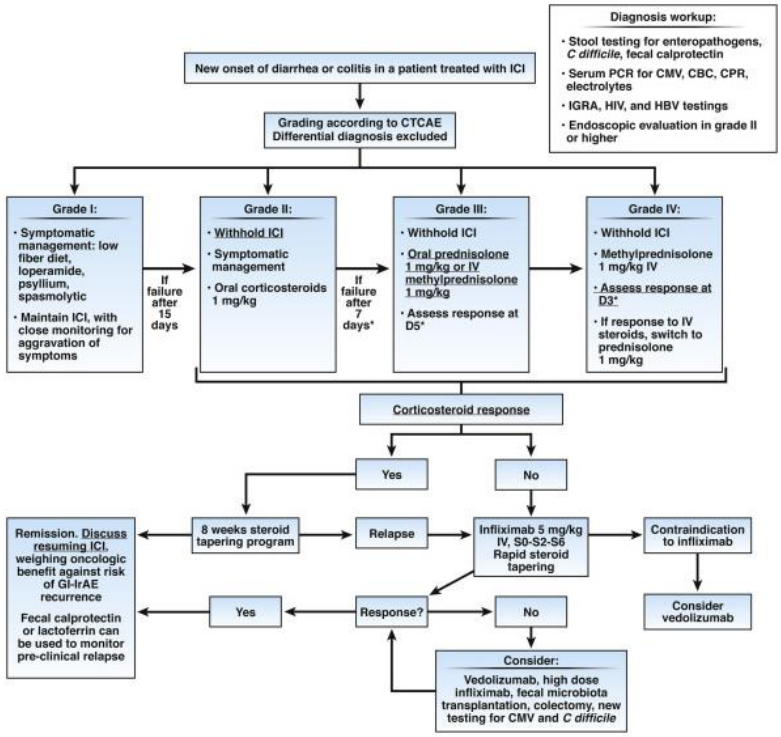
"*Immune checkpoint inhibitors-induced colitis are one of the most frequent adverse events observed with these very effective and important oncology treatments. However, today, there is a need for a new treatment approach which could prevent physicians from using the immunosuppresive drugs, such as corticosteroids, that are antagonist to the beneficial effect expected with immune checkpoint inhibitors. OPM-101, an inhibitor of the RIPK2 pathway, is a promising candidate for becoming this new drug as it has shown immunomodulatory properties. This new product represents a great hope for patients*".

So far, the space has gained little attention with only a few industry-sponsored clinical trials conducted so far. We consider this a direct consequence of our still relatively limited knowledge of the immunopathogenesis of ICI-induced colitis as ICIs are a relatively novel class of therapeutic agents for cancers as described above.

- Last year, Janssen completed the observational TENOR study[12] with ustekinumab for ICI-AC. 19 patients were treated with ustekinumab for ICI-AC refractory to steroids plus infliximab and/or vedolizumab. Most of them had grade ≥3 diarrhea (84.2%), and colitis with ulceration was present in 42.1%. 13 patients (68.4%) attained clinical remission with ustekinumab and mean fecal calprotectin levels dropped significantly after treatment (629 ± 101.5 mcg/mg to 92.0 ± 21.7 mcg/mg, P = 0.0004)[13].
- USA-based First Wave Biosciences, on the other hand, announced an agreement with AzurRx Biopharma in 2021 for its niclosamide formulations to treat ICI-AC (and COVID-19 gastrointestinal infections). AzurRx was granted a worldwide, exclusive right to develop, manufacture, and commercialize First Wave's proprietary immediate release oral and enema formulations of niclosamide for the treatment of ICI-AC and COVID-19 GI infections. The agreement consisted of an upfront payment of USD 10.3m, USD 10.3m in additional payments, and USD 3m of convertible junior preferred stock + up to USD 74m in potential development and commercial milestones, as well as mid-single digit royalties on product sales for the ICI-AC and COVID-19 GI indications. Since then, the companies announced FDA clearance of their IND application for the Ph2a PASSPORT trial investigating FW-ICI-AC as a treatment for Grade 1 and Grade 2 colitis and diarrhea in oncology patients receiving treatment with ICIs. FW-ICI-AC is a proprietary oral immediate-release tablet formulation of niclosamide.

  Value Vision estimates that the ICI-AC market will grow to USD 4.4bn by 2030 with the majority of sales stemming from use in the treatment setting (EUR 4.1bn).

Exhibit 15 Algorithm of diagnosis workup and treatment ICI-induced diarrhea and colitis



Source: Collins et al. (2020)

[12] NCT03606499
[13] Thomas et al. (2023). IL12/23 Blockade for Refractory Immune-Mediated Colitis: 2-Center Experience. Am J Gastroenterol 118(9).

4.3 OPM-101: a potential first-in-class oral immunomodulator for ICI-AC and IBD

4.3.1 Scientific rationale for targeting RIPK2[14]

4.3.1.1 RIPK2 activation crucial in the innate immune system but at the origin of autoimmune and inflammatory diseases when dysregulated

Receptor-interacting serine/threonine kinase 2 (RIPK2), also known as receptor-interacting protein 2 (RIP2), is a downstream signaling molecule for nucleotide-binding oligomerization domain 1 (NOD1) and NOD2. RIPK2 is expressed in the cytoplasm of antigen-presenting cells (APCs), such as dendritic cells (DCs) and macrophages, and is also expressed in T cells. In addition to hematopoietic cells, epithelial cells also express functional RIPK2. Thus, innate immune cells, including APCs, and epithelial cells express functional RIPK2.

Recognition of microbe-associated molecular patterns by NOD1 and NOD2 leads to the interaction between RIPK2 and these innate immune receptors, followed by the release of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-12/23p40 through the activation of nuclear factor kappa B (NF-κB) and mitogen-activated protein kinases (MAPK). **Thus, activation of RIPK2 plays a critical role in host defense against microbial infections**.

Recent experimental and clinical studies have provided evidence that activation of RIPK2 is involved in the development of autoimmune diseases, especially IBDs (see also further down). Indeed, the colonic mucosa of patients with IBD exhibits enhanced expression of RIPK2 and associated signaling molecules. Furthermore, the blockage of RIPK2 activation ameliorates the development of experimental murine colitis. Thus, **excessive activation of RIPK2 seems to underly IBD immunopathogenesis**.

RIPK2 serves as a central protein hub in NOD-mediated cytokine signaling[15]

RIPK2 is an obligate signaling molecule downstream of NOD1 and NOD2. It is composed of a kinase domain (KD), an intermediate domain (INTD), and a caspase activation and recruitment domain (CARD). NOD1 and NOD2 bind to the CARD of RIPK2 through a CARD–CARD interaction. The interaction between ATG16L1 and RIPK2 is mediated by the KD whereas interferon regulatory factor 4 (IRF4) binds to the KD and INTD of RIPK2. As such, RIPK2 serves as a scaffolding protein and each domain of RIPK2 plays an indispensable role in protein–protein interactions (Exhibit 16).

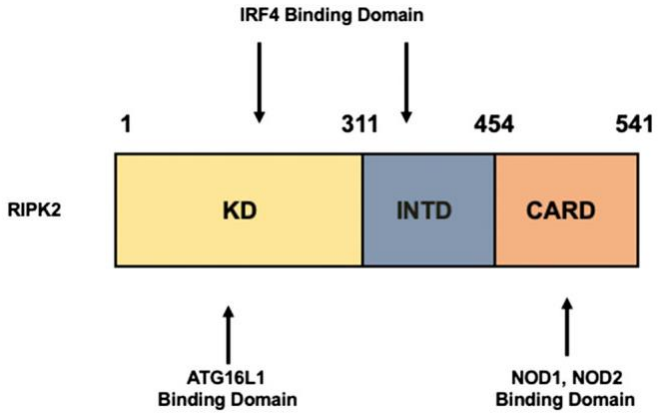
RIPK2 is controlled by complex posttranslational modification events, including autophosphorylation at several sites. Best described are the phosphorylation events at S176 and Y474, which are associated with activity and structural changes. The role and outcome of these phosphorylation events is not entirely understood. On the one hand, it was shown that kinase activity of RIPK2 is dispensable for signaling and might only affect protein stability. On the other hand, in addition to resulting in protein instability, inhibition of kinase activity by the tyrosine kinase inhibitors gefitinib and erlotinib or the RIPK2-specific compounds WEHI-345 and GSK583 was shown to reduce signaling (see also below). Some insight into this controversy was provided by the identification that **RIPK2 inhibitors can also block interaction of RIPK2 with the E3 ubiquitin ligase X-linked inhibitor of apoptosis (XIAP), essential for RIPK2-mediated NF-κB activation.**

XIAP is the essential E3 for RIPK2 ubiquitination and interacts with RIPK2 through its baculoviral IAP-repeat (BIR) 2 domain. XIAP also ubiquitinates K410 and K538 with K63-linked ubiquitin, which was shown to be important for NOD2 signaling.

[14] Honjo et al. (2021). RIPK2 as a New Therapeutic Target in Inflammatory Bowel Diseases. Front Pharmacol.; 12: 650403.
[15] Ellwanger et al. (2019). XIAP controls RIPK2 signaling by preventing its deposition in speck-like structures. Life Sci Alliance. 2(4).

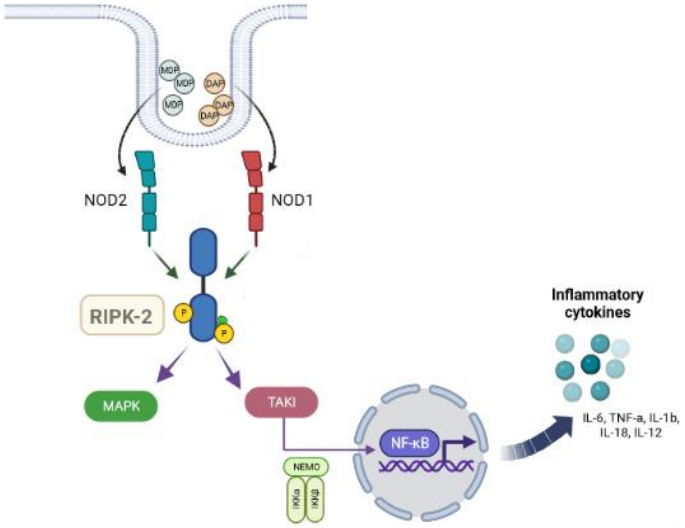
XIAP binding to RIPK2 recruits the linear ubiquitin chain assembly complex (LUBAC)[16]. Ubiquitination of RIPK2 leads to recruitment of the transforming growth factor β-activated kinase 1 (TAK1). This ultimately triggers the activation of the IκB kinase complex (the signal integration hub for NF-κB activation), leading to cytokine production, and MAPK signaling (Exhibit 17).

Exhibit 16 RIPK2 structure



Source: Honjo et al. (2021)

Exhibit 17 Signaling pathways mediated by RIPK2



Source: OPM
RIPK2 is a signaling molecule downstream of NOD1 and NOD2. Activation of RIPK2 results in a robust production of pro-inflammatory cytokines, including TNF-α and ILs, through the nuclear translocation of nuclear factor-κB (NF-κB) subunits.

RIPK2's pathogenic role in IBDs[17]

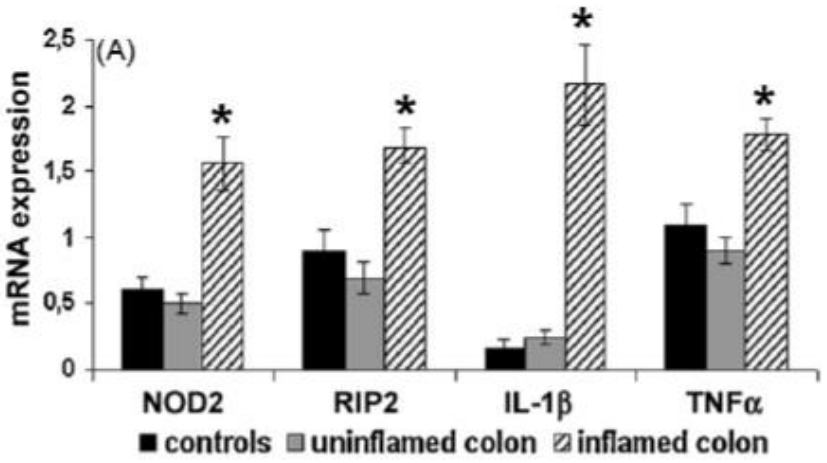
While loss-of-function, defective NOD2 signaling is associated with the development of CD, patients who have "normal" NOD2 generally show too much activity and elevated pro-inflammatory cytokine production in response to NOD2 activation. This NOD2-driven cytokine production is dependent on the protein kinase, RIPK2, as cells without RIPK2 do not respond to NOD2-activating signals.

The clinical relevance of RIPK2 activation in the generation of colitogenic cytokine responses was examined by using colonic biopsy samples obtained from CD and UC patients during colonoscopy:

- As determined by qPCR, expression of RIPK2 and RIPK2-related signaling molecules such as cIAP1, cIAP2, TRAF6, and TAK1 was much higher in colonic lesions of patients with CD and UC than in normal colonic mucosa. Both NOD2 and RIPK2 expression positively correlated with that of pro-inflammatory cytokines in the colonic mucosa of patients with CD and UC.

[16] E3 ubiquitin ligases cIAP1 & cIAP2, TRAF2 & TRAF5, and ITCH were shown to participate in RIPK2 ubiquitination but their physiological roles remain to be clarified.
[17] Lai et al. (2023). Discovery of a novel RIPK2 inhibitor for the treatment of inflammatory bowel disease. Biochemical Pharmacology 214.

Exhibit 18 Increased expression of NOD2/RIPK2 in colon biopsies from IBD patients



Source: GSK

- Consistent with qPCR data, immunofluorescence studies showed that colonic dendritic cells expressing RIPK2 and cIAP2 produce TNF-α. Moreover, the intensity of the molecular interaction between cIAP2 and RIPK2 and between RIPK2 and TAK1 is positively correlated with expression levels of IL-6 and TNF-α in the inflamed colonic mucosa of patients with CD and UC.

Taken together, these studies utilizing human IBD samples fully support the view that activation of RIPK2 plays a pathogenic role in the development of human IBD by promoting the production of pro-inflammatory cytokines. This observation sparked interest around RIPK2 as a target for pharmacological intervention and **numerous studies have now shown that inactivating RIPK2, either pharmacologically or genetically, limits both NOD1 and NOD2 signaling pathways.**

Excitement also centers on the fact that RIPK2 inhibition is distinct from pathways already targeted in inflammatory disease such as TNF or JAK/STAT. Thus, **RIPK2 inhibition may have efficacy either alone or in combination with existing inflammatory disease treatments.**

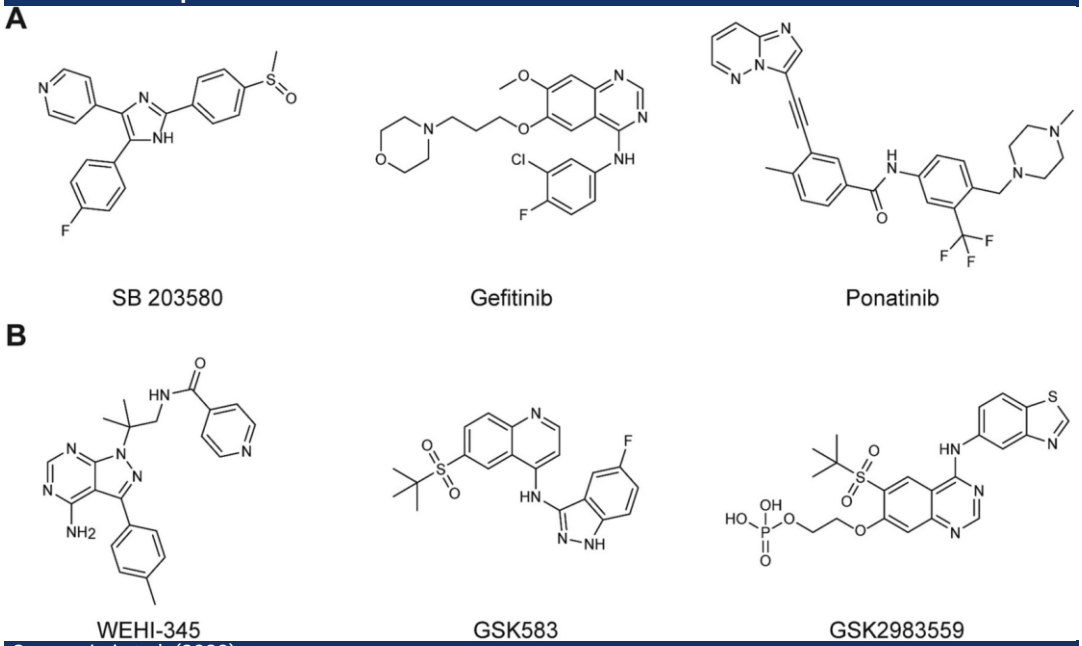
Current RIPK2 inhibitor landscape

A number of RIPK2 inhibitors have been developed so far:

- The p38 MAPK inhibitor SB 203580, the EGFR tyrosine kinase inhibitor gefitinib and the type II inhibitor ponatinib were identified to show inhibitory activities against RIPK2. These inhibitors, however, might not be suitable for further application due to their pan-inhibitions (Exhibit 19, A).
- Selective RIPK2 inhibitors including WEHI-345 and GSK583 exhibit great activities and better specificity to RIPK2, but they have not yet entered the clinic. The optimization of GSK583 resulted in the non-prodrug parent compound 5, which showed increased inhibition activity against the release of inflammatory cytokines in human whole blood, while significantly reducing activity against hERG. However, the parent compound 5 has poor solubility, leading to the development of a prodrug GSK2983559 with increased solubility (Exhibit 19, B).

- GSK2983559 was the first RIPK2 inhibitor that advanced into Ph1 clinical trial for the treatment of IBD. Unfortunately, the trial was terminated due to non-clinical toxicology findings and reduced safety margins[18], which are indicative of toxicity related to the compound. A relatively recent paper described the discovery of a new RIPK2 inhibitor 'Zharp2-1', which exhibited 1/ superior solubility vs. GSK2983559, 2/ excellent *in vivo* pharmacokinetic profiles, and 3/ superior inhibition of MDP-induced production of pro-inflammatory cytokines.
- OPM's 'OPM-101', in fact, is a type 1 kinase inhibitor. The kinase function as such seems not important, RIPK2 is a scaffolding protein, leading to complexation upon activation with the BIR domain of XIAP and generating a protein complex called the riposome (similar to inflammazome) that start the cascade. OPM-101 is thus a scaffolding inhibitor that stops the cascade, probably by generating a RIPK2 conformation that stops the activation. We are generating further data on this.
- **Apart from OPM-101, the only other RIPK2 inhibitor currently in clinical development is Boehringer Ingelheim's 'BI 706321', which is in a Ph2a for CD with readout expected mid-2024[19] (Exhibit 20, top)**.

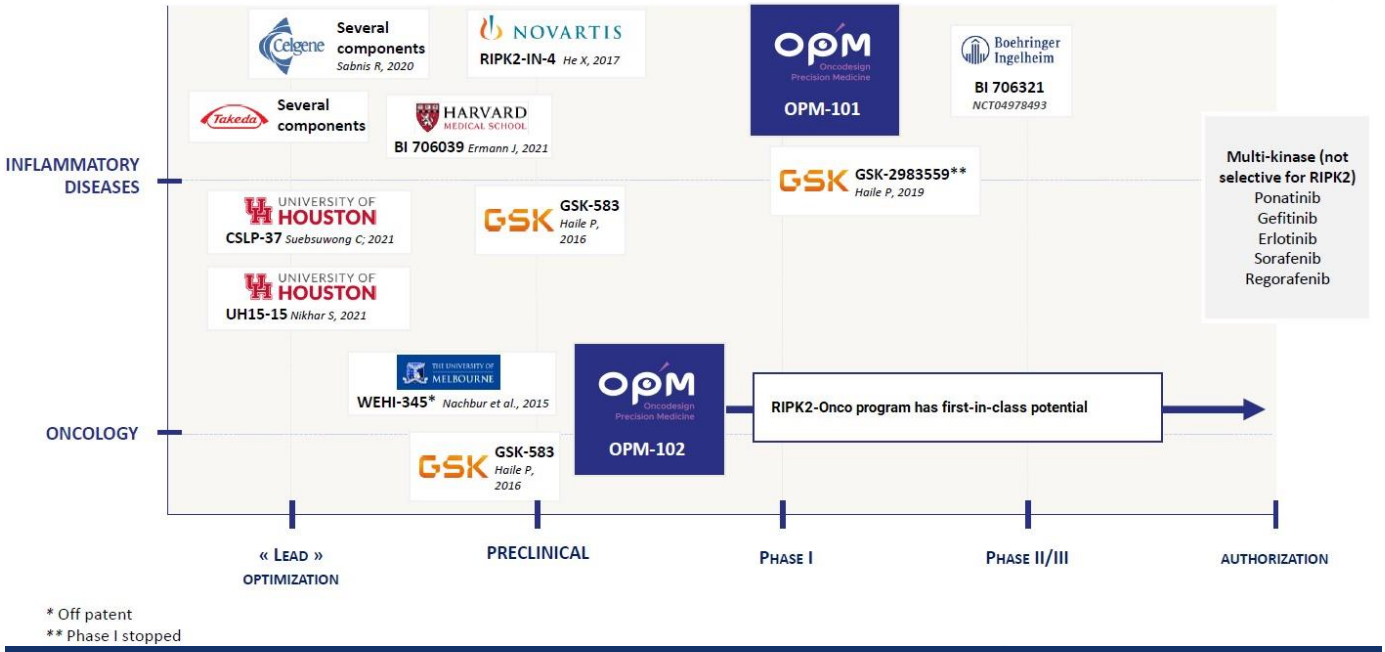
Exhibit 19 Reported RIPK2 inhibitors



Source: Lai et al. (2023).
(A) Chemical structure of non-selective RIPK2 inhibitors. (B) Chemical structure of selective RIPK2 inhibitors.

[18] ClinicalTrials.gov identifier NCT03358407
[19] ClinicalTrials.gov identifier NCT04978493

Exhibit 20 RIPK2 competitive environment: OPM either runner-up (OPM-101 for inflammatory diseases) or first-in-class (OPM-102 for oncology)



* Off patent
** Phase I stopped

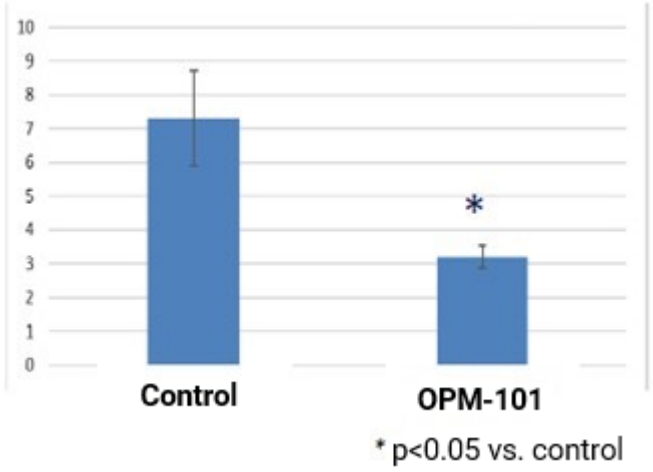
Source: OPM

4.3.2 Data & development status

4.3.2.1 Preclinical data

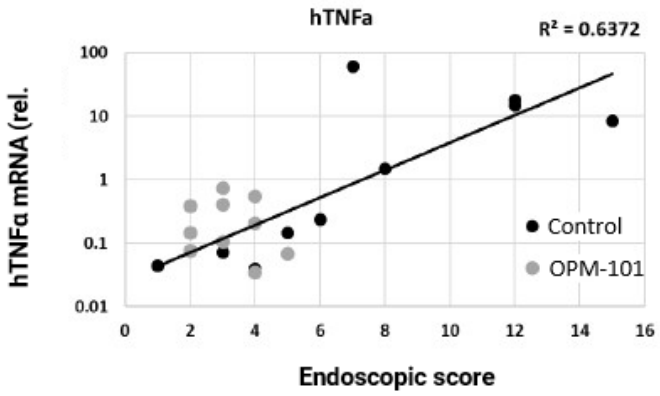
Based on the strong scientific rationale to target RIPK2, OPM conducted a variety of preclinical experiments to validate their proprietary RIPK2 inhibitor. As shown below, OPM-101 (100 mg/kg (2x/d)) significantly reduced the endoscopic score in an acute mouse model[20], developed by Transcure (France), thereby establishing preclinical proof-of-concept.

Exhibit 21 Endoscopic score on Day 12



Source: OPM

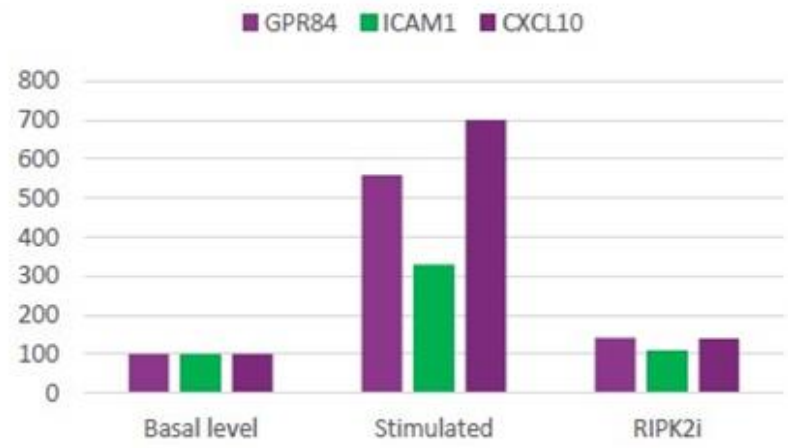
Exhibit 22 OPM-101 protects the colon from inflammation by preventing local production of hTNFα, which correlated with reduced endoscopic score



Source: OPM

Moreover, *in vitro* inhibition of RIPK2 by OPM-101 lowered levels of proteins which are commonly found mutated in IBD patients (Exhibit 23).

Exhibit 23 Modulation of innate immunity via inhibition of the NOD2-RIPK2 pathway

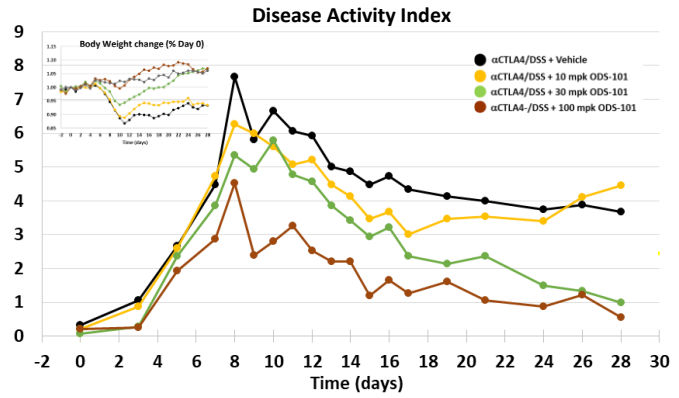


Source: OPM

[20] Humanized mouse model of DSS-induced acute colitis and sensitive to adalimumab (Humira®). Administration of DSS in mice causes human ulcerative colitis-like pathologies due to its toxicity to colonic epithelial cells, which results in compromised mucosal barrier function.

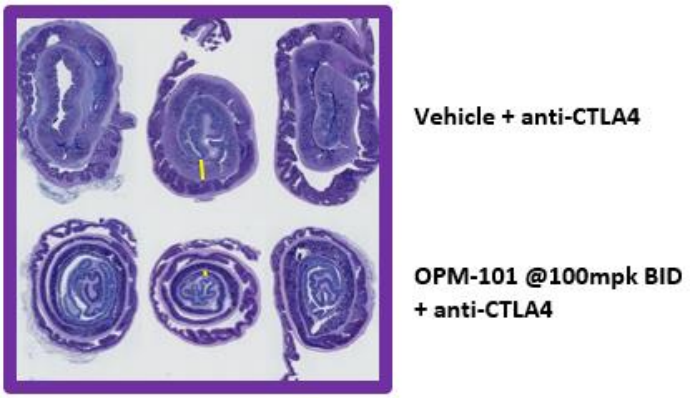
Also, using a DSS+CTLA4-induced colitis mouse model (displays a more severe form of the disease), OPM-101 was shown to protect from acute and chronic colitis and increased recovery rate and mice body weight (Exhibit 24), protects the colon from inflammation-driven epithelial thickening (Exhibit 25), and reduces TNFα and IL-1β expression (Exhibit 26). Hence, this preclinical works provides a great foundation to advance the asset in clinical development for ICI-AC.

Exhibit 24 OPM-101 protects from acute and chronic colitis



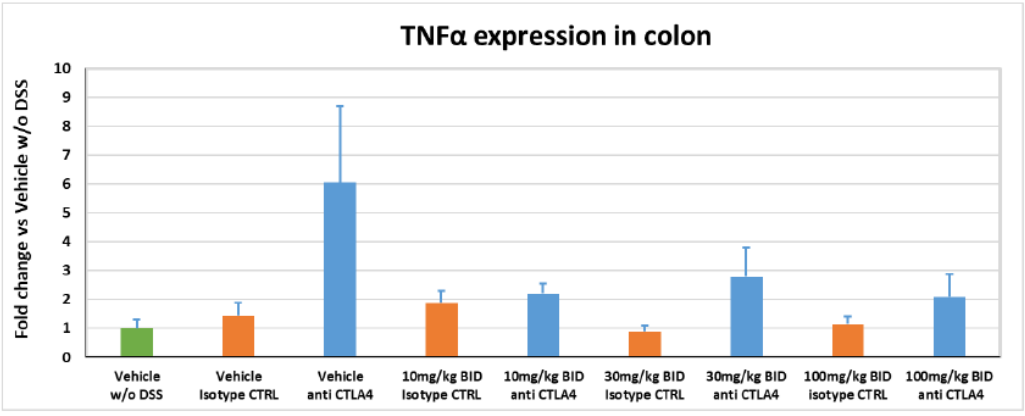
Source: OPM
ODS-101=OPM-101

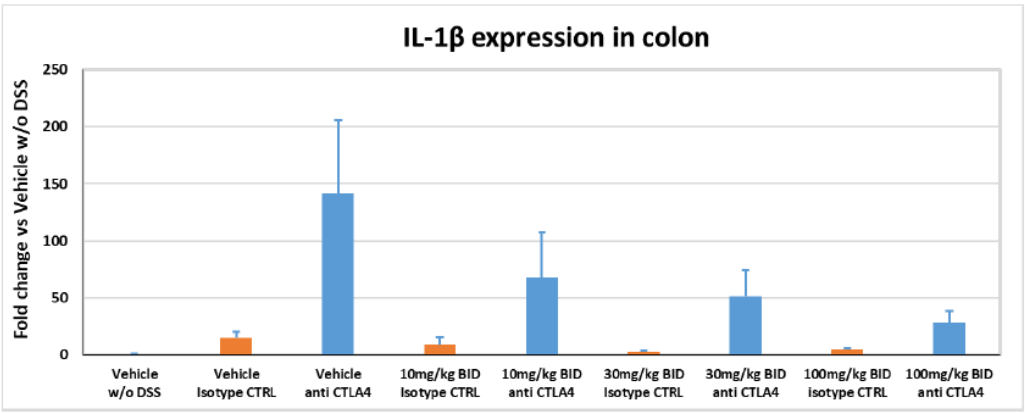
Exhibit 25 OPM-101 protects the colon from inflammation-driven epithelial thickening



Source: OPM
BID: twice daily

Exhibit 26 OPM-101 reduces TNFα and IL-1β expression in a DSS+CTLA4-induced colitis mouse model



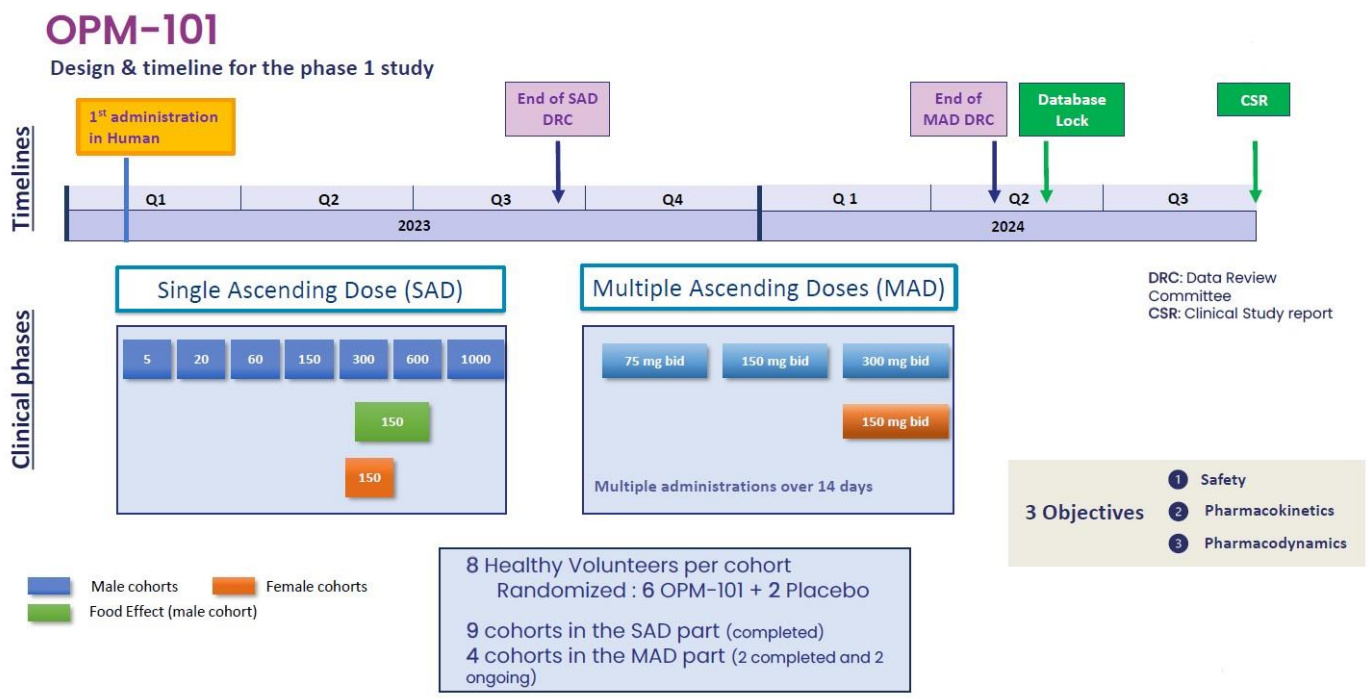


Source: OPM

4.3.2.2 Ph1 study in healthy volunteers currently ongoing

Following these promising preclinical data, OPM launched a Ph1 study in healthy volunteers in 2023 with topline results expected around June/July 2024. This first-in-human study is a randomized, double-blind, placebo-controlled study, consisting of a single and multiple ascending dose phase, to study the safety, tolerability, pharmacokinetic and pharmacodynamic profile of OPM-101 (Exhibit 27). This Ph1 also includes a study of the food effect and a study of the gender effect in order to best prepare the future clinical development of the molecule.

Exhibit 27 OPM-101 Ph1 in healthy volunteers: design



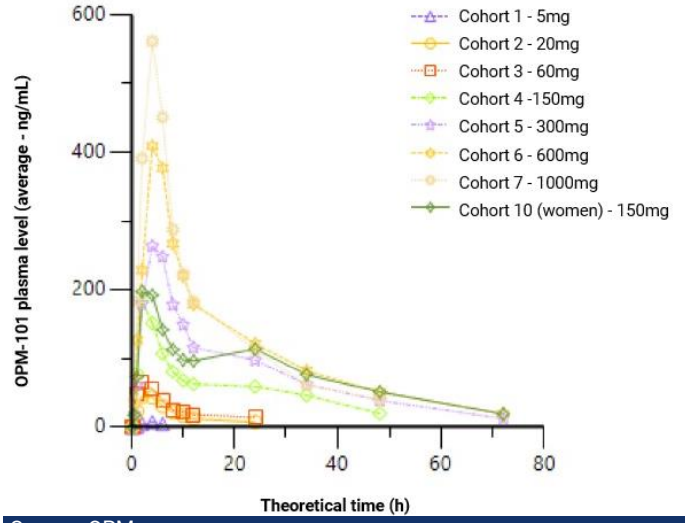
Source: OPM

In October 2023, OPM announced positive interim results at the end of the first part of the Ph1 SAD study. This first part of the Ph1 trial was completed in 7 months. 72 healthy volunteers were randomized in 9 cohorts and OPM-101 was evaluated against placebo using single oral administration at escalating doses.

This study demonstrated that:

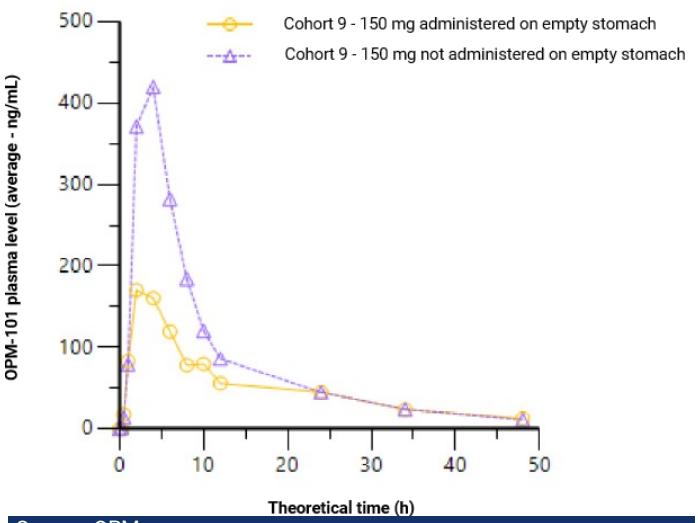
- OPM-101 is rapidly absorbed orally, with an **estimated half-life elimination of 12 to 15 hours (Exhibit 28, rapid clearance is an attractive feature in light of combo therapy with biologics), enabling once-daily administration with target engagement above 80%** (Exhibit 31).
- Taking a fat-rich breakfast increased peak concentrations (Cmax) and total exposure (AUC_{0-t}) to the product (Exhibit 29). Administering OPM-101 after breakfast therefore offers the possibility of administrating lower doses to achieve equivalent levels of target inhibition.

Exhibit 28 Ph1 SAD: OPM-101 plasma kinetics



Source: OPM

Exhibit 29 Ph1 SAD: Food effect



Source: OPM

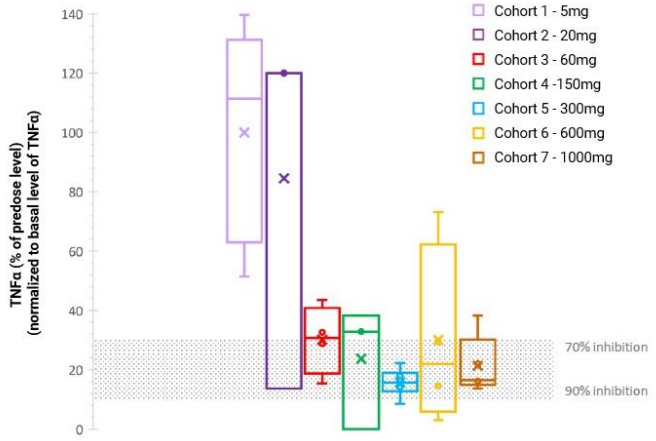
- **OPM-101 had a significant safety range, as doses tested varied from 5 to 1000 mg, and the maximum tolerated dose was not reached** (Exhibit 30).
- **No serious or severe adverse events or dose-limiting toxicities leading to study discontinuation were observed** during the SAD part of the study, which we believe can be attributed to OPM's proprietary medicinal chemistry platform. The few adverse events possibly related to the product were mainly minor, allowing repeated oral administration to be envisaged with confidence (Exhibit 30).
- Significant target engagement (measured through TNFα level reduction) over a 24-hour period, starting with low doses. After a single-dose oral administration of OPM-101 (at doses from 5 to 1000 mg), **target engagement was observed at low doses as early as 1h after administration and maintained at a very significant level over 24h (Exhibit 31)**. We find the statistically significant reduction in TNFα levels upon treatment with low doses (60mg) of OPM-101 encouraging result but it remains to be seen, of course, to what extent this translates in a clinically meaningful benefit for UC patients.
- Exhibit 32 nicely illustrates the immunomodulative character of OPM-101 as it reduces the TNFα to basal levels, rather than depleting levels entirely as immunosuppressors do.

Exhibit 30 Ph1 SAD: OPM-101 exhibits an excellent tolerability profile

Study part	Group	Dose (mg)	Number of subjects with at least 1 TEAE	Number of TEAEs	Treatment-related TEAEs	Severity of treatment-related TEAEs	SAEs
SAD	1	5	1	1	0	-	0
	2	20	0	0	0	-	0
	3	60	1	1	0	-	0
	4	150	1	1	0	-	0
	5	300	2	3	1	Moderate	0
	6	600	4	6	3	Mild	0
	7	1000	3	3	1	Mild	0
	9 (FE)	150	4	5	2	Mild	0
	10 (F)	150	1	4	1	Moderate	0
MAD	1	75 (bid)	4	6	4	Mild (3) Moderate (1)	0
	2	150 (bid)	3	3	2	Mild	0
	3	300 (bid)	0	0	0	-	0
	4 (F)	150 (bid)	2	2	2	Moderate (2)	0
			TOTAL	31	14	Mild (11) Moderate (5)	0

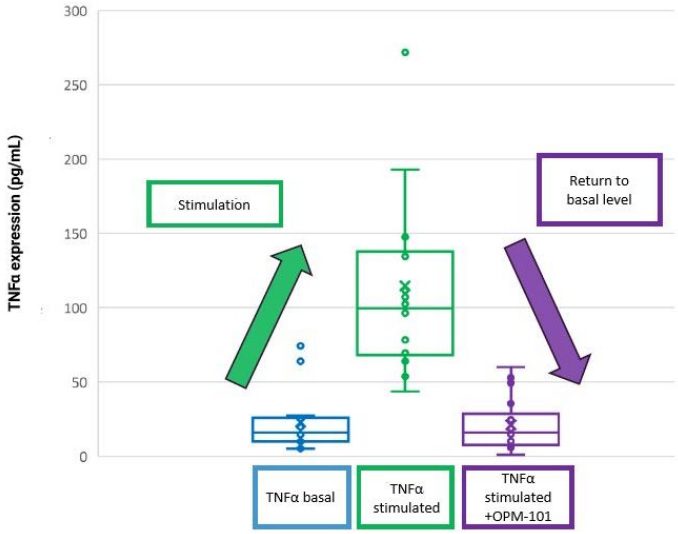
Source: OPM

Exhibit 31 Ph1 SAD: pharmacodynamics at 24h – significant inhibition of TNFα mRNA levels already at low dosing



Source: OPM
TNFa expression *ex vivo* stimulated by L18-MDP

Exhibit 32 Ph1 SAD: OPM-101 reduces TNFα expression levels through immunomodulation rather than immunosuppression



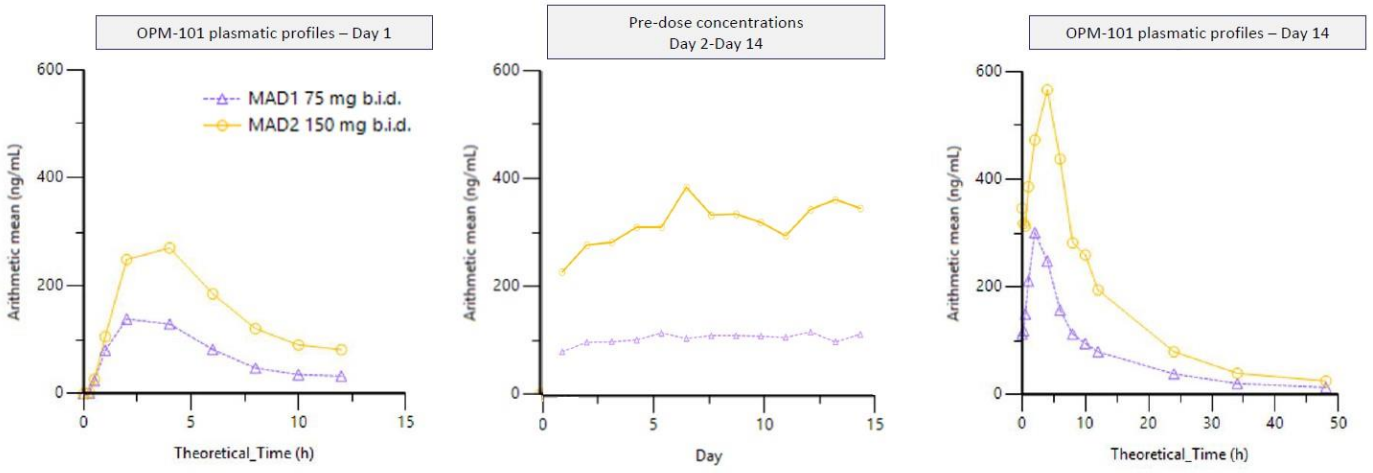
Source: OPM
TNFa expression *ex vivo* stimulated by L18-MDP
Pooled data from all male cohorts.

OPM capitalized on the analysis of OPM-101 data obtained during the SAD to optimize preparation of the second part of the study, which started in Q4 2023, following ANSM approval. In this part of the study, OPM-101 is administered twice a day[21], at 75-300 mg doses, for 14 days. (Exhibit 27). Data obtained so far confirms/indicates that:

- OPM-101 is orally bioavailable and rapidly absorbed (Tmax between 2-4h, Exhibit 33 left)
- C_{max} and AUC_{0-t} are increasing dose-proportionally on both Day 1 and Day 14 (Exhibit 33 left and right).
- Drug exposure on Day 14 is approximately twice that of Day 1: c. 600 ng/mL vs. c. 300 ng/mL for 150 mg BID and c. 300 ng/mL vs. c. 150 ng/mL for 75 mg BID (Exhibit 33 left and right).
- A steady-state drug concentration is reached after 3-4 days (c. 300 ng/mL for 150 mg BID and c. 100 ng/mL for 75 mg BID) (Exhibit 33 middle).
- The half-life elimination of 12-15h (Exhibit 33 left and right).
- Rapid onset of target engagement within the first 2h and high and consistent target engagement (c. 80%) over 14 days (Exhibit 34).

[21] Twice-a-day to ensure target engagement for 24h a day for 2 weeks. OPM indicated that they're going to do the necessary formulation work to allow once-a-day administration.

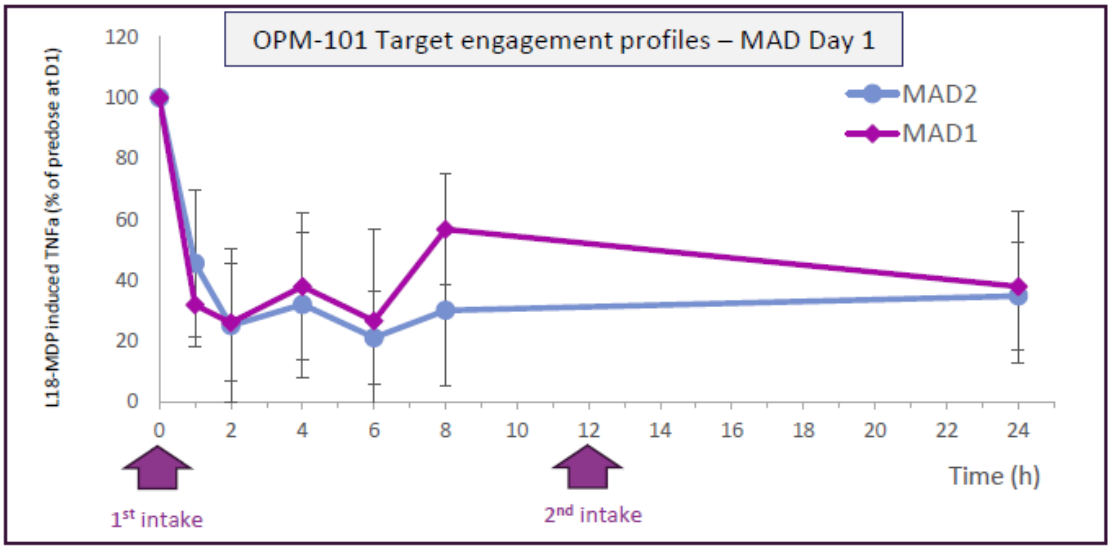
Exhibit 33 Ph1 MAD: pharmacokinetics of OPM-101 Day 1-14

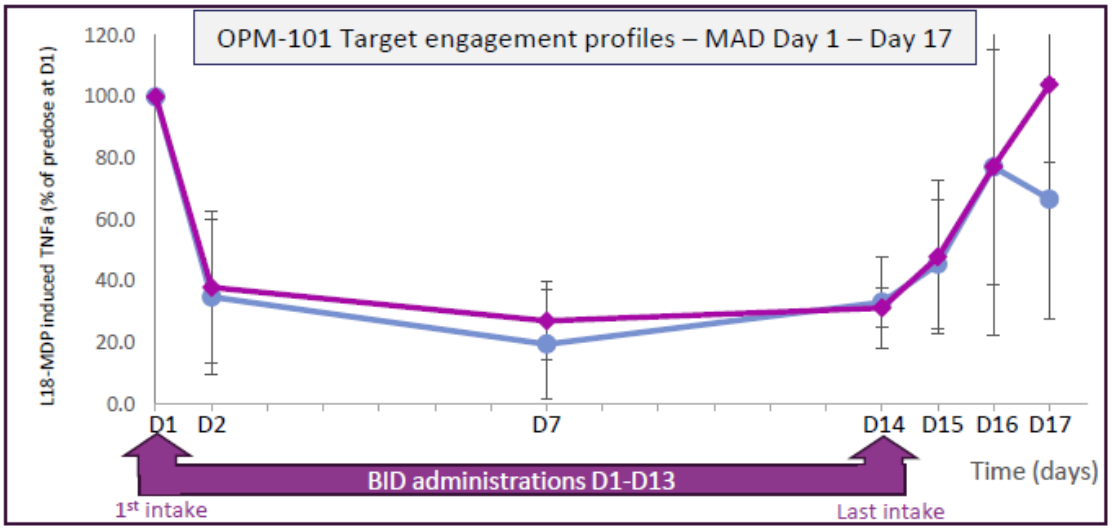


n=6 in each cohort

Source: OPM

Exhibit 34 Ph1 MAD: Rapid onset of target engagement within the first 2h and high and consistent target engagement (c. 80%) over 14 days





Source: OPM

Due to the lack of clinical (especially efficacy) data from IBD patients, we consider it too early to make definitive statements about the therapeutic potential of the drug and, hence, look forward to the first efficacy results from a Ph2 study. OPM prioritizes the ICI-AC opportunity as it aims to launch a Ph2a trial for this indication by late '24/early '25 and only around mid-'25 for IBD (Exhibit 65 in addendum).

Nevertheless, we believe that OPM-101 is well positioned for clinical success taking into account:

1/ the sound scientific rationale behind selecting the RIPK2 target

2/ its proprietary medicinal chemistry platform favoring target selectivity (thereby also avoiding pitfalls other RIPK2 inhibitors faced)

3/ the limited encouraging (pre)clinical efficacy and safety data generated by the compound so far.

As OPM-101 is a small molecule immunomodulator (rather than immunosuppressor) allowing for convenient oral administration while preserving the immune system's ability to fight infections, we find it sufficiently differentiated to break into both the (crowded, hence it makes sense to prioritize ICI-AC) IBD and ICI-AC markets as both mono & (potentially) combo therapy.

4.3.3 RIPK2 as an oncology target

OPM is also exploring RIPK2 as a target for oncology. Indeed, RIPK2 is highly expressed in various tumor types, including ovarian, bladder and colon tumors. The molecular mechanisms by which **RIPK2 promotes tumor progression and resistance** are manifold:

- Regulation of the immune microenvironment of the immune microenvironment[22].
- Mechanisms linked to amplification of oncogenes or dependence on dependence on transcription factors independent of its initial immune regulatory function[23].
- Increased RIPK2 function appears to be linked to resistance to PD-1[24,26].

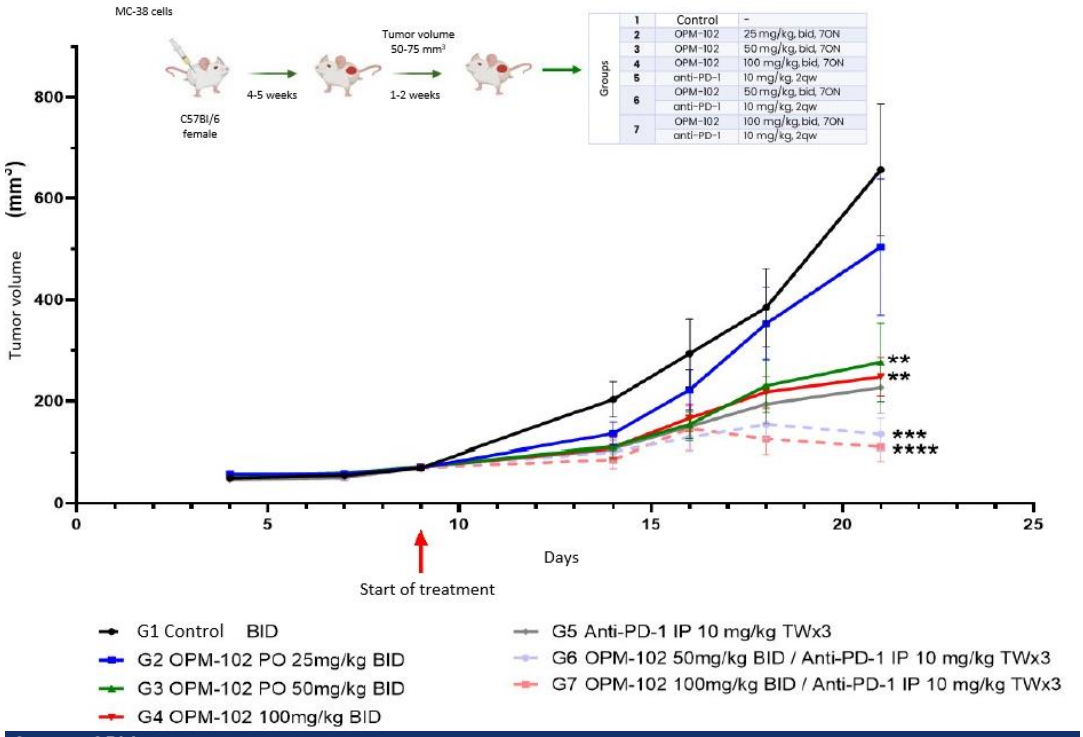
As Exhibit 35 indicates, OPM-102[25] treatment reduces tumor volume in a dose-dependent and statistically significant (from 50mg/kg dose) manner in mice. Moreover, OPM-102 negatively affects cytokine levels (Exhibit 36). Finally, OPM-102 seems to synergize with anti-PD-1 treatment resulting into a statistically significant reduction in tumor volume vs. anti-PD-1 monotherapy. A recently publication indicated that RIPK2 inibition seems to render cancer cells vulnerable to the immune system by enhancing epitope presentation on their cell membrane through a MHC/HLA mechanism[26].

We look forward to gaining more insight on the precise mechanism-of-action underlying this effect (OPM is currently advancing the asset in preclinical studies, Exhibit 65 in addendum)) but already want to point out that **1/ OPM-102 has first-in-class potential in oncology as RIPK2 inhibitor** (Exhibit 20, bottom) and **2/ this synergy could be very relevant in the context of preventing/treating ICI-AC as ICI dosing could potentially be lowered thereby preventing off-target immune activation.**

Other clinical-stage precision oncology companies, applying a comparable targeted approach like OPM, include Acrivon, Repare Therapeutics, Ikena Oncology (USA), and Cantargia (Sweden).

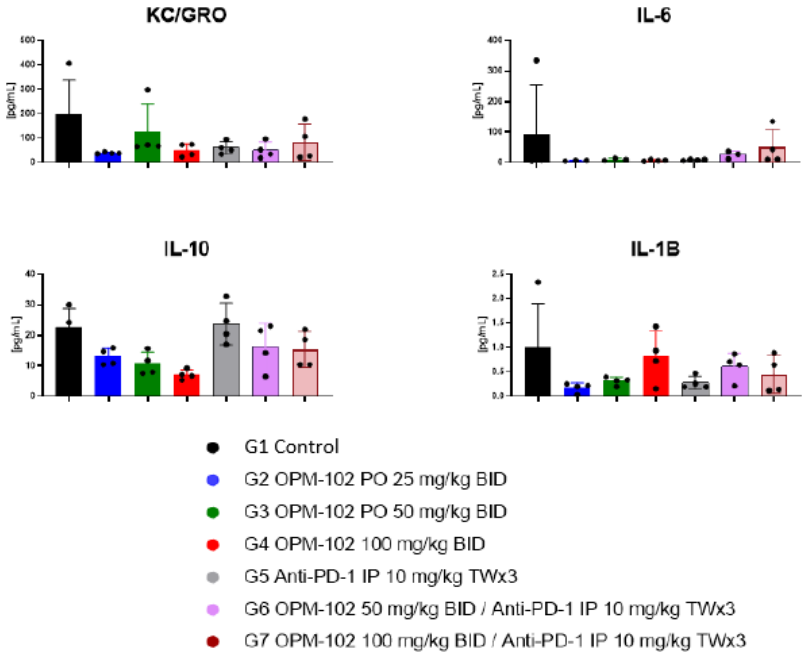
[22] Song et al. (2022). Pan-cancer analysis reveals RIPK2 predicts prognosis and promotes immune therapy resistance via triggering cytotoxic T lymphocytes dysfunction. Molecular Medicine 28 (47).
[23] Yan et al. (2022). Receptor-interacting protein kinase 2 (RIPK2) stabilizes c-Myc and is a therapeutic target in prostate cancer metastasis. Nature Communications 13 (669).
[24] Barnett et al. ASCO, 2023.
[25] OPM-102 and OPM-101 are closely related but structurally different RIPK2 inhibitors.
[26] Sang et al. (2024). Receptor-interacting Protein Kinase 2 Is an Immunotherapy Target in Pancreatic Cancer. Cancer Discov 14.

Exhibit 35 ***In vivo*** **efficacy of OPM-102 as monotherapy or in combination with anti-PD-1 in mice with MC38 tumors**



Source: OPM
One-way ANOVA test (** p < 0.01, *** p < 0.001, **** p < 0.0001 vs. control group).
C57BL/6 is the most widely used genetic background for genetically modified mice for use as models of human disease. The MC38 adenocarcinoma colorectal cell line is a well-established and often used tumor model for pre-clinical studies of neoantigens and immunotherapeutic approaches.

Exhibit 36 **Plasma cytokine levels upon treatment with OPM-102 as monotherapy or in combination with anti-PD-1 in mice with MC38 tumors**



Source: OPM
KC/GRO: Keratinocyte chemoattractant/human growth-regulated oncogene

5/ OPM-201: LRRK2 inhibitor for PD

5.1 Epidemiology

PD is a chronic degenerative disorder of the central nervous system that affects both the motor system and non-motor systems. **Nearly one million people in the U.S. and more than 10 million worldwide are living with the disease**, making it the second-most common neurodegenerative disease after Alzheimer's disease. Nearly 90k people in the U.S. are diagnosed with PD each year. The incidence of PD increases with age, but an estimated 4% of people with PD are diagnosed before age 50. Men are 1.5 times more likely to have the disease than women.

The symptoms usually emerge slowly and, as the disease progresses, non-motor symptoms become more common. Early symptoms are tremor, rigidity, slowness of movement, and difficulty with walking. Problems may also arise with cognition, behavior, sleep, and sensory systems. PD dementia is common in advanced stages.

The motor symptoms of the disease result from the nerve cell death in the *substantia nigra*, a midbrain region that supplies dopamine to the basal ganglia. The cause of this cell death is poorly understood but involves the aggregation of the protein alpha synuclein into Lewy bodies within the dopaminergic neurons. Collectively, the main motor symptoms are known as parkinsonism.

Contributing factors include a combination of age, genetic and environmental factors:

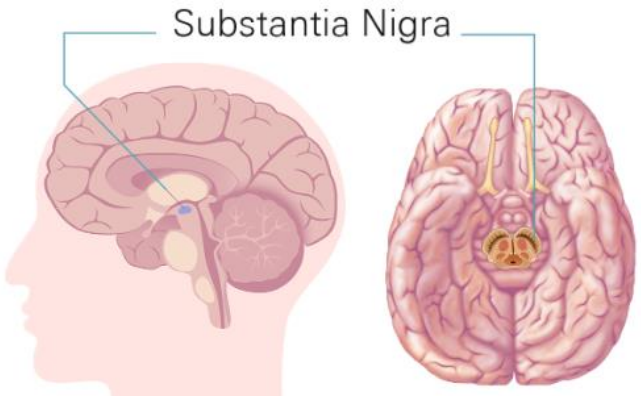
- Approximately 10-15% of people with PD have a family history of this disorder. Familial cases of PD (autosomal dominant inheritance) can be caused by **mutations in the LRRK2 (leucine-rich repeat kinase 2, see below), PARK7, PINK1, PRKN, or SNCA gene**, or by alterations in genes that have not been identified. Variants in some of these genes (incl. LRRK2) may also play a role in cases that appear to be sporadic/idiopathic (iPD) (not inherited).
- Environmental factors identified as disease risk factors include for example exposure to pesticides and prior head injuries.

PD diagnosis is mainly based on symptoms, usually motor-related. PD typically occurs in people over the age of 60, of whom about 1% are affected. In those younger than 50, it is termed early-onset PD. The average post-diagnosis life expectancy is 7–15 years.

5.2 Pathophysiology

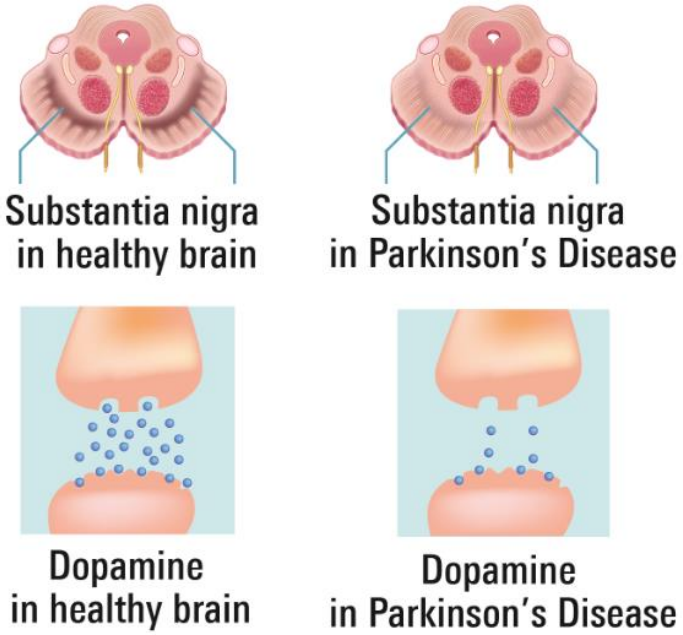
The main pathological characteristics of PD are cell death in the brain's basal ganglia (affecting up to 70% of the dopamine-secreting neurons in the *substantia nigra pars compacta* by the end of life, Exhibit 37, Exhibit 38). **In PD, alpha-synuclein, a protein encoded by the SNCA gene, becomes misfolded and clumps together with other alpha-synuclein (αSyn). Cells are unable to remove these clumps, and the αSyn becomes cytotoxic, damaging the cells.** These clumps can be seen in neurons under a microscope and are called Lewy bodies. Loss of neurons is accompanied by the death of astrocytes (star-shaped glial cells) and an increase in the number of microglia (another type of glial cell) in the *substantia nigra*.

Exhibit 37 The substantia nigra produces dopamine which controls movements and muscle tone



Source: Marley Drug

Exhibit 38 PD is characterized by loss in dopamine-producing cells in the substantia nigra leading to movement disorders



Source: Marley Drug

5.2.1 Pathological LRRK2 activity contributes to PD

5.2.1.1 LRRK2 is a widely distributed protein with numerous physiological roles

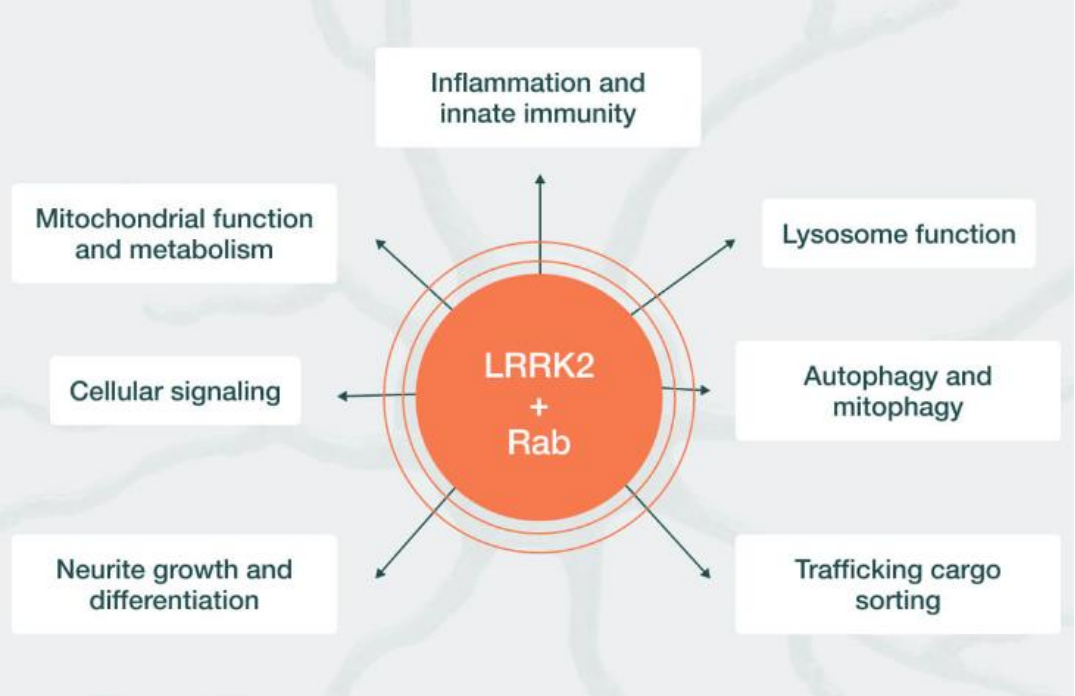
The LRRK2 gene, discovered in 2004, is located on chromosome 12, contains 51 exons spanning 144 kb and encodes for a large 286 kDa / 2527 amino acid-long multidomain protein of the same name (Exhibit 40). The central portion of LRRK2 contains a Ras of Complex (Roc) GTPase and a C-terminus of Roc (COR) domain, followed by serine-threonine kinase domains. The ROC-COR bidomain and kinase region together constitute the catalytic core of LRRK2, which therefore encompasses two enzymatic activities. In addition, there are several protein–protein interaction domains including ankyrin and leucine-rich repeat motifs at the N-terminus, and WD40 repeats at the C-terminus.

LRRK2 is widely expressed in many tissues such as brain, heart, kidney and lungs. In the mammalian brain, both mRNA and protein of LRRK2 have been detected highly expressed in dopamine-innervated areas such as cerebral cortex, striatum as well as in the cerebellum and hippocampus, while at low levels in dopaminergic neurons of the *substantia nigra* and ventral tegmental area.

At the cellular level, LRRK2 expression has been reported in astrocytes, microglia, neurons, endothelial cells and peripheral immune cells. In cells, LRRK2 is mainly found throughout the cytoplasm associated with various intracellular membranes and vesicular structures, such as lipid raft, early endosomes, lysosomes, plasma membrane and synaptic vesicles, as well as in the endoplasmic reticulum, Golgi complex and outer mitochondrial membrane.

Despite not yet having a detailed picture of the normal function of LRRK2, it has shown to be involved in the cytoskeleton and in membrane trafficking, iron homoeostasis and mitochondrial function among others (Exhibit 39**Error! Reference source not found.** and Exhibit 66 in addendum).

Exhibit 39 Elevated LRRK2 kinase activity can disrupt numerous cellular processes

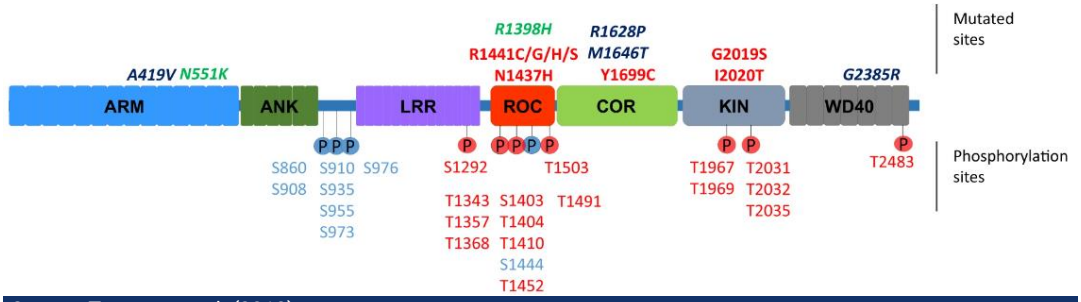


Source: Neuron23
Rab8A and Rab10 are physiological substrates of LRRK2

5.2.1.2 LRRK2 mutations linked to PD

Several mutations have been documented in the LRRK2 gene with seven of these missense mutations identified as pathogenic[27], including R1441G, R1441C, R1441H, Y1699C, G2019S, R1628P, G2385R and I2020T (Exhibit 40). **All of these, except G2385R[28], result in a toxic gain-of-function: elevated kinase activity**. The **G2019S mutation in the LRRK2 protein is the most common pathogenic mutation**, accounting for 3–19% of familial and 1–6% of sporadic PD cases[29].

Exhibit 40 Pathogenic LRRK2 mutations (red) contribute to PD pathophysiology



Source: Taymans et al. (2018).
Key amino acid substitutions are indicated that alter risk for PD, including mutations that increase risk for PD such as pathogenic mutations (red) and risk factor mutations (blue) as well as mutations that confer reduced risk for PD (green). Phosphorylated residues are given below the schematic, with heterologous phosphosites give in blue and autophosphorylation sites in red.

[27] The phenotypic penetrance of the LRRK2 gene is incomplete meaning that not all individuals carrying a mutation develop PD.
[28] Mutation in the WD40 domain that actually decreases the kinase activity of LRRK2.
[29] Other risk factors for iPD are oxidative stress, endolysosomal impairment, and environmental toxicants.

LRRK2 has been revealed to co-localize with early stages of aggregating αSyn in lower brainstem of PD and dementia with Lewy body patients. **Current studies indicate that mutant LRRK2 exacerbates αSyn neuropathology, most likely via an indirect interaction involving Rab GTPases**[30] and chaperones, in a cell type, brain region and patient age-dependent manner. Work to date also indicates that LRRK2 and α-synuclein converge on common mechanisms that lead to neuronal death, particularly by affecting the autophagy lysosomal pathway. It was also suggested that **mutant LRRK2 can mediate neurodegeneration independent of large αSyn aggregates** as autopsy studies revealed that an appreciable subset of LRRK2 PD cases can have dopaminergic neuron loss but lack Lewy body pathology. Therefore, further research is needed to determine why αSyn does not appear to aggregate into insoluble forms in a proportion of LRRK2 PD cases and to characterize the presence and roles of different αSyn aggregates in LRRK2 PD.

Both increased LRRK2 activity and phosphorylated Rab proteins have also been observed in PD patients independent of LRRK2 mutation status. The molecular mechanisms by which LRRK2 is activated by e.g. environmental contaminants (rather than genetics), however, still remain to be delineated.

5.2.2 LRRK2 as a therapeutic target[31]

Considering its link with PD, LRRK2 has been prioritized as a PD target since its discovery in 2004 and it has been shown that inhibiting the kinase domain of LRRK2 has neuroprotective effects and prevents endolysosomal deficits. However, LRRK2 inhibitor development has been facing significant challenges related to effectiveness and safety. In fact, the most important unresolved medicinal chemistry challenge is the lack of a crystal structure of the LRRK2 kinase domain, which hampers drug development efforts. However, recent developments in low-resolution, cryo-EM-based LRRK2 structures have resolved this to some extent with experimental work to obtain a high-resolution structure still ongoing.

An overview of the small molecule inhibitors (3) and anti-sense oligonucleotide (1) in clinical trial development as potential treatments for PD can be found in Exhibit 41.

Exhibit 41 LRRK2-targeted therapeutics: currently ongoing trials

Asset	MoA	Company	Ongoing Trials	Topline readout	ClinicalTrials.gov Identifier
OPM-201		OPM/Servier	Ph1	H1 2025	N/A
DNL151/BIIB122	Small molecule inhibitor	Denali Tx/Biogen	Ph2b	Aug-25	NCT05348785
NEU-723		Neuron23	Ph1	Jun-23*	NCT05633745
ION859/BIIB094	antisense oligonucleotide	Ionis Pharmaceuticals/Biogen	Ph1	Dec-24	NCT03976349

Source: Taymans et al. (2018), ClinicalTrials.gov
*Neuron23 announced first dosing in the Ph1 in Feb 2023 but has not reported results since.

Given the expression of LRRK2 in tissues other than the brain, especially the lungs, there is justified concern about the potential for 'on-target' (LRRK2-specific) toxicity, such as pulmonary toxicity. However, based on studies in rodents and non-human primates, and the fact that humans with LRRK2 loss of function mutations are not known to have deleterious health effects, **blockade of LRRK2 kinase activity seems to be reasonably safe**.

[30] Increased kinase activity of mutant LRRK2 was shown to phosphorylate Rab35, affecting its interaction with its substrates, eventually preventing the endosome-lysosomal degradation of αSyn aggregates.
[31] Taymans et al. (2023). Perspective on the current state of the LRRK2 field. npj Parkinson's Disease 9 (104).

This was also illustrated by the Ph1b results in PD patients with DNL151/BIIB122, the most advanced LRRK2 inhibitor from Biogen/Denali Tx currently in Ph2 development for PD (and Exhibit 67 in addendum)[32]. **Ph1(b)33 biomarker data of DNL151/BIIB122 provided initial proof-of-concept supporting continued clinical development of LRRK2 inhibitors.** More specifically, Biomarker results demonstrated dose-dependent peripheral LRRK2 kinase inhibition based on reduction in whole-blood pS935 LRRK234 and PBMC35 pT73 Rab1036, modulation of the lysosomal pathway downstream of LRRK2 based on reduction in urine BMP37, and central LRRK2 kinase inhibition based on reduction in CSF tLRRK2. Thus, in these early-phase studies, LRRK2 kinase inhibition levels sufficient to modulate lysosomal pathways downstream of LRRK2 were safely achieved with daily oral dosing of BIIB122 (Exhibit 68 in addendum).

It does remain to be seen, however, to what extent this will translate in a clinically meaningful benefit, e.g. improve mobility through measuring MDS-UPDRS, especially since the degenerative process is already underway (hence a thorough patient selection strategy will need to be applied).

To investigate this, Biogen & Denali launched two global late-stage clinical trials following successful completion of the Ph1(b): the **Ph2b LUMA study** in participants with early-stage Parkinson's disease, which commenced in May 2022; and the Ph3 LIGHTHOUSE study in participants with PD related to LRRK2 mutations, which commenced in September 2022.

Mid-2023, finally, Biogen and Denali agreed to, in consideration of the LIGHTHOUSE study's complexity including the long timeline with anticipated study completion in 2031, to discontinue the study and amend the protocol for the LUMA study to now include eligible patients with a LRRK2 genetic mutation in addition to continuing to enrol eligible patients with early-stage idiopathic PD. Patients already enrolled and randomized in LIGHTHOUSE were offered the opportunity to join the LUMA study, which is now meant to serve as a registrational trial.

5.2.3 OPM-201 partnered with Servier in > EUR 300m deal

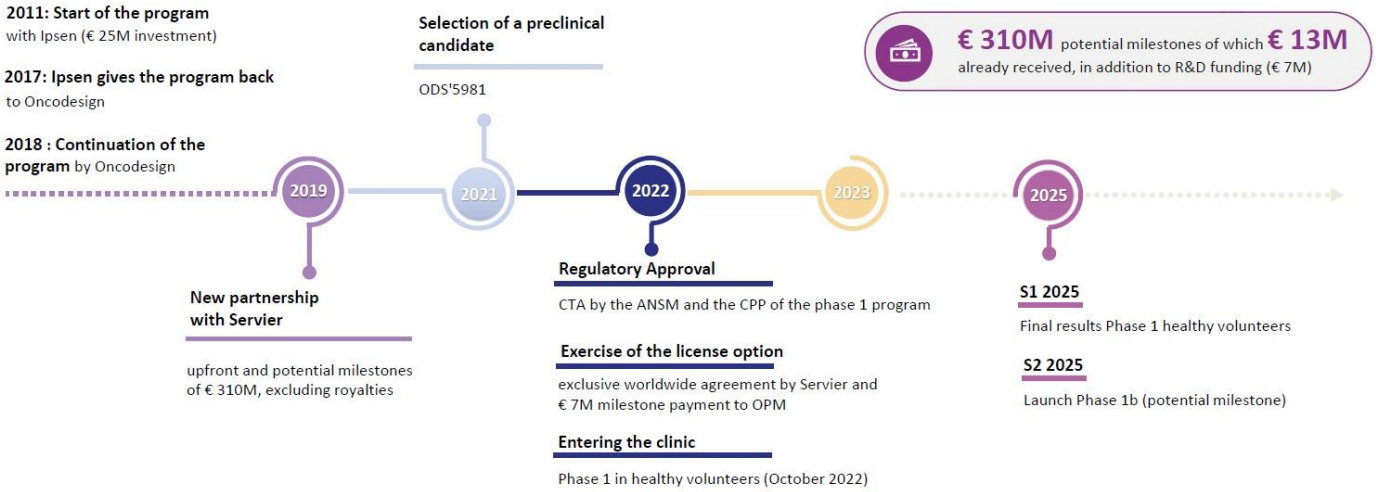
In March 2019, Servier and OPM entered into a research collaboration (with licensing option)[38] on LRRK2 kinase inhibitors worth EUR 310m in upfront & milestone payment + (unspecified) royalties on net sales, as potential therapeutic agents for PD. In 2022, Servier exercised the licence option, triggering a EUR 7m milestone payment to OPM, and a Ph1 in healthy volunteers was launched which is expected to readout in H1 2025. Servier aims to launch the subsequent Ph1b in H2 2025 (Exhibit 42).

We consider OPM-201 favourably positioned for success as a disease-modifying treatment (DMT) for PD, even being 2nd in the race behind DNL151 (if not first-in-class, OPM-201 can still be best-in-class). **A DMT is a therapy that changes the course of the disease, rather than merely providing symptomatic relief as the currently available treatments do**. **Our conviction is based on the unique features of Nanocyclix® molecules and their ability to 1/ precisely target intractable and unexplored kinases in various kinase families and 2/ easily cross cell membranes and even the blood-brain barrier due to their small size and limited conformational space.**

[32] Two patients in the Ph1b study discontinued on the first study day: one who received 130 mg once daily experienced severe asymptomatic hypotension, considered by the investigator as being unrelated to study drug (pre-existing hypotension), and another patient who received 300 mg once daily experienced mild hypotension and orthostatic hypotension with mild dizziness. In all discontinuations, symptoms resolved with discontinuation of therapy. There were no clinically meaningful changes in pulmonary or renal function in either study.
[33] The Ph1 enrolled 184 healthy volunteers and Ph1b 36 PD patients.
[34] a phosphorylated form of LRRK2 that is reduced following LRRK2 kinase inhibition
[35] peripheral blood mononuclear cells
[36] direct LRRK2 substrate
[37] marker of peripheral lysosomal function
[38] The initial LRRK2 program at Oncodesign/OPM was funded by Ipsen in a similar deal. Ipsen retracted after a strategic change and the program came back to OPM.

Early 2024, Servier announced another, OPM complementary, partnership with Aitia with the aim to leverage Aitia's 'Gemini Digital Twins' to identify patients most likely to respond positively to LRRK2i. Under the terms of the collaboration, Servier will combine data from its previous work in the field of neuroscience and PD with Aitia's expertise in AI-enabled drug discovery. Aitia's Gemini Digital Twins, computational representations of disease that capture genetic and molecular interactions that causally drive clinical and physiological outcomes, will simulate the mechanisms of action of LRRK2 inhibitor treatment to highlight biomarkers in patients. Ultimately, these discoveries may make it possible to define subpopulations of patients who will respond favourably to LRRK2 inhibition.

Exhibit 42 Lucrative partnership with Servier for LRRK2 inhibitor OPM-201



Source:OPM

5.3 Current PD treatments[39]

PD cannot be cured, but medicines can help control the symptoms, often dramatically. **There are currently no DMTs approved for PD**. The number of currently ongoing clinical trials assessing symptomatic and disease-modifying treatments is about equal and testing agents targeting αSyn (either by preventing its aggregation or clearing existing aggregates) maintain a large presence in the pipeline. Considering its strong link with αSyn neuropathology, we believe this trend provides strong validation for the LRRK2 inhibition approach. Examples of other DMT approaches under clinical study, often with a connection to αSyn pathology as well, are centered around neuroinflammation, mitochondrial dysfunction, and glucocerebrosidase activity.

5.3.1 Current drug interventions

People with PD have low levels of brain dopamine. However, dopamine cannot be given directly because it cannot enter the brain. Hence, medicines are administered to increase or substitute for dopamine. **Although significant symptom improvement can often be observed following initial treatment, benefits of medicines frequently diminish or become less consistent over time as dopaminergic neurones continue to decline. Also, side effects such as vomiting, hallucinations, compulsive behaviour among other are frequently detected.**

[39] McFarthing et al. (2023). Parkinson's Disease Drug Therapies in the Clinical Trial Pipeline: 2023 Update. J Parkinsons Dis. 13(4).

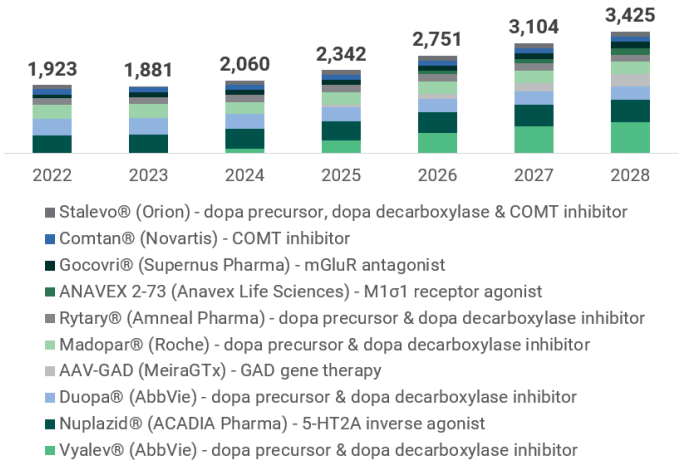
The most-commonly prescribed PD medicines can be categorized in the following groups:

- **Carbidopa-levodopa**: **Levodopa/L-DOPA is currently still the most effective PD medicine**. It is a natural chemical that passes into the brain and is converted to dopamine. Levodopa can be combined with carbidopa, which protects levodopa from early conversion to dopamine outside the brain thereby preventing or lessening side effects. After years, as your disease progresses, the benefit from levodopa may lessen. Carbidopa-levodopa can also be taken in an inhaled and infused form. It may be helpful in managing symptoms that arise when medicines taken by mouth suddenly stop working during the day.
- **Dopamine agonists.** Unlike levodopa, dopamine agonists do not change into dopamine. Instead, they mimic dopamine effects in the brain. Dopamine agonists aren't as effective as levodopa in treating symptoms. However, they last longer and may be used with levodopa to smooth the sometimes off-and-on effect of levodopa.
- **Monoamine oxidase B inhibitors.** They help prevent the breakdown of brain dopamine by inhibiting the brain enzyme monoamine oxidase B (MAO B).
- **Catechol O-methyltransferase (COMT) inhibitors.** This medicine mildly prolongs the effect of levodopa therapy by blocking an enzyme that breaks down dopamine.

Exhibit 43 and Exhibit 44 provide an overview of the total world-wide market value of the top 10 PD drugs, based on annual sales in the period 2022-2028. Levodopa (i.e. dopamine precursor)-containing treatments currently dominate this multi-billion dollar market and are expected to continue to gain market share in the years to come in absence of DMTs.

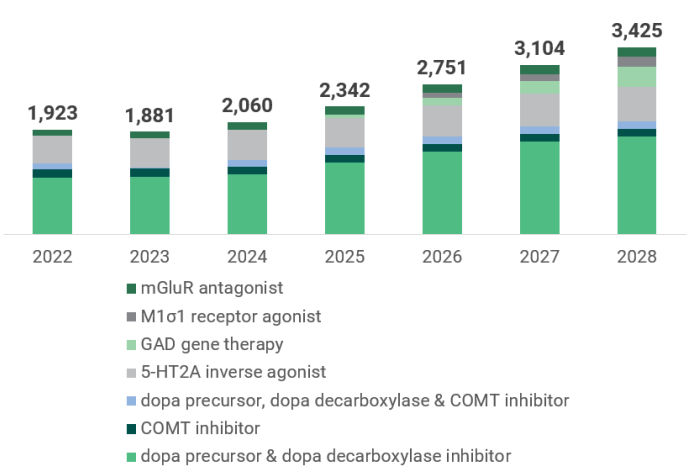
Summarized, the clear need for a DMT prompts development of OPM-201, especially keeping in mind its small molecule character allowing 1/ convenient oral (rather than IV as for biologics) administration, and 2/ enhanced BBB penetration ability, and 3/ cheaper production vs. biologics targeting α-synuclein.

Exhibit 43 Total world-wide market value of top 10 PD drugs 2022-2028 (USD m)



Source: Evaluate Pharma

Exhibit 44 Total world-wide market value of top 10 PD drugs 2020-2026 by drug class (USD m)



Source: Evaluate Pharma

5.3.2 Surgical procedures

- **Deep brain stimulation (DBS).** This intervention involves the implantation of electrodes into a specific part of the brain. The electrodes are connected to a generator implanted in the chest near the collarbone. The generator sends electrical pulses to the brain and may reduce PD symptoms. This highly invasive surgery involves risks including infections, stroke or brain hemorrhage. Some people experience problems with the DBS system or have complications due to stimulation. DBS is most often offered to people with advanced PD who have unstable responses to levodopa. **Although DBS may provide sustained benefit for Parkinson's symptoms, it does not keep PD from progressing**.

5.3.3 Other treatments

MRI-guided focused ultrasound (MRgFUS) is a minimally invasive treatment that has helped some PD patients manage tremors. Ultrasound is guided by an MRI to the area in the brain where the tremors start. The ultrasound waves are at a very high temperature and burn areas that are contributing to the tremors.

6/ Sales and revenue projections

6.1 IBD and ICI-AC opportunities expected to yield EUR 400m in combined revenue for OPM

Our net sales projections for OPM-101 for IBD and ICI-AC amount to > EUR 1bn and EUR 350m (see also Exhibit 9 and Exhibit 10 for (peak) sales estimates of IBD therapies as a reference), respectively, and are displayed in Exhibit 45 and Exhibit 46.

IBD projections:

- As OPM-101 could, pending Ph1 data, be advanced into a Ph2a for either UC or CD (and potentially even both) mid-2025, we took an average of both disease prevalence numbers to arrive at our 'diagnosed IBD cases' estimate.
- In line with French biotech Abivax's clinical development strategy for obefazimod for IBD, we model a separate Ph2b study. On the basis thereof, we anticipate a big pharma to in-license the asset for subsequent development and commercialization.
- Market share: peak penetration of 7.5% of the biologics-refractory moderate-severe patient population, keeping in mind the current and expected intense (small molecule) competition (JAKi, S1P receptor modulators…) by the time of approval. We anticipate OPM-101 to reach peak penetration 1 year later in EU5 vs. USA and JPN based on the expected country-by-country launch cascade and pricing and reimbursement discussions.
- Pricing: List price/patient/year and discount % based on alternative small molecule treatments for IBD[40]. We include a gross-to-net adjustment of 25% in the USA to account for rebates, discounts, and other reductions. We model a 30% price discount in EU5 and Japan.

[40] Rinvoq®: USD 72.5, Xeljanz®: USD 63.3k (Evaluate Pharma)

Exhibit 45 OPM-101 net sales projections in IBD (EUR m)

		2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040
years from now		0.75	1.75	2.75	3.75	4.75	5.75	6.75	7.75	8.75	9.75	10.75	11.75	12.75	13.75	14.75	15.75	16.75
stage		Ph1	Ph2a	Ph2a	Ph2b	Ph2b	Ph3	Ph3	Ph3	Filing					Market			
		2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040
USA																		
Population (m)		258.1	260.2	262.2	264.1	266.0	267.9	269.7	271.3	272.8	274.2	275.7	277.2	278.6	280.0	281.5	283.0	284.5
Diagnosed IBD cases		775,613	790,349	805,366	820,668	836,260	852,149	868,340	884,839	901,651	918,782	936,239	954,027	972,154	990,625	1,009,447	1,028,626	1,048,170
Incl. moderate to severe symptoms	*55%*	426,587	434,692	442,951	451,367	459,943	468,682	477,587	486,661	495,908	505,330	514,931	524,715	534,685	544,844	555,196	565,744	576,494
Targeted therapy-treated (%)		*35.0%*	*35.5%*	*36.0%*	*36.5%*	*37.0%*	*37.5%*	*38.0%*	*38.5%*	*39.0%*	*39.5%*	*40.0%*	*40.5%*	*41.0%*	*41.5%*	*42.0%*	*42.5%*	*43.0%*
Targeted therapy-treated		149,305	154,316	159,462	164,749	170,179	175,756	181,483	187,365	193,404	199,605	205,973	212,510	219,221	226,110	233,182	240,441	247,892
Biologics-refractory population	*60%*																	
OPM-101 eligible		89,583	92,589	95,677	98,849	102,107	105,453	108,890	112,419	116,042	119,763	123,584	127,506	131,532	135,666	139,909	144,265	148,735
Market share		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0.4%*	*1.2%*	*3.1%*	*5.4%*	*6.8%*	*7.3%*	**7.5%**	*7.5%*
OPM101-treated		0	0	0	0	0	0	0	0	0	456	1522	4010	7166	9229	10209	10820	11132
List price/y/pt (EUR)	70,000																	
Discount	*25%*																	
Net price/y/pt (EUR)	52,500																	
Net sales USA		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**24**	**80**	**211**	**376**	**485**	**536**	**568**	**584**
EU5																		
IBD diagnosed prevalence	*0.3%*	776,177	790,925	805,952	821,265	836,870	852,770	868,973	885,483	902,307	919,451	936,921	954,722	972,862	991,346	1,010,182	1,029,375	1,048,934
Incl. moderate to severe symptoms	*55%*	426,898	435,009	443,274	451,696	460,278	469,024	477,935	487,016	496,269	505,698	515,306	525,097	535,074	545,240	555,600	566,156	576,913
Targeted therapy-treated (%)		*30.0%*	*30.5%*	*31.0%*	*31.5%*	*32.0%*	*32.5%*	*33.0%*	*33.5%*	*34.0%*	*34.5%*	*35.0%*	*35.5%*	*36.0%*	*36.5%*	*37.0%*	*37.5%*	*38.0%*
Targeted therapy-treated		128,069	132,678	137,415	142,284	147,289	152,433	157,719	163,150	168,731	174,466	180,357	186,410	192,627	199,013	205,572	212,309	219,227
Biologics-refractory population	*60%*																	
OPM-101 eligible		76,842	79,607	82,449	85,371	88,373	91,460	94,631	97,890	101,239	104,680	108,214	111,846	115,576	119,408	123,343	127,385	131,536
Market share		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0.2%*	*1.0%*	*2.3%*	*4.2%*	*5.9%*	*6.9%*	*7.3%*	**7.5%**
OPM101-treated		0	0	0	0	0	0	0	0	0	209	1090	2603	4908	7084	8479	9263	9865
Price/y/pt (EUR)	36,750																	
Net sales EU5		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**8**	**40**	**96**	**180**	**260**	**312**	**340**	**363**
Japan																		
IBD diagnosed prevalence	*0.3%*	308,542	314,404	320,378	326,465	332,668	338,989	345,429	351,993	358,680	365,495	372,440	379,516	386,727	394,075	401,562	409,192	416,967
Incl. moderate to severe symptoms	*55%*	169,698	172,922	176,208	179,556	182,967	186,444	189,986	193,596	197,274	201,022	204,842	208,734	212,700	216,741	220,859	225,056	229,332
Targeted therapy-treated (%)		*30.0%*	*30.5%*	*31.0%*	*31.5%*	*32.0%*	*32.5%*	*33.0%*	*33.5%*	*34.0%*	*34.5%*	*35.0%*	*35.5%*	*36.0%*	*36.5%*	*37.0%*	*37.5%*	*38.0%*
Targeted therapy-treated		50,909	52,741	54,624	56,560	58,550	60,594	62,695	64,855	67,073	69,353	71,695	74,101	76,572	79,111	81,718	84,396	87,146
Biologics-refractory population	*60%*																	
OPM-101 eligible		30,546	31,645	32,775	33,936	35,130	36,357	37,617	38,913	40,244	41,612	43,017	44,460	45,943	47,466	49,031	50,637	52,288
Market share		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0.4%*	*1.2%*	*3.1%*	*5.4%*	*6.8%*	*7.3%*	**7.5%**	*7.5%*
OPM101-treated		0	0	0	0	0	0	0	0	0	158	530	1398	2503	3229	3578	3798	3913
Price/y/pt (EUR)	36,750																	
Net sales JPN		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**6**	**19**	**51**	**92**	**119**	**131**	**140**	**144**
Net sales OPM-101 in IBD		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**37**	**139**	**358**	**649**	**864**	**979**	**1,048**	**1,091**

Source: Degroof Petercam estimates
Diagnosed IBD cases number based on average of UC and CD numbers.
Patent expiration expected in 2040 (Exhibit 69 in addendum).

ICI-AC projections:

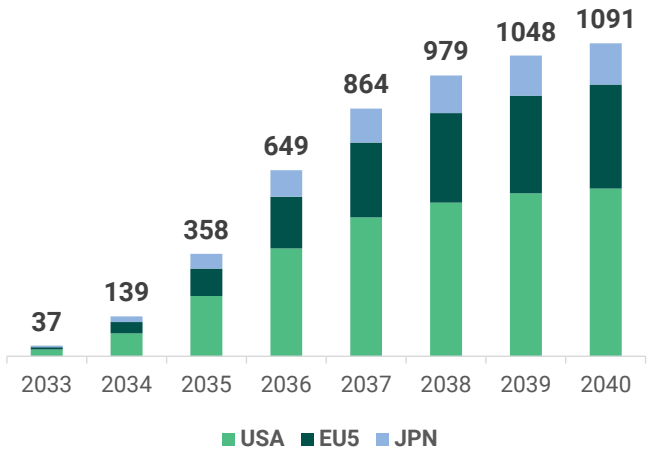
- For the time being, we only take into account sales stemming from use in the treatment setting:
  - Peak penetration of 30% of the ICI-treated population which either develops diarrhea (i.e. 30% of ICI-treated population), which often leads to colitis, or has colitis (c. 10% of ICI-treated patients) and this categorized as grade II-IV (ICI treatment interrupted). We anticipate OPM-101 to reach peak penetration 1 year later in EU5 vs. USA and JPN based on the expected country-by-country launch cascade and pricing and reimbursement discussions.
  - If 'OPM-102' would confirm its synergism with ICIs in clinical trials, we anticipate uptake in the preventive setting as well as RIPK2 inhibition would reduce the risk for ICI-AC both directly and indirectly (by lowering ICI dosing).
- Pricing: price/patient/year in line with our estimate for IBD (Exhibit 45).

Exhibit 46 OPM-101 net sales projections in ICI-AC (EUR m)

		2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040
years from now		0.75	1.75	2.75	3.75	4.75	5.75	6.75	7.75	8.75	9.75	10.75	11.75	12.75	13.75	14.75	15.75	16.75
stage		Ph1/2a	Ph2a	Ph2b	Ph2b	Ph3 ready	Ph3	Ph3	Ph3	Filing				Market				
		2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040
USA																		
ICI-treated population		17,000	17,850	18,743	19,680	20,664	21,697	22,782	23,921	25,117	26,373	27,691	29,076	30,530	32,056	33,659	35,342	37,109
ICI-associated diarrhea/colitis prevalence	*40%*																	
Grade II-IV	*75%*																	
Market share treatment setting		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*1.5%*	*4.4%*	*10.7%*	*19.3%*	*25.6%*	*29.0%*	***30.0%***	*30.0%*
OPM101-treated		0	0	0	0	0	0	0	0	0	120	367	936	1,765	2,461	2,928	3,181	3,340
Price/y/pt (EUR)	52,500																	
Net sales USA		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**6**	**19**	**49**	**93**	**129**	**154**	**167**	**175**
EU5																		
ICI-treated population		17,012	17,863	18,756	19,694	20,679	21,713	22,798	23,938	25,135	26,392	27,711	29,097	30,552	32,079	33,683	35,368	37,136
ICI-associated diarrhea/colitis prevalence	*40%*																	
Grade II-IV	*75%*																	
Market share		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*1.0%*	*3.7%*	*8.2%*	*15.0%*	*21.8%*	*26.3%*	*28.5%*	***30.0%***
OPM101-treated		0	0	0	0	0	0	0	0	0	79	310	717	1,375	2,097	2,655	3,022	3,342
Price/y/pt (EUR)	36,750																	
Net sales EU5		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**3**	**11**	**26**	**51**	**77**	**98**	**111**	**123**
Japan																		
ICI-treated population		6,763	7,101	7,456	7,829	8,220	8,631	9,063	9,516	9,992	10,491	11,016	11,566	12,145	12,752	13,390	14,059	14,762
ICI-associated diarrhea/colitis prevalence	*40%*																	
Grade II-IV	*75%*																	
Market share		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*1.5%*	*4.4%*	*10.7%*	*19.3%*	*25.6%*	*29.0%*	***30.0%***	*30.0%*
OPM101-treated		0	0	0	0	0	0	0	0	0	48	146	372	702	979	1,165	1,265	1,329
Price/y/pt (EUR)	36,750																	
Net sales JPN		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**2**	**5**	**14**	**26**	**36**	**43**	**47**	**49**
Net sales OPM-101 in ICI-AC		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**11**	**36**	**89**	**169**	**242**	**294**	**325**	**347**

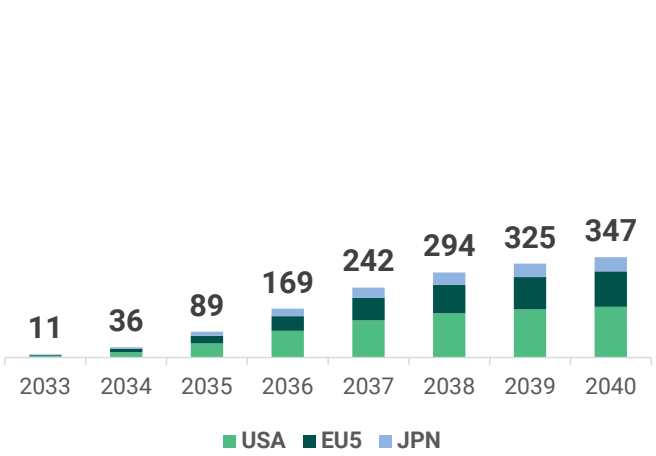
Source: Degroof Petercam estimates
Patent expiration expected in 2040 (Exhibit 69 in addendum).
We expect the Ph3 to commence in partnership with big pharma following Ph2b completion for IBD in 2028.

Exhibit 47 OPM-101 net sales projections in IBD



Source: Degroof Petercam estimates
Patent expiration expected in 2040 (Exhibit 69 in addendum).

Exhibit 48 OPM-101 net sales projections in ICI-AC



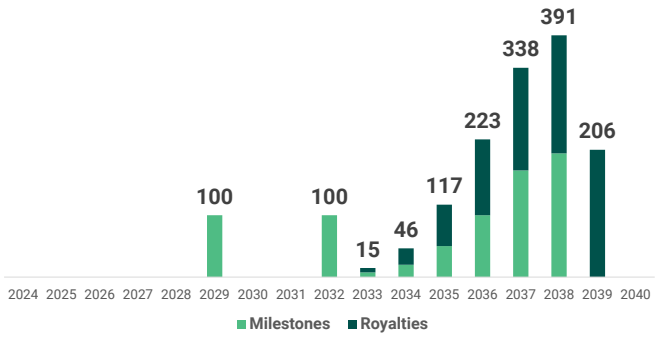
Source: Degroof Petercam estimates
Patent expiration expected in 2040 (Exhibit 69 in addendum).

Exhibit 49 OPM-101 revenue projections for OPM (EUR m)

	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040
years from now	0.75	1.75	2.75	3.75	4.75	5.75	6.75	7.75	8.75	9.75	10.75	11.75	12.75	13.75	14.75	15.75	16.75
stage IBD	Ph1	Ph2a	Ph2a	Ph2b	Ph2b	Ph3	Ph3	Ph3	Filing				Market				
stage ICI-AC	Ph1/2a	Ph2a	Ph2b	Ph2b	Ph3 ready	Ph3	Ph3	Ph3	Filing				Market				
Net sales OPM-101	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**48**	**175**	**447**	**818**	**1,106**	**1,273**	**1,373**	**1,438**
OPM-101 advanced by			OPM								Pharma						
Royalty	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*0%*
Royalty	0	0	0	0	0	0	0	0	0	7	26	67	123	166	191	206	0
Milestone payments (EUR 750m)	0	0	0	0	0	100	0	0	100	7.5	20	50	100	173	200	0	0
OPM revenue	**0**	**0**	**0**	**0**	**0**	**100**	**0**	**0**	**100**	**15**	**46**	**117**	**223**	**338**	**391**	**206**	**0**

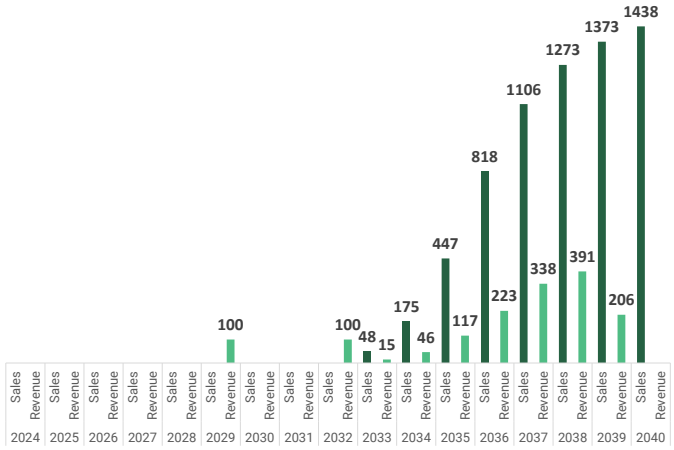
Source: Degroof Petercam estimates
Vertical line indicates transition to partnership.
Milestone payment amount based on gastrointestinal deal values for small molecules and biologics period 2012-2024 (Evaluate Pharma).
Patent expiration expected in 2040 (Exhibit 69 in addendum).

Exhibit 50 Combined OPM-101 revenue projections (EUR m)



Source: Degroof Petercam estimates
Patent expiration expected in 2040 (Exhibit 69 in addendum).

Exhibit 51 Combined OPM-101 net sales & revenue projections (EUR m)



Source: Degroof Petercam estimates
Patent expiration expected in 2040 (Exhibit 69 in addendum).

6.2 OPM-201: multi-blockbuster potential but clinical development path to be confirmed

Our net sales/royalty revenue projections for OPM-201 for PD amount to EUR 3.4bn/328m and EUR 3.1bn/258m for our base-case (Exhibit 52) and bear-case scenario (Exhibit 53), respectively.

PD projections:

- In line with the design of the Ph2b LUMA study with DNL151/BIIB122, we anticipate for our base-case scenario a registrational Ph2b/3 study with both PD patients with (familial+sporadic) and w/o (sporadic) LRRK2 mutations, following successful completion of the Ph1b. Our alternative bear-case scenario consists of a Ph2b followed by a stand-alone Ph3 study, pushing out the time-to-market with 3 years.
- Market share: peak penetration of 15% of the LRRK2 mutation-positive PD population and 5% of the LRRK2 mutation-negative PD population, as we anticipate some label restrictions (i.e. only patients meeting specific diagnostic criteria are treatment-eligible) and could envision other PD drugs to be approved by that time (including Denali/Biogen's LRRK2 inhibitor).

- Pricing: List price/patient/year in line with Leqembi®, a DMT for Alzheimer's disease (similar as PD a neurodegenerative disease). We include a gross-to-net adjustment of 10% in the USA to account for rebates, discounts, and other reductions. 30% price discount in EU5 and Japan. However, we admit that OPM-201 pricing is difficult to estimate as 1/ there is no DMT marketed for PD yet and 2/ this will be highly dependent on the clinical benefit it offers for patients. Hence, we conducted a sensitivity analysis to assess the impact of OPM-201 pricing and WACC on OPM-201 enterprise value (Exhibit 61, Exhibit 62 and Exhibit 70, Exhibit 71 in addendum).

Exhibit 52 OPM-201 net sales and revenue projections in PD (base-case) (EUR m)

		2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040
years from now		0.75	1.75	2.75	3.75	4.75	5.75	6.75	7.75	8.75	9.75	10.75	11.75	12.75	13.75	14.75	15.75	16.75
stage		Ph1	Ph1b	Ph1b	Ph2b/3	Ph2b/3	Ph2b/3	Ph2b/3	Filing					Market				
		2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040
USA																		
Population (m)		258.1	260.2	262.2	264.1	266.0	267.9	269.7	271.3	272.8	274.2	275.7	277.2	278.6	280.0	281.5	283.0	284.5
PD prevalence		1,000,000	1,030,000	1,061,415	1,094,319	1,128,790	1,164,911	1,202,771	1,242,462	1,284,085	1,327,744	1,373,551	1,421,625	1,472,093	1,525,088	1,580,754	1,639,242	1,700,713
% sporadic PD	85%																	
% sporadic PD with LRRK2 mutation	2%																	
Sporadic PD patients with LRRK2 mutation		17,000	17,510	18,044	18,603	19,189	19,803	20,447	21,122	21,829	22,572	23,350	24,168	25,026	25,926	26,873	27,867	28,912
Sporadic PD patients w/o LRRK2 mutation		833,000	857,990	884,159	911,568	940,282	970,371	1,001,908	1,034,971	1,069,643	1,106,010	1,144,168	1,184,214	1,226,253	1,270,398	1,316,768	1,365,488	1,416,694
% familial PD	15%																	
% familial PD with LRRK2 mutation	5%																	
Familial PD patients with LRRK2 mutation		7,500	7,725	7,961	8,207	8,466	8,737	9,021	9,318	9,631	9,958	10,302	10,662	11,041	11,438	11,856	12,294	12,755
Total PD patient population with LRRK2 mutation		24,500	25,235	26,005	26,811	27,655	28,540	29,468	30,440	31,460	32,530	33,652	34,830	36,066	37,365	38,728	40,161	41,667
Market share		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0.8%*	*2.3%*	*5.8%*	*10.3%*	*13.2%*	*14.4%*	*14.8%*	***15.0%***	*15.0%*
OPM201-treated		0	0	0	0	0	0	0	0	239	756	1950	3,572	4,767	5,393	5,744	6,004	6,244
Eligible PD patient population w/o LRRK2 mutation		833,000	857,990	884,159	911,568	940,282	970,371	1,001,908	1,034,971	1,069,643	1,106,010	1,144,168	1,184,214	1,226,253	1,270,398	1,316,768	1,365,488	1,416,694
Market share		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0.3%*	*0.7%*	*1.8%*	*3.2%*	*4.3%*	*4.7%*	*4.9%*	***5.0%***	*5.0%*
OPM-201-treated		0	0	0	0	0	0	0	0	2714	8,136	20,458	38,037	52,292	60,297	64,766	67,926	70,722
List price/y/pt (EUR)	25,000																	
Discount	*10%*																	
Net price/y/pt (EUR)	22,500																	
Net sales USA		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**66**	**200**	**504**	**936**	**1,284**	**1,478**	**1,586**	**1,663**	**1,732**
EU5																		
Total PD patient population with LRRK2 mutation		24,518	25,253	26,024	26,830	27,675	28,561	29,489	30,462	31,483	32,553	33,677	34,855	36,093	37,392	38,757	40,191	41,698
Market share		*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.4%*	*0.8%*	*2.3%*	*5.8%*	*10.3%*	*13.2%*	*14.4%*	*14.8%*	***15.0%***
OPM-201-treated		0	0	0	0	0	0	0	0	126	248	783	2,020	3,701	4,943	5,594	5,960	6,234
Eligible PD patient population w/o LRRK2 mutation		833,607	858,615	884,803	912,232	940,967	971,078	1,002,638	1,035,725	1,070,422	1,106,816	1,145,001	1,185,076	1,227,146	1,271,324	1,317,727	1,366,483	1,417,726
Market share		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0.1%*	*0.3%*	*0.7%*	*1.8%*	*3.2%*	*4.3%*	*4.7%*	*4.9%*	***5.0%***
OPM-201-treated		0	0	0	0	0	0	0	0	1358	2808	8423	21,189	39,416	54,214	62,543	67,211	70,524
Price/y/pt (EUR)	15,750																	
Net sales EU5		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**23**	**48**	**145**	**366**	**679**	**932**	**1,073**	**1,152**	**1,209**
Japan																		
Total PD patient population with LRRK2 mutation		9,746	10,039	10,345	10,665	11,001	11,353	11,722	12,109	12,515	12,940	13,387	13,855	14,347	14,864	15,406	15,976	16,575
Market share		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0.8%*	*2.3%*	*5.8%*	*10.3%*	*13.2%*	*14.4%*	*14.8%*	***15.0%***	*15.0%*
OPM-201-treated		0	0	0	0	0	0	0	0	95	301	776	1,421	1,896	2,145	2,285	2,388	2,484
Eligible PD patient population w/o LRRK2 mutation		331,371	341,312	351,722	362,625	374,048	386,018	398,563	411,716	425,508	439,976	455,155	471,085	487,809	505,370	523,816	543,197	563,567
Market share		*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.3%*	*0.7%*	*1.8%*	*3.2%*	*4.3%*	*4.7%*	*4.9%*	***5.0%***	*5.0%*
OPM-201-treated		0	0	0	0	0	0	0	0	1080	3236	8138	15,131	20,802	23,986	25,764	27,021	28,134
Price/y/pt (EUR)	15,750																	
Net sales JPN		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**19**	**56**	**140**	**261**	**358**	**412**	**442**	**463**	**482**
Net sales OPM-201		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**108**	**304**	**790**	**1,562**	**2,320**	**2,821**	**3,101**	**3,279**	**3,423**
Royalty		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*0%*
Royalty		0	0	0	0	0	0	0	0	11	30	79	156	232	282	310	328	0
Milestone payments			10		15				22.5	35	20	75	120					
OPM-201 revenue		**0**	**10**	**0**	**15**	**0**	**0**	**0**	**23**	**46**	**50**	**154**	**276**	**232**	**282**	**310**	**328**	**0**

Source: Degroof Petercam estimates

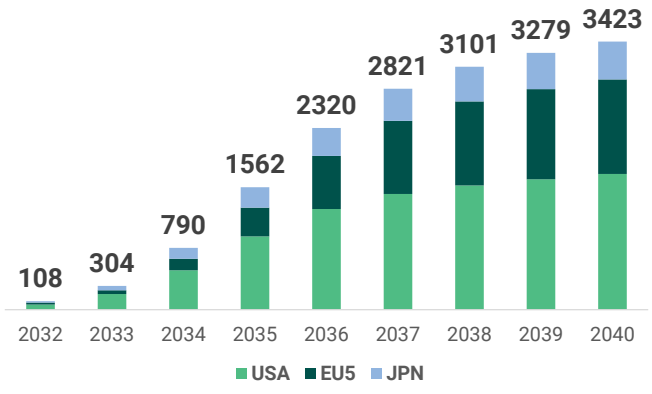
Patent expiration expected in 2040 (Exhibit 69 in addendum).

Exhibit 53 OPM-201 net sales and revenue projections in PD (bear-case) (EUR m)

		2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040
years from now		0.75	1.75	2.75	3.75	4.75	5.75	6.75	7.75	8.75	9.75	10.75	11.75	12.75	13.75	14.75	15.75	16.75
stage		Ph1	Ph1b	Ph1b	Ph2b	Ph2b	Ph2b	Ph3	Ph3	Ph3	Ph3	Filing				Market		
		2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040
USA																		
Population (m)		258.1	260.2	262.2	264.1	266.0	267.9	269.7	271.3	272.8	274.2	275.7	277.2	278.6	280.0	281.5	283.0	284.5
PD prevalence		1,000,000	1,030,000	1,061,415	1,094,319	1,128,790	1,164,911	1,202,771	1,242,462	1,284,085	1,327,744	1,373,551	1,421,625	1,472,093	1,525,088	1,580,754	1,639,242	1,700,713
% sporadic PD	*85%*																	
% sporadic PD with LRRK2 mutation	*2%*																	
Sporadic PD patients with LRRK2 mutation		17,000	17,510	18,044	18,603	19,189	19,803	20,447	21,122	21,829	22,572	23,350	24,168	25,026	25,926	26,873	27,867	28,912
Sporadic PD patients w/o LRRK2 mutation		833,000	857,990	884,159	911,568	940,282	970,371	1,001,908	1,034,971	1,069,643	1,106,010	1,144,168	1,184,214	1,226,253	1,270,398	1,316,768	1,365,488	1,416,694
% familial PD	*15%*																	
% familial PD with LRRK2 mutation	*5%*																	
Familial PD patients with LRRK2 mutation		7,500	7,725	7,961	8,207	8,466	8,737	9,021	9,318	9,631	9,958	10,302	10,662	11,041	11,438	11,856	12,294	12,755
Total PD patient population with LRRK2 mutation		24,500	25,235	26,005	26,811	27,655	28,540	29,468	30,440	31,460	32,530	33,652	34,830	36,066	37,365	38,728	40,161	41,667
Market share		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0.0%*	*0.0%*	*0.0%*	*0.8%*	*2.3%*	*5.8%*	*10.3%*	*13.2%*	***14.4%***
OPM201-treated		0	0	0	0	0	0	0	0	0	0	0	265	839	2,166	3,972	5,309	6,014
Eligible PD patient population w/o LRRK2 mutation		833,000	857,990	884,159	911,568	940,282	970,371	1,001,908	1,034,971	1,069,643	1,106,010	1,144,168	1,184,214	1,226,253	1,270,398	1,316,768	1,365,488	1,416,694
Market share		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0.0%*	*0.0%*	*0.0%*	*0.3%*	*0.7%*	*1.8%*	*3.2%*	*4.3%*	***4.7%***
OPM-201-treated		0	0	0	0	0	0	0	0	0	0	0	3,004	9,020	22,715	42,295	58,230	67,241
List price/y/pt (EUR)	25,000																	
Discount	*10%*																	
Net price/y/pt (EUR)	22,500																	
Net sales USA		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**74**	**222**	**560**	**1,041**	**1,430**	**1,648**
EU5																		
Total PD patient population with LRRK2 mutation		24,518	25,253	26,024	26,830	27,675	28,561	29,489	30,462	31,483	32,553	33,677	34,855	36,093	37,392	38,757	40,191	41,698
Market share		*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.4%*	*0.8%*	*2.3%*	*5.8%*	*10.3%*	***13.2%***
OPM-201-treated		0	0	0	0	0	0	0	0	0	0	0	139	275	870	2,246	4,122	5,512
Eligible PD patient population w/o LRRK2 mutation		833,607	858,615	884,803	912,232	940,967	971,078	1,002,638	1,035,725	1,070,422	1,106,816	1,145,001	1,185,076	1,227,146	1,271,324	1,317,727	1,366,483	1,417,726
Market share		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0.0%*	*0.0%*	*0.0%*	*0.1%*	*0.3%*	*0.7%*	*1.8%*	*3.2%*	***4.3%***
OPM-201-treated		0	0	0	0	0	0	0	0	0	0	0	1,503	3,113	9,352	23,561	43,891	60,458
Price/y/pt (EUR)	15,750																	
Net sales EU5		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**26**	**53**	**161**	**406**	**756**	**1,039**
Japan																		
Total PD patient population with LRRK2 mutation		9,746	10,039	10,345	10,665	11,001	11,353	11,722	12,109	12,515	12,940	13,387	13,855	14,347	14,864	15,406	15,976	16,575
Market share		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0.8%*	*2.3%*	*5.8%*	*10.3%*	*13.2%*	***14.4%***
OPM-201-treated		0	0	0	0	0	0	0	0	0	0	0	105	334	862	1,580	2,112	2,392
Eligible PD patient population w/o LRRK2 mutation		331,371	341,312	351,722	362,625	374,048	386,018	398,563	411,716	425,508	439,976	455,155	471,085	487,809	505,370	523,816	543,197	563,567
Market share		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0.3%*	*0.7%*	*1.8%*	*3.2%*	*4.3%*	***4.7%***
OPM-201-treated		0	0	0	0	0	0	0	0	0	0	0	1,195	3,588	9,036	16,825	23,164	26,749
Price/y/pt (EUR)	15,750																	
Net sales JPN		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**20**	**62**	**156**	**290**	**398**	**459**
Net sales OPM-201		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**120**	**337**	**877**	**1,737**	**2,584**	**3,146**
Royalty		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*10%*	*10%*	*10%*	*10%*	*10%*	*0%*
Royalty		0	0	0	0	0	0	0	0	0	0	0	12	34	88	174	258	0
Milestone payments			10		15							22.5	35	20	75	120		
OPM-201 revenue		**0**	**10**	**0**	**15**	**0**	**0**	**0**	**0**	**0**	**0**	**23**	**47**	**54**	**163**	**294**	**258**	**0**

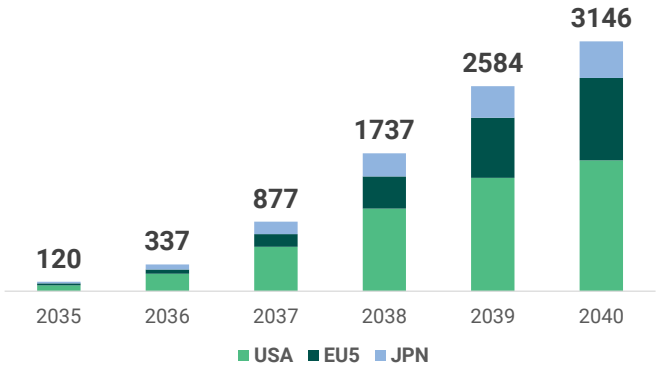
Source: Degroof Petercam estimates
Patent expiration expected in 2040 (Exhibit 69 in addendum).

Exhibit 54 OPM-201 net sales projections in PD (base-case, EUR m)



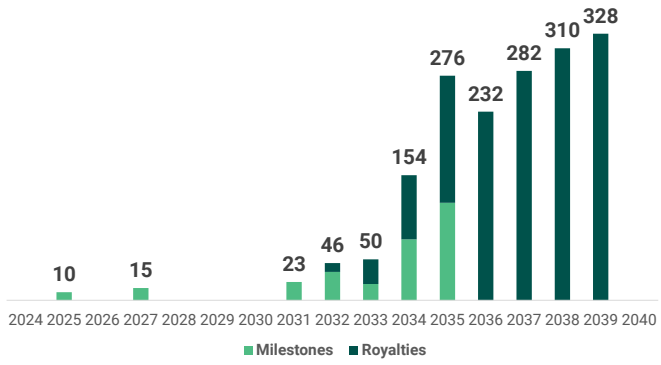
Source: Degroof Petercam estimates
Patent expiration expected in 2040 (Exhibit 69 in addendum).

Exhibit 55 OPM-201 net sales projections in PD (bear-case, EUR m)



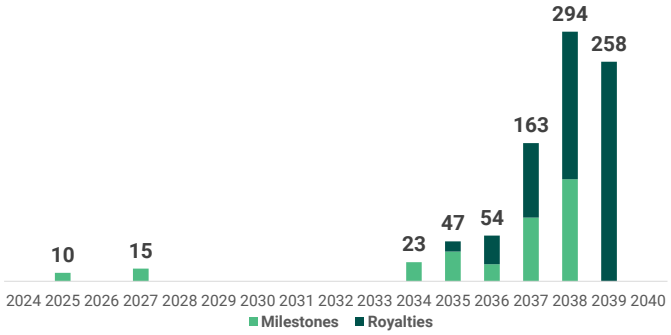
Source: Degroof Petercam estimates
Patent expiration expected in 2040 (Exhibit 69 in addendum).

Exhibit 56 OPM-201 revenue projections in PD (base-case, EUR m)



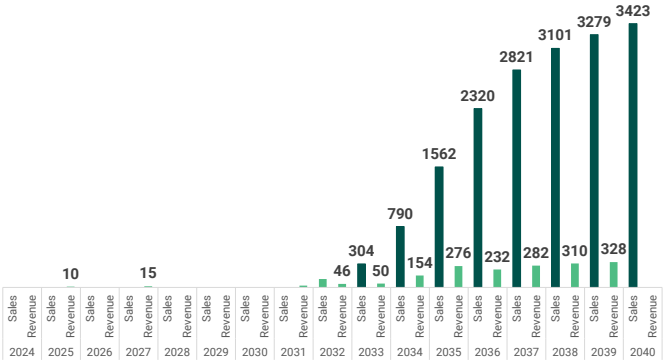
Source: Degroof Petercam estimates
Patent expiration expected in 2040 (Exhibit 69 in addendum).

Exhibit 57 OPM-201 revenue projections in PD (bear-case, EUR m)



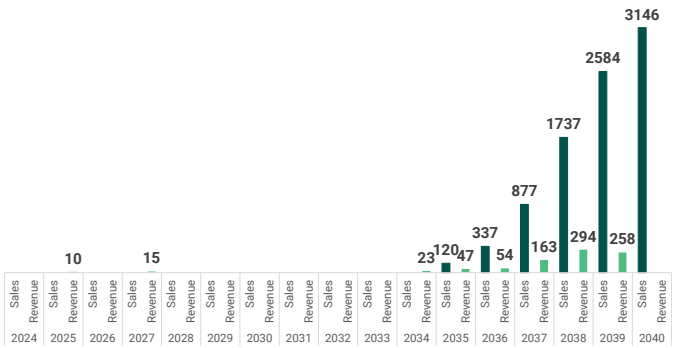
Source: Degroof Petercam estimates
Patent expiration expected in 2040 (Exhibit 69 in addendum).

Exhibit 58 OPM-201 net sales & revenue projections in PD (base-case, EUR m)



Source: Degroof Petercam estimates
Patent expiration expected in 2040 (Exhibit 69 in addendum).

Exhibit 59 OPM-201 net sales & revenue projections in PD (bear-case, EUR m)



Source: Degroof Petercam estimates
Patent expiration expected in 2040 (Exhibit 69 in addendum).

7/ Valuation

We value OPM using a Sum-of-the-Parts (rNPV-based, projection period until 2040) based on OPM-101 (IBD and ICI-AC opportunities) and OPM-201 and implement a WACC in line with the risk profile of the company expected to advance the asset in the respective year: 15% in case of OPM and 9% for a (big) pharma partner. We account for both clinical and partnership risk by incorporating success rates for 1/ each clinical study and regulatory decision step, and 2/ the occurrence of an out-licensing event for OPM-101 post-Ph2b. We currently omit any potential additional (royalty) revenues and costs stemming from discovery/preclinical-stage oncology programs.

7.1/ Costs assumptions

- OPM-101 for IBD and ICI-AC:
  - We omit COGS and S&M expenses given the (expected) commercial partnership from Ph3 onwards.
  - We include a G&A cost of EUR 3.2m for 2024 (i.e. c. 85%[41] of estimated 2024 G&A cost of EUR 3.7m for the whole company which we model 10% higher vs. the 2023 G&A cost) gradually evolving to EUR 6.8m by 2028 (year before expected partnership).
  - Our DPe for the remaining cost of the Ph1 and expenses related to the follow-up Ph2a+b studies for IBD and ICI-AC amount to close to EUR 40m[42].
- OPM-201 for PD:
  - Since OPM-201 is already Servier-partnered, we omit operational expenses (COGS, SG&A, & R&D costs), D&A, and CAPEX from our rNPV calculation.

7.2/ Tax rate

We include a tax rate of 15% (based on the French tax policy for licensing-related revenues including upfront and milestone payments, and royalties) and offset this with any amassed tax credits.

[41] Given the ongoing Ph1 in healthy volunteers and planned Ph2a for ICI-AC, we anticipate the majority of G&A costs to stem from OPM-101 clinical development activities.
[42] Based on company guidance + estimates indicated on 'fromsciencetopharma.com'.

Exhibit 60 OPM-101 valuation (EUR m)

		2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040
years from now		0.75	1.75	2.75	3.75	4.75	5.75	6.75	7.75	8.75	9.75	10.75	11.75	12.75	13.75	14.75	15.75	16.75
stage IBD		Ph1	Ph2a	Ph2a	Ph2b	Ph2b	Ph3	Ph3	Ph3	Filing				Market				
stage ICI-AC		Ph1/2a	Ph2a	Ph2b	Ph2b	Ph3 ready	Ph3	Ph3	Ph3	Filing				Market				
Net sales OPM-101		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**48**	**175**	**447**	**818**	**1,106**	**1,273**	**1,373**	**1,438**
OPM-101 advanced by				OPM								Pharma						
Royalty		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*0%*
Royalty		0	0	0	0	0	0	0	0	0	7	26	67	123	166	191	206	0
Milestone payments (EUR 750m)		0	0	0	0	0	100	0	0	100	7.5	20	50	100	173	200	0	0
OPM revenue		**0**	**0**	**0**	**0**	**0**	**100**	**0**	**0**	**100**	**15**	**46**	**117**	**223**	**338**	**391**	**206**	**0**
COGS																		
Gross profit		0	0	0	0	0	100	0	0	100	15	46	117	223	338	391	206	0
G&A		-3.2	-4.9	-5.5	-6.3	-6.8	0											
R&D		-2.8	-9.0	-10.0	-11.25	-6.3												
S&M																		
OPEX		-6	-14	-15	-18	-13.1	0	0	0	0	0	0	0	0	0	0	0	0
Operating profit/EBITDA		-6	-14	-15	-18	-13	100	0	0	100	15	46	117	223	338	391	206	0
D&A		-0.4	-0.5	-0.6	-0.7	-0.8												
EBIT		-6	-14	-16	-18	-14	100	0	0	100	15	46	117	223	338	391	206	0
Tax expense	*15%*	0	0	0	0	0	-6.9	0	0	-15	-2	-7	-18	-33	-51	-59	-31	0
EBI(T)		-6	-14	-16	-18	-14	93	0	0	85	13	39	99	189	288	332	175	0
D&A		0.4	0.5	0.6	0.7	0.8												
CAPEX		-2.7	-3.0	-3.3	-3.6	-4.0												
FCF		**-9**	**-17**	**-19**	**-21**	**-17**	**93**	**0**	**0**	**85**	**13**	**39**	**99**	**189**	**288**	**332**	**175**	**0**
Likelihood of success		*95%*	*95%*	*81%*	*81%*	*100%*	*35%*	*100%*	*100%*	*65%*	*90%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*
Cumulative success rate		*95%*	*90%*	*73%*	*60%*	*60%*	*21%*	*21%*	*21%*	*14%*	*12%*	*12%*	*12%*	*12%*	*12%*	*12%*	*12%*	*12%*
rFCF		**-8**	**-15**	**-14**	**-13**	**-10**	**19**	**0**	**0**	**12**	**2**	**5**	**12**	**23**	**35**	**41**	**21**	**0**
WACC		*15%*	*15%*	*15%*	*15%*	*15%*	*9.0%*	*9.0%*	*9.0%*	*9.0%*	*9.0%*	*9.0%*	*9.0%*	*9.0%*	*9.0%*	*9.0%*	*9.0%*	*9.0%*
Discounted rFCF		**-7.4**	**-11.9**	**-9.3**	**-7.5**	**-5.2**	**11.8**	**0.0**	**0.0**	**5.4**	**0.7**	**1.9**	**4.4**	**7.7**	**10.7**	**11.4**	**5.5**	**0.0**
Advancing OPM-101				OPM								Pharma partner						
Success rate partnership	*75%*																	
Adjusted discouted rFCF		-7.4	-11.9	-9.3	-7.5	-5.2	8.9	0.0	0.0	4.1	0.5	1.4	3.3	5.8	8.0	8.5	4.1	0.0

rNPV	**3.4**

Source: Degroof Petercam estimates
Vertical line indicates transition to partnership.
Patent expiration expected in 2040 (Exhibit 69 in addendum).

Exhibit 61 OPM-201 valuation (base-case, EUR m)

		2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040
years from now		0.75	1.75	2.75	3.75	4.75	5.75	6.75	7.75	8.75	9.75	10.75	11.75	12.75	13.75	14.75	15.75	16.75
stage		Ph1	Ph1b	Ph1b	Ph2b/3	Ph2b/3	Ph2b/3	Ph2b/3	Filing					Market				
Net sales OPM-201		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**108**	**304**	**790**	**1,562**	**2,320**	**2,821**	**3,101**	**3,279**	**3,423**
Royalty		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*0%*
Royalty		0	0	0	0	0	0	0	0	11	30	79	156	232	282	310	328	0
Milestone payments			10		15				22.5	35	20	75	120					
OPM-201 revenue		**0**	**10**	**0**	**15**	**0**	**0**	**0**	**23**	**46**	**50**	**154**	**276**	**232**	**282**	**310**	**328**	**0**
Gross profit		0	10	0	15	0	0	0	23	46	50	154	276	232	282	310	328	0
Operating profit/EBITDA		0	10	0	15	0	0	0	23	46	50	154	276	232	282	310	328	0
EBIT		0	10	0	15	0	0	0	23	46	50	154	276	232	282	310	328	0
Tax expense	*15%*	0	0	0	0	0	0	0	-1	-7	-8	-23	-41	-35	-42	-47	-49	0
EBI(T)		0	10	0	15	0	0	0	22	39	43	131	235	197	240	264	279	0
FCF		**0**	**10**	**0**	**15**	**0**	**0**	**0**	**22**	**39**	**43**	**131**	**235**	**197**	**240**	**264**	**279**	**0**
Likelihood of success		*100%*	*90%*	*100%*	*59%*	*100%*	*100%*	*100%*	*12%*	*85%*	*100%*	*100.0%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*
Cumulative success rate		*100%*	*90%*	*90%*	*53%*	*53%*	*53%*	*53%*	*6%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*
rFCF		**0**	**9**	**0**	**8**	**0**	**0**	**0**	**1**	**2**	**2**	**7**	**13**	**11**	**13**	**14**	**15**	**0**
WACC	*9%*																	
Discounted rFCF		**0.0**	**7.7**	**0.0**	**5.7**	**0.0**	**0.0**	**0.0**	**0.7**	**1.0**	**1.0**	**2.7**	**4.5**	**3.4**	**3.8**	**3.8**	**3.7**	**0.0**

rNPV	**38.1**

Source: Degroof Petercam estimates
Patent expiration expected in 2040 (Exhibit 69 in addendum).

Exhibit 62 OPM-201 valuation (bear-case, EUR m)

		2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040
years from now		0.75	1.75	2.75	3.75	4.75	5.75	6.75	7.75	8.75	9.75	10.75	11.75	12.75	13.75	14.75	15.75	16.75
stage		Ph1	Ph1b	Ph1b	Ph2b	Ph2b	Ph2b	Ph3	Ph3	Ph3	Ph3	Filing			Market			
Net sales OPM-201		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**120**	**337**	**877**	**1,737**	**2,584**	**3,146**
Royalty		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*10%*	*10%*	*10%*	*10%*	*10%*	*0%*
Royalty		0	0	0	0	0	0	0	0	0	0	0	12	34	88	174	258	0
Milestone payments			10		15							22.5	35	20	75	120		
% of net sales														*6%*	*9%*	*7%*		
OPM-201 revenue		**0**	**10**	**0**	**15**	**0**	**0**	**0**	**0**	**0**	**0**	**23**	**47**	**54**	**163**	**294**	**258**	**0**
Gross profit		0	10	0	15	0	0	0	0	0	0	23	47	54	163	294	258	0
Operating profit/EBITDA		0	10	0	15	0	0	0	0	0	0	23	47	54	163	294	258	0
EBIT		0	10	0	15	0	0	0	0	0	0	23	47	54	163	294	258	0
Tax expense	*15%*	0	0	0	0	0	0	0	0	0	0	-1	-7	-8	-24	-44	-39	0
EBI(T)		0	10	0	15	0	0	0	0	0	0	22	40	46	138	250	220	0
FCF		**0**	**10**	**0**	**15**	**0**	**0**	**0**	**0**	**0**	**0**	**22**	**40**	**46**	**138**	**250**	**220**	**0**
Likelihood of success		*100%*	*90%*	*100%*	*59%*	*100%*	*100%*	*27%*	*100%*	*100%*	*100%*	*45.9%*	*85%*	*100%*	*100%*	*100%*	*100%*	*100%*
Cumulative success rate		*100%*	*90%*	*90%*	*53%*	*53%*	*53%*	*14%*	*14%*	*14%*	*14%*	*6%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*
rFCF		**0**	**9**	**0**	**8**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**2**	**3**	**8**	**14**	**12**	**0**
WACC	*9%*																	
Discounted rFCF		**0.0**	**7.7**	**0.0**	**5.7**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.5**	**0.8**	**0.8**	**2.2**	**3.6**	**2.9**	**0.0**

rNPV	**24.2**

Source: Degroof Petercam estimates

Patent expiration expected in 2040 (Exhibit 69 in addendum).

Based on a net cash position of EUR 6.8m[43] and 18.2m[44] outstanding shares, we arrive at an equity value range of EUR 34.5-48.3m translating into a target valuation range of EUR 1.9-2.7 (Exhibit 63). We do want to point out that this range does not include the dilutive impact of any potential capital raises in the future.

Exhibit 63 Valuation summary

Asset	Indication	Scenario	Launch	LoA	Peak Sales (EUR m)	Peak Revenue (EUR m)	rNPV (EUR m)
OPM-101	IBD	N/A	2033	12%	1091	391	3.4
	ICI-AC	N/A	2033	12%	347		
OPM-201	Parkinson's disease	base-case	2032	5%	3423	328	38.1
	Parkinson's disease	bear-case	2035	5%	3146	294	24.2

Enterprise value (base case, EUR m)	41.5
Enterprise value (bear-case, EUR m)	27.6
Net cash (EUR m)	6.8
Equity value (base case, EUR m)	48.3
Equity value (bear case, EUR m)	34.5
Outstanding shares (m)	18.2
Target valuation range (EUR)	**1.9-2.7**

Source: Degroof Petercam estimates

[43] (EUR 10m at 2023 end + EUR 2.1m ERDF funding + EUR 1.7m net proceeds from fundraising + EUR 750k DTD grant funding) – (EUR 6m bank loan + EUR 1.75m BPI loan)

[44] Bloomberg April 9, 2024

8/ Investment conclusion

We consider OPM an attractive investment opportunity considering the following elements:

- **OPM-101: RIPK2 inhibitor for immune checkpoint inhibitor-associated colitis (ICI-AC) and inflammatory bowel diseases (IBDs)**
  - Compelling scientific rationale and (pre)clinical data, indicating safety, preliminary efficacy, and selectivity, support RIPK2 inhibition as a mechanism of action to target both ICI-AC and IBD (UC and CD).
  - **Immunomodulator** (rather than immunosuppressor), acting via a **distinct molecular pathway**, allowing for convenient **oral administration potentially in combo therapy** while preserving the immune system's ability to fight infections. Hence, differentiated enough to break into both the (crowded) IBD and ICI-AC markets.
  - We project EUR 400m in revenue at peak for OPM, based on an envisioned (big) pharma partnership for ICI-AC and IBD post-Ph2b.

- **OPM-201: lucrative partnership since 2019 with French pharma company Servier on LRRK2 kinase inhibitors for Parkinson's disease (PD)**
  - Servier-launched Ph1 in healthy volunteers expected to readout in H1 2025.
  - **EUR 300m in biobucks + royalties on net sales** offering significant financial upside for OPM and external validation for its innovative technology suite.
  - **PD is a blockbuster opportunity** for which we model at least EUR 3bn in peak sales translating into > EUR 300m in royalty revenue for OPM.

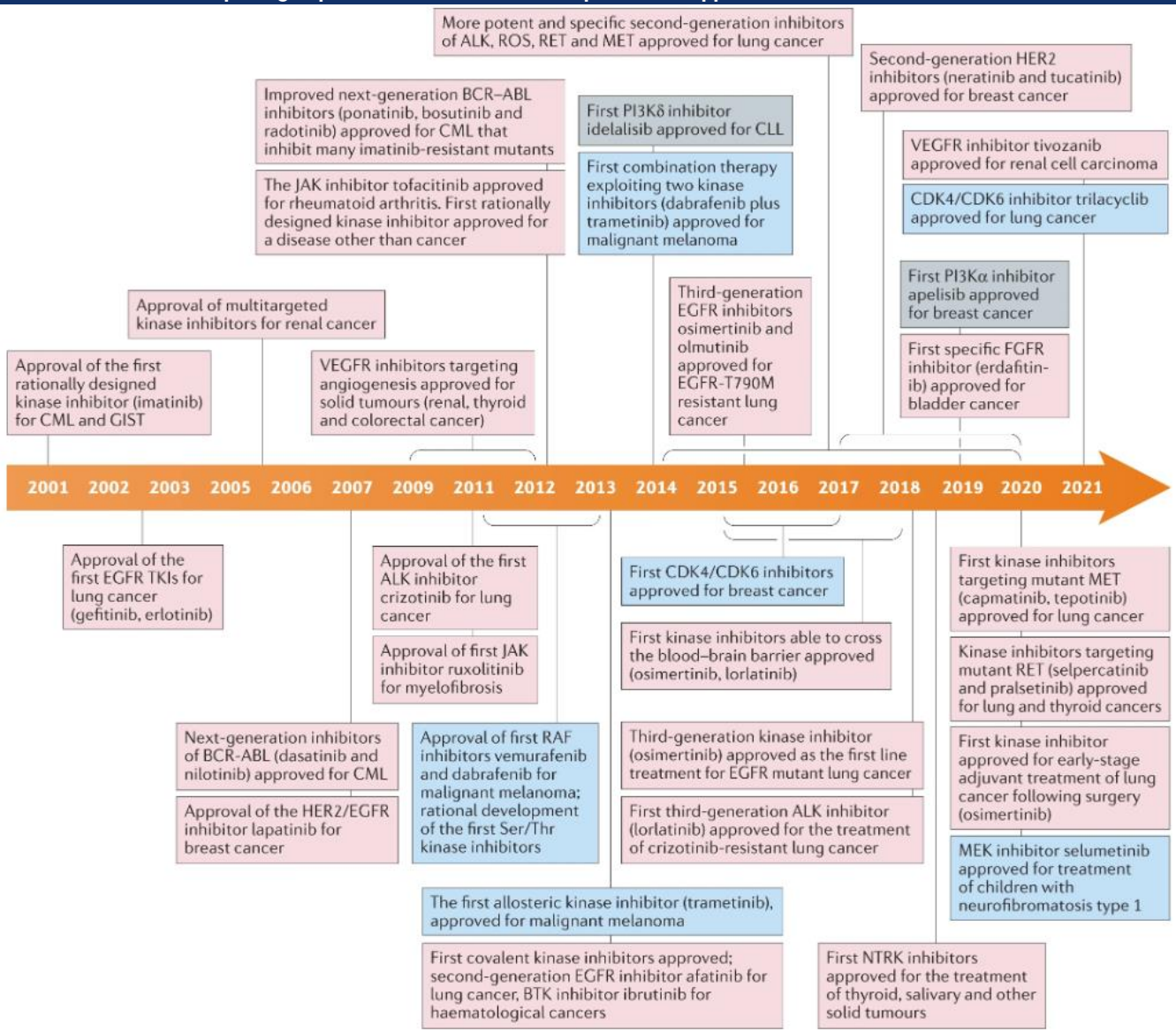
- **Industry-unique small molecule database** offering opportunities for new pipeline additions and potential out-licensing.

- **Seasoned management team** with a strong entrepreneurial track record.

- **Attractive 12-month news flow** including two Ph1 study readouts with both OPM-101 and OPM-201 which increase our target valuation range, which already offers a > 25% upside to the last closing price, with c.10% if successful.

9/ Addendum

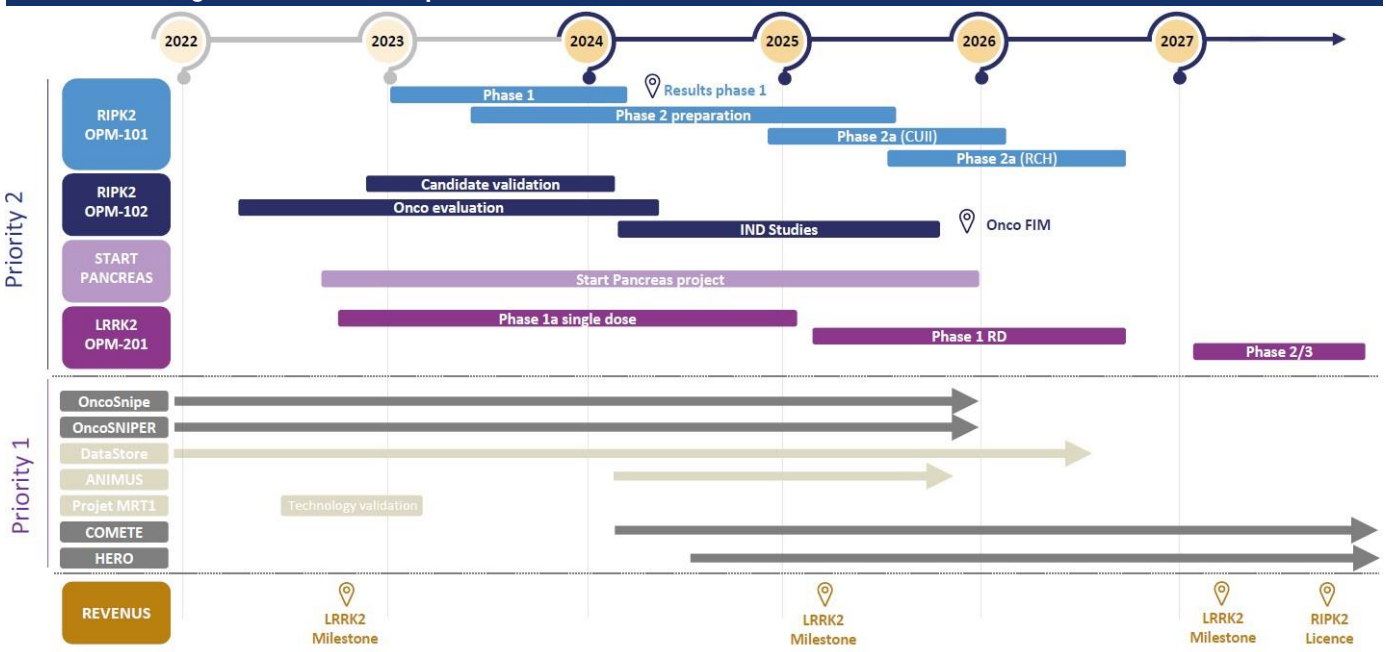
Exhibit 64 Timeline depicting important events in the development and approval of kinase inhibitors



Source: Cohen et al. (2021)

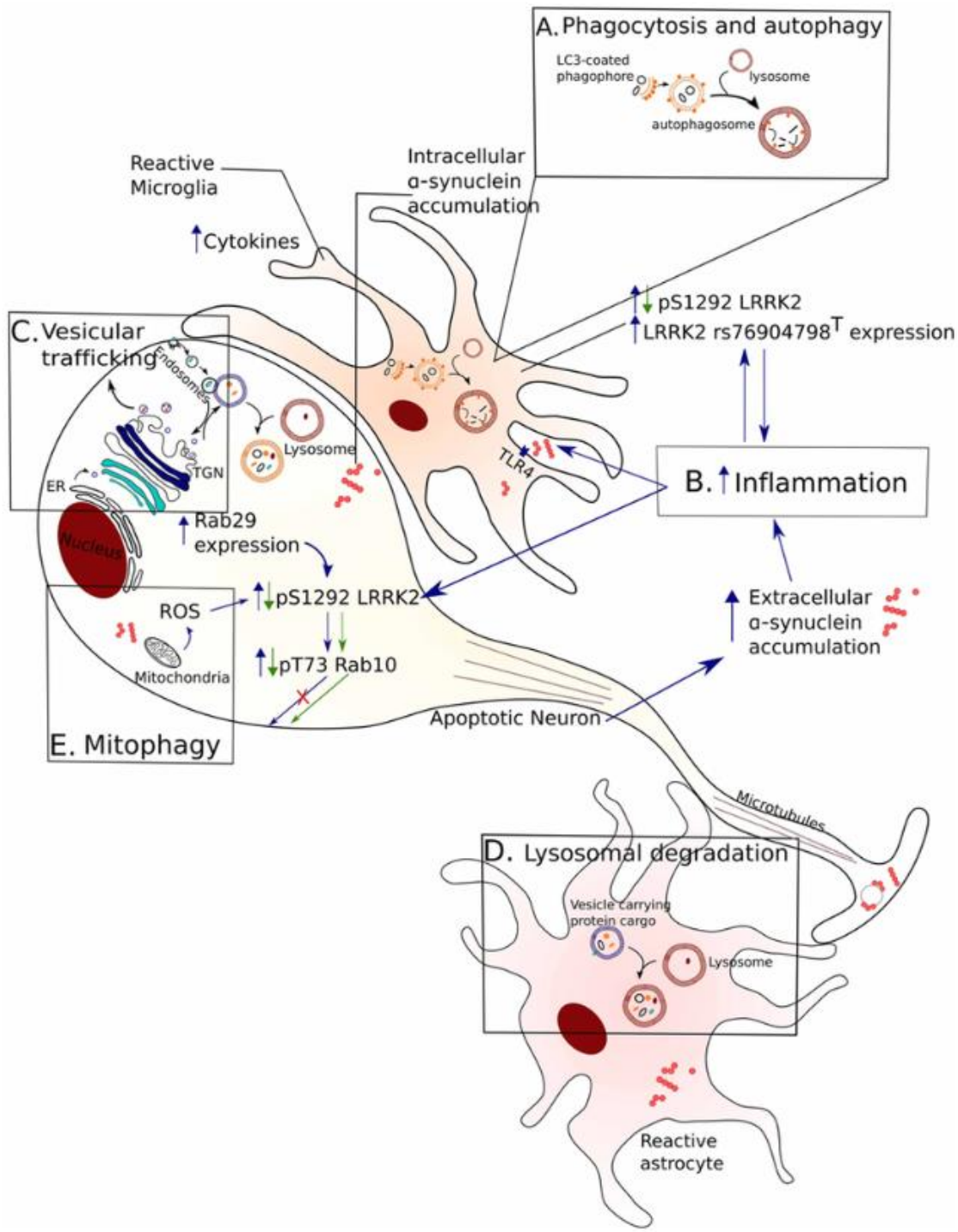
Events involving tyrosine kinases are in pink boxes, those involving serine/threonine-specific protein kinases are in blue boxes and those involving phosphatidylinositol 3-kinases (PI3Ks) are in grey boxes. BTK, Bruton's tyrosine kinase; CML, chronic myeloid leukaemia; CLL, chronic lymphocytic leukaemia; EGFR, epidermal growth factor receptor; FGFR, fibroblast growth factor receptor; GIST, gastrointestinal tumour; NTRK, neurotrophic receptor tyrosine kinase; TKI, tyrosine kinase inhibitor.

Exhibit 65 Program Gantt chart and prioritization



Source: OPM
CUII: immune checkpoint inhibitor-associated colitis
RCH: ulcerative colitis
FIM: first-in-man

Exhibit 66 Physiological pathways of LRRK2 activity



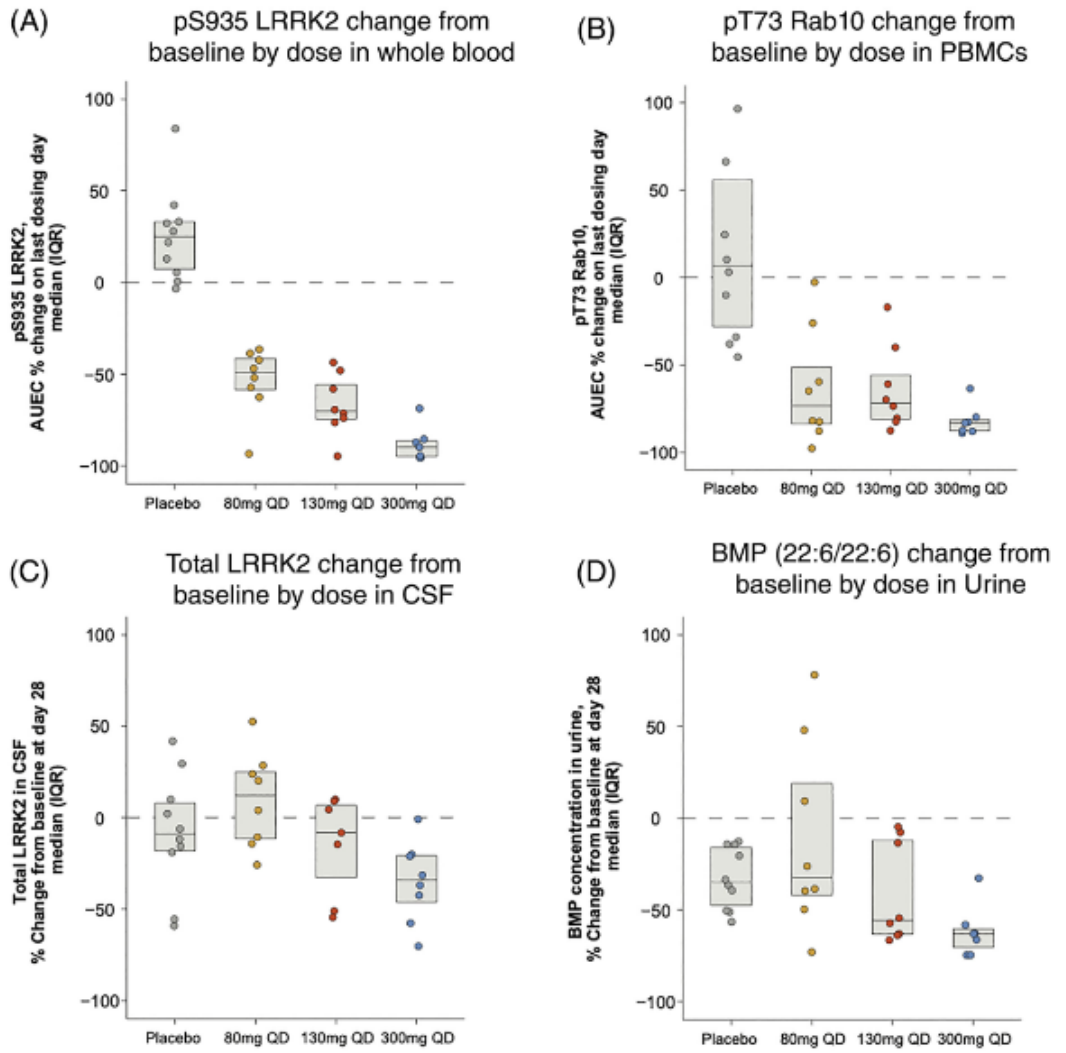
Source: A common function of LRRK2 in genetic and sporadic PD can be modelled on physiological signaling pathways important for neuronal survival. A generic apoptotic neuron (without dendrites for simplicity) and reactive glial cells are depicted and highlighted pathways are shown along with downstream effects of increased LRRK2 activity. Blue arrows indicate a gain-of-function pathway where increased LRRK2 kinase activity may drive dysfunction while green arrows highlight the molecular events of pharmacological LRRK2 inhibition. (A) LRRK2 has been linked to autophagosome maturation and impaired phagocytosis nominating these processes as possible culprits in the clearance of aggregated synuclein. (B) LRRK2 is activated in systems of induced inflammation while higher LRRK2 levels are seen in immune cells from idiopathic PD patients compared with healthy controls. Accumulation of extracellular synuclein can further induce an inflammatory response and this, in turn, can lead to LRRK2 activation. (C) LRRK2 interacts with Rab29 and mediates TGN dynamics while Rab29 expression can drive LRRK2 activation. Active LRRK2 phosphorylates Rab GTPases with downstream effects on vesicular trafficking as well as impaired autophagy/lysosomal pathways (D) that can impair clearance of aggregated proteins. (E) Progressive increase in ROS with ageing can activate LRRK2 that in turn can affect mitochondrial function and impair mitochondrial clearance through mitophagy.

Exhibit 67 Ph1b results indicate DNL151/BIIB122 administration is well tolerated in PD patients

	Placebo QD (N = 10)	BIIB122 QD 80 mg (N = 8)	BIIB122 QD 130 mg (N = 9)	BIIB122 QD 300 mg (N = 9)	BIIB122 Total (N = 26)
Any TEAE (n [%])[a]	5 (50.0)	8 (100.0)	8 (88.9)	7 (77.8)	23 (88.5)
Severe	0	0	1 (11.1)[b]	1 (11.1)[c]	2 (7.7)
Moderate	1 (10.0)	1 (12.5)	2 (22.2)	2 (22.2)	5 (19.2)
Mild	4 (40.0)	7 (87.5)	5 (55.6)	4 (44.4)	16 (61.5)
Study drug–related TEAE (n [%])	3 (30.0)	4 (50.0)	3 (33.3)	7 (77.8)	14 (53.8)
TEAE leading to study drug discontinuation (n [%])	0	0	1 (11.1)	1 (11.1)	2 (7.7)
Most Common TEAEs (Reported for ≥5% Patients Overall) by Preferred Term (n [%])					
Headache	2 (20.0)	4 (50.0)	2 (22.2)	5 (55.6)	11 (42.3)
Back pain	0	1 (12.5)	3 (33.3)	2 (22.2)	6 (23.1)
Tremor	2 (20.0)	1 (12.5)	2 (22.2)	1 (11.1)	4 (15.4)
Nasopharyngitis	0	2 (25.0)	3 (33.3)	0	5 (19.2)
Procedural pain	1 (10.0)	2 (25.0)	1 (11.1)	1 (11.1)	4 (15.4)
Nausea	0	1 (12.5)	1 (11.1)	2 (22.2)	4 (15.4)
Myalgia	1 (10.0)	1 (12.5)	1 (11.1)	1 (11.1)	3 (11.5)
Dizziness	0	0	1 (11.1)	2 (22.2)	3 (11.5)
Hypotension	0	0	1 (11.1)	2 (22.2)	3 (11.5)
Orthostatic hypotension	0	1 (12.5)	0	2 (22.2)	3 (11.5)
Hyperhidrosis	1 (10.0)	0	0	2 (22.2)	2 (7.7)
Cough	2 (20.0)	0	1 (11.1)	0	1 (3.8)
Fatigue	0	2 (25.0)	0	0	2 (7.7)
Gastrooesophageal reflux disease	0	0	1 (11.1)	1 (11.1)	2 (7.7)
Insomnia	0	1 (12.5)	0	1 (11.1)	2 (7.7)
Vomiting	0	1 (12.5)	0	1 (11.1)	2 (7.7)
Dizziness postural	1 (10.0)	1 (12.5)	0	0	1 (3.8)
Hypoacusis	1 (10.0)	0	0	1 (11.1)	1 (3.8)
Tinnitus	1 (10.0)	0	0	1 (11.1)	1 (3.8)

Source: Jennings et al. (2022).
Abbreviations: QD = once daily; TEAE = treatment-emergent adverse event.
Data are n (%) of patients.
TEAE Preferred Terms are shown in order of decreasing frequency overall.
No deaths or serious adverse events were reported in the study.
a Each patient is counted only once, in the highest severity category.
b Severe TEAE (asymptomatic hypotension) in one patient randomized to BIIB122 130 mg QD, reported as not related to study drug, led to early discontinuation of study drug.
c Severe TEAE (headache) in one patient randomized to BIIB122 300 mg QD, onset after last dose study drug, reported as not related to study drug.

Exhibit 68 Ph1b study: dose-dependent target and pathway engagement in patients with PD in multiple-dose cohorts



Source: Jennings et al. (2023).
Pharmacodynamics of LRRK2 inhibition in patients with PD in the phase 1b study. (A) pS935 LRRK2 reduction from baseline in whole blood. (B) pT73 Rab10 reduction from baseline in PBMCs. One placebo outlier for pT73 Rab10 with > 100% increase is not shown. Inhibition of LRRK2 over the dosing interval at steady state, as measured by average reduction in whole-blood pS935 LRRK2 and PBMC pT73 Rab10, was calculated as the median percent change from baseline time-adjusted AUEC on the last dosing day. Whole-blood and PBMC samples were collected at the following time points: day −1, day 1 predose, and on the last dosing day at predose and 1, 3, 8, and 24 hours postdose. Baseline was calculated as the average of day −1 and day 1 predose values. (C) Total LRRK2 reduction from baseline in CSF in response to LRRK2 inhibition. CSF was collected at day −1 and day 28 3 hours postdose. (D) Urine BMP reduction from baseline in response to LRRK2 inhibition. Urine samples were collected on day −1 and 1–6 hours postdose on the last day of dosing. Urine BMP concentrations were reported as a ratio to urine creatinine concentrations (ng BMP/mg creatinine). AUEC, area under the effect curve from time 0 to 24 hours (or 12 hours for Part E); BMP, bis(monoacylglycerol)phosphate; BMP(22:6/22:6), di-docosahexaenoyl bis(monoacylglycerol)phosphate; CSF, cerebrospinal fluid; IQR, interquartile range; LRRK2, leucine-rich repeat kinase 2; PBMC, peripheral blood mononuclear cell; PD, Parkinson's disease; pS935, phosphorylated serine 935; pT73, phosphorylated threonine 73; qd, once daily.

Exhibit 69 OPM's intellectual property position

Patent	Application number	Target	Date of registration	Expiry date	Publication date	Status
ONC-026	WO2016042087	RIPK2 Rig.	17/09/2014	17/09/2034	24/03/2016	National phase
ONC-027	WO2017148925	PET Tracer	29/02/2016	29/02/2036	08/09/2017	National phase
ONC-036	WO2021152165	RIPK2 ONN Lactams	31/01/2020	31/01/2040(1)	05/08/2021	National phase
ODS1(2)	WO2021224320	LRRK2 Carbamates	06/05/2020	06/05/2040(1)	11/11/2021	National phase
ODS2(2)	WO2022194976	LRRK2 Ethers/Amides/Amines	18/03/2021	18/03/2041(1)	22/09/2022	Published

Source:OPM

Exhibit 70 OPM-201 sensitivity analysis (base-case)

		List price (EUR)								
	38.1	15,000	**25,000**	35,000	45,000	55,000	65,000	75,000	85,000	95,000
WACC	7%	35.3	45.4	55.4	65.5	75.6	85.6	95.7	105.8	115.8
	8%	32.6	41.5	50.4	59.3	68.1	77.0	85.9	94.8	103.6
	9%	30.2	**38.1**	45.9	53.8	61.6	69.4	77.3	85.1	93.0
	10%	28.1	35.0	42.0	48.9	55.9	62.8	69.7	76.7	83.6
	11%	26.2	32.3	38.5	44.6	50.8	56.9	63.1	69.2	75.4

Source: Degroof Petercam estimates

Exhibit 71 OPM-201 sensitivity analysis (bear-case)

		List price (EUR)								
	24.2	15,000	**25,000**	35,000	45,000	55,000	65,000	75,000	85,000	95,000
WACC	7%	24.5	28.2	31.8	35.5	39.2	42.8	46.5	50.1	53.8
	8%	22.9	26.1	29.3	32.5	35.7	38.9	42.0	45.2	48.4
	9%	21.4	**24.2**	27.0	29.8	32.6	35.4	38.2	41.0	43.8
	10%	20.2	22.6	25.0	27.5	29.9	32.4	34.8	37.2	39.7
	11%	19.0	21.1	23.3	25.4	27.6	29.7	31.8	34.0	36.1

Source: Degroof Petercam estimates

Profit & loss (EUR m)	12/22a	12/23e	12/24e	12/25e	12/26e
Revenues	**8.3**	**1.8**	**4.7**	**11.8**	**1.8**
of which Sales	8.0	1.1	1.1	1.1	1.1
of which Other revenues	0.3	0.7	3.6	10.7	0.7
Total operating costs	-9.1	-12.2	-12.8	-20.7	-23.2
of which R&D costs	-7.0	-8.8	-9.1	-16.6	-18.7
EBITDA	-0.6	-10.1	-7.8	-8.4	-20.9
EBIT	**-0.8**	**-10.4**	**-8.2**	**-8.9**	**-21.4**
Net financial result	-0.1	0.1	-0.2	-0.0	0.2
Pre-tax result	**-0.9**	**-10.3**	**-8.4**	**-8.9**	**-21.2**
Taxes	1.5	1.8	1.5	1.6	3.7
Tax rate	*160.9%*	*17.5%*	*17.7%*	*17.6%*	*17.2%*
Associates	0.0	0.0	0.0	0.0	0.0
Minorities	0.0	0.0	0.0	0.0	0.0
Discontinued & exceptional items	0.0	0.0	0.0	0.0	0.0
Net profit	**0.6**	**-8.5**	**-6.9**	**-7.3**	**-17.5**
Adjusted net profit	**0.8**	**-8.2**	**-7.3**	**-7.8**	**-18.1**

Balance sheet (EUR m)	12/22a	12/23e	12/24e	12/25e	12/26e
Tangible fixed assets	0.9	2.0	3.3	4.4	5.6
Right of use assets	1.6	1.6	1.6	1.6	1.6
Goodwill	0.0	0.0	0.0	0.0	0.0
Other intangible assets	4.0	5.1	6.4	7.5	8.7
Financial fixed assets	0.1	0.3	0.3	0.3	0.3
Deferred tax assets	0.4	1.6	1.6	1.6	1.6
Total fixed assets	**7.1**	**10.5**	**13.2**	**15.4**	**17.8**
Inventories	0.0	0.0	0.0	0.0	0.0
Trade receivables	0.5	0.9	1.1	1.5	1.9
Other current assets	2.6	2.5	2.5	2.5	2.5
Cash & cash equivalents	13.4	10.0	1.2	-11.0	-33.0
Total current assets	**16.4**	**13.3**	**4.8**	**-7.0**	**-28.6**
Assets held for sale	0.0	0.0	0.0	0.0	0.0
Total assets	23.5	23.9	17.9	8.4	-10.9
Equity	10.3	5.7	0.5	-7.0	-24.9
Minorities & preference shares	0.0	0.0	0.0	0.0	0.0
Total Equity	**10.3**	**5.7**	**0.5**	**-7.0**	**-24.9**
Long-term interest-bearing debt	4.5	10.1	6.8	3.6	3.4
Long-term lease debt	0.0	0.0	0.0	0.0	0.0
Employee benefit provisions	0.0	0.0	0.0	0.0	0.0
Other provisions	0.0	0.0	0.0	0.0	0.0
Deferred taxed liabilities	0.8	1.4	1.4	1.4	1.4
Other long-term liabilities	0.0	0.0	0.0	0.0	0.0
Total non-current liabilities	**5.3**	**11.5**	**8.2**	**5.0**	**4.8**
Short-term interest-bearing debt	1.7	1.8	3.3	3.2	0.2
Short term lease debt	0.0	0.0	0.0	0.0	0.0
Accounts payable	3.0	3.6	4.6	6.0	7.8
Other current liabilities	0.9	1.2	1.2	1.2	1.2
Total current liabilities	**5.6**	**6.5**	**9.1**	**10.4**	**9.2**
Liabilities held for sale	0.0	0.0	0.0	0.0	0.0
Total equity & liabilities	**21.2**	**23.7**	**17.8**	**8.3**	**-10.9**

Source: Oncodesign Precision Medicine/Degroof Petercam estimates

Cash Flow (EUR m)	12/22a	12/23e	12/24e	12/25e	12/26e
EBIT	-0.8	-10.4	-8.2	-8.9	-21.4
Depreciations	0.1	0.2	0.2	0.2	0.3
Amortization	0.1	0.2	0.2	0.2	0.3
Impairment	0.0	0.0	0.0	0.0	0.0
Changes in working capital	0.0	0.4	0.8	1.0	1.4
Other operational cash flow	1.4	1.9	-0.2	-0.0	0.2
Operational Cash Flow	**0.8**	**-7.8**	**-7.2**	**-7.4**	**-19.3**
Taxes paid	1.1	1.8	1.5	1.6	3.7
Dividends from associates	0.0	0.0	0.0	0.0	0.0
Net interest paid	0.1	0.1	0.4	0.2	0.0
Other cash from operating activities	-1.1	-2.1	-1.3	-1.4	-3.4
CF from operating activities	**0.9**	**-7.9**	**-6.6**	**-7.0**	**-19.1**
CAPEX	-1.8	-1.2	-1.5	-1.4	-1.4
Capex/depreciation	1,688.9%	820.0%	829.6%	630.4%	550.7%
Investments in intangibles	-1.8	-1.2	-1.5	-1.4	-1.4
Acquisitions	0.0	0.0	0.0	0.0	0.0
Divestments	0.0	0.0	0.0	0.0	0.0
Other investing cash flow	0.0	-0.1	-0.0	-0.0	-0.0
CF from investing activities	**-3.5**	**-2.5**	**-3.0**	**-2.8**	**-2.9**
Dividends paid	0.0	0.0	0.0	0.0	0.0
Minority & preference dividends	0.0	0.0	0.0	0.0	0.0
Share buybacks	0.0	0.0	0.0	0.0	0.0
Equity financing	7.7	0.0	2.0	0.0	0.0
Payments on lease liabilities	0.0	0.0	0.0	0.0	0.0
Other financing cash flow	4.2	7.5	-2.2	-3.5	-3.2
CF from financing activities	**11.9**	**7.5**	**-0.2**	**-3.5**	**-3.2**
Changes in consolidation & currencies	0.0	0.0	0.0	0.0	0.0
Change in net cash (debt)	**9.3**	**-3.0**	**-9.8**	**-13.3**	**-25.2**
FCF to Enterprise	-1.6	-8.4	-8.7	-8.6	-18.5
FCF to Equity	-2.6	-10.4	-9.6	-9.7	-22.0

Enterprise Value & Capital Employed (EUR m)	12/22a	12/23e	12/24e	12/25e	12/26e
Market capitalization	8.4	25.3	27.7	27.7	27.7
Long-term debt	4.5	10.1	6.8	3.6	3.4
Short-term debt	1.7	1.8	3.3	3.2	0.2
Lease debt	0.0	0.0	0.0	0.0	0.0
Cash position	13.4	10.0	1.2	-11.0	-33.0
Net financial debt	-7.2	1.9	8.9	17.7	36.6
Minorities & preference shares	0.0	0.0	0.0	0.0	0.0
EV adjustments	0.0	0.0	0.0	0.0	0.0
Enterprise Value	1.2	27.2	36.7	45.5	64.3
Equity (group share)	10.3	5.7	0.5	-7.0	-24.9
Net financial debt	-7.2	1.9	8.9	17.7	36.6
Minorities	0.0	0.0	0.0	0.0	0.0
Adjustments capital employed	0.0	0.0	0.0	0.0	0.0
Capital employed (ROCE)	3.1	7.6	9.4	10.7	11.7

Source: Oncodesign Precision Medicine/Degroof Petercam estimates

Figures per share (EUR m)	12/22a	12/23e	12/24e	12/25e	12/26e
Adjusted EPS	0.16	-0.49	-0.40	-0.43	-0.99
Adjusted EPS fully diluted	0.16	-0.49	-0.40	-0.43	-0.99
Declared EPS	0.11	-0.51	-0.38	-0.40	-0.96
Cash flow per share	0.16	-0.49	-0.36	-0.38	-0.94
FCF to equity per share	-0.53	-0.63	-0.53	-0.53	-1.21
Dividend per share	0.00	0.00	0.00	0.00	0.00
Book value per share	2.08	0.34	0.03	-0.39	-1.37
Shares (m)					
Number of shares at year-end	4.950	16.590	18.190	18.190	18.190
Average number of shares	4.950	16.590	18.190	18.190	18.190
Average number of shares diluted	4.950	16.590	18.190	18.190	18.190

Ratios	12/22a	12/23e	12/24e	12/25e	12/26e
Adjusted P/E	10.8	-3.1	-3.8	-3.6	-1.5
Price/Book	0.8	4.5	55.3	-3.9	-1.1
EV/Sales	0.2	24.7	33.3	41.3	58.5
EV/R&D	-0.2	-3.1	-4.0	-2.7	-3.4
EV/EBIT	-1.4	-2.6	-4.5	-5.1	-3.0
EV/CE	0.4	3.6	3.9	4.3	5.5
Dividend yield	-	-	-	-	-

Source:Oncodesign Precision Medicine/Degroof Petercam estimates

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This report was first disseminated by Degroof Petercam on 17 April 2024 14:30 CET

Valuations are continuously reviewed by the analyst and will be updated and/or refreshed regularly. The rationale behind a change in target valuation will be explained in such a refresher/update.
An overview of the research published on this company can be found on our website:
https://research.degroofpetercam.com/portail/societe/news.php?id=248&type=0

This report has been reviewed by the company prior to publication and has been subsequently amended.
The report has been reviewed by Laura Roba, Equity Analyst.

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