Årsstämma 2026

Sofia Heigis, vd

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About Oncopeptides

A Swedish biotech specializing in difficult-to-treat cancers through a **commercialized therapy**, Pepaxti, and an **innovative pipeline**. In the early stages of a strategic expansion driven by **European commercialization, global partnerships** and **next-generation innovations**.

2000

FOUNDED
in 2000

≈70
employees

HQ in Sweden
DE, AT, ES & IT

FULL APPROVAL
Pepaxti in Europe 2022

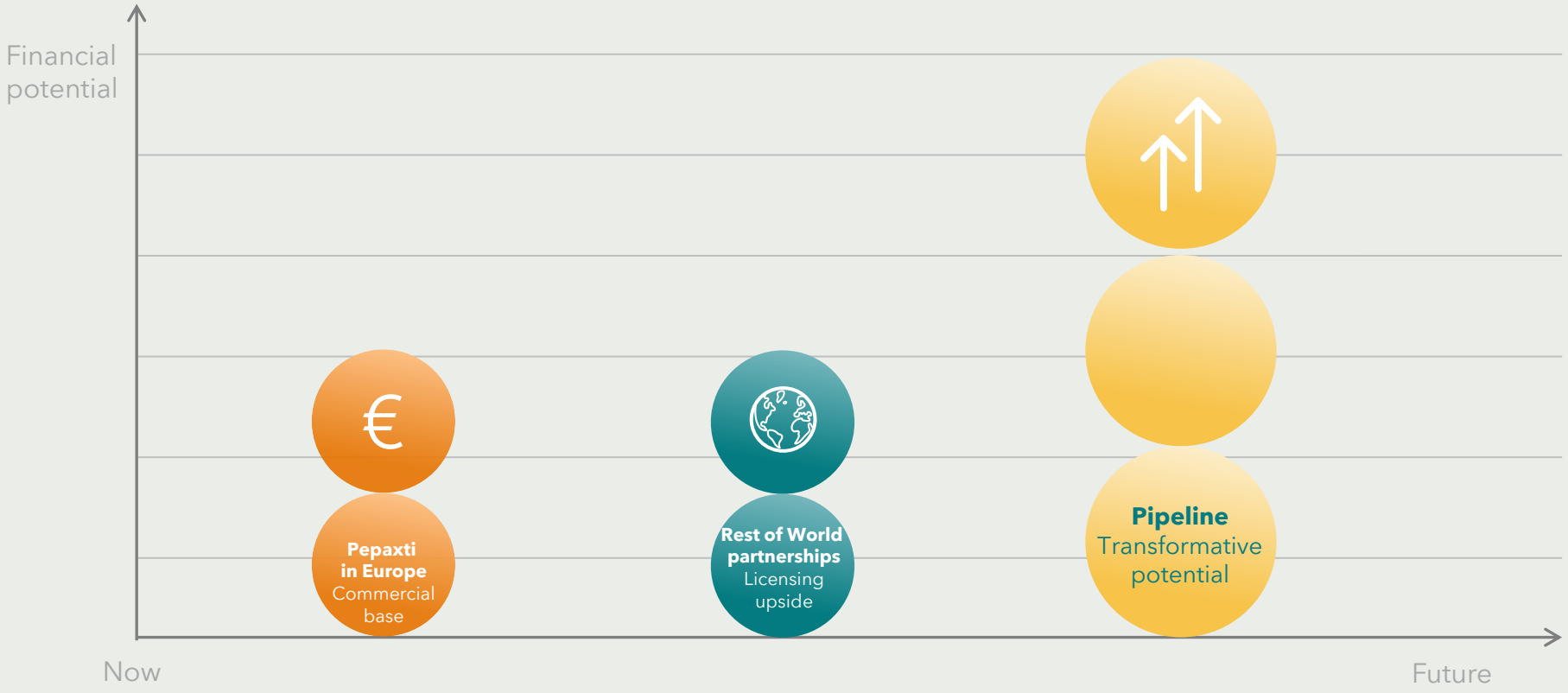
LISTED
Nasdaq Stockholm
since 2017

PARTNERS
South Korea, Greece, MENA, Eurasia, Africa with more ongoing

VISION
Bringing hope through science

PIPELINE
Drug candidates with potential within multiple indications

Our potential



A **global biotech** with a marketed **product**, **expanding indications**, and a proprietary platform unlocking future therapies

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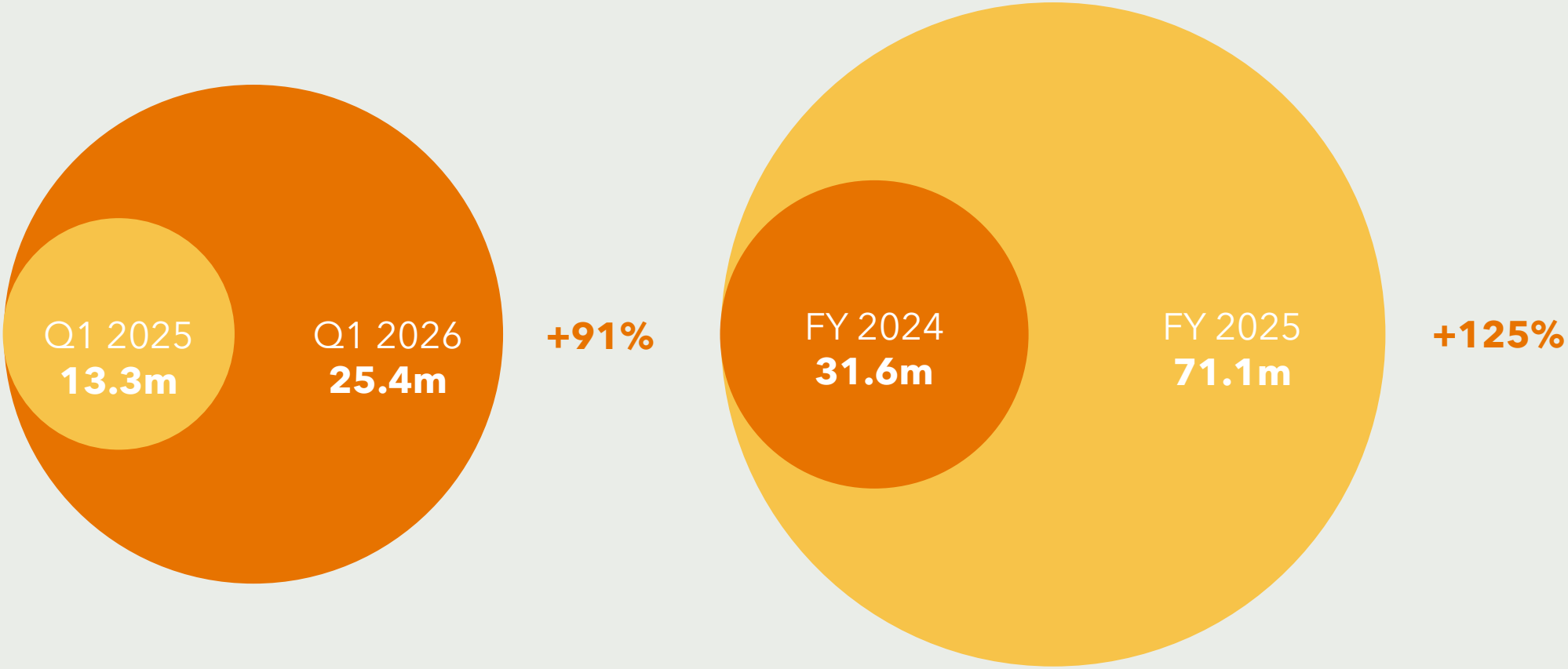
Where we are right now



All figures in SEK.

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Why invest in Oncopeptides?

Growth momentum in Europe

SEK ≈1.5B European market potential with fully approved product

Pipeline potential in $8B+ Glioblastoma global market

Strategic expansion through partnerships

Pipeline assets in multiple potential indications

Recent announcements strengthening our investment case

91 % growth in Q1 YoY

Growth momentum i Europe

Application to enter third line would, following approval and patient access, significantly increase addressable market for Pepaxti

SEK ≈1.5B European et potential ully approved product

Pipeline potential in $8B+ Glioblastoma global market

Several partnership discussions ongoing

Strategic expansion through partnerships

Window-of-opportunity study to launch in summer

Pipeline assets in multiple potential indications

Pepaxti in Europe

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PDCs enhance alkylation through enzymatic enrichment and dual targeting of both nuclear and mitochondrial DNA

1 Melflufen enters cells freely due to its lipophilicity, without the need of transporter proteins.

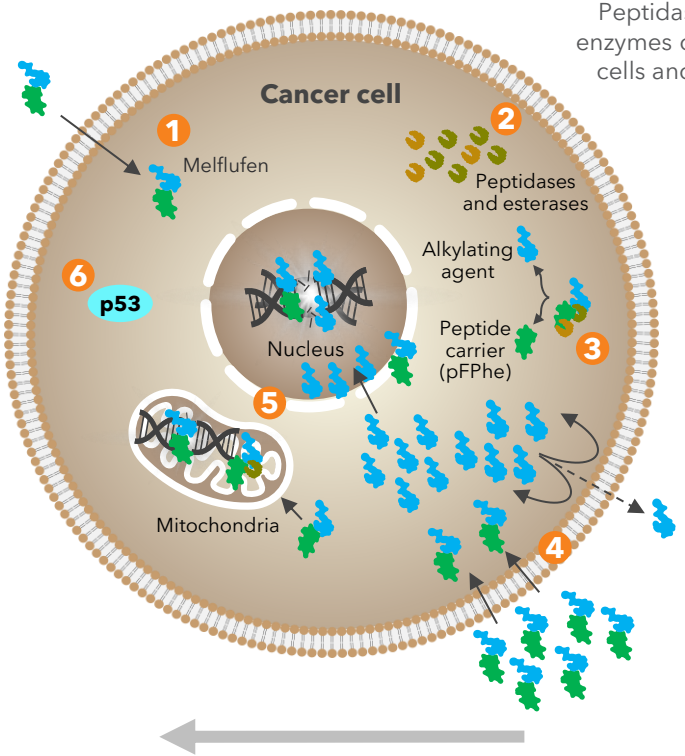
2 Peptidases and esterases are enzymes overexpressed in tumor cells and important in protein homeostasis

3 Melflufen is a PDC that utilizes the overexpression of peptidases inside tumor cells and is rapidly hydrolyzed to release cytotoxic hydrophilic alkylating agents

4 The rapid hydrolysis of melflufen creates a concentration gradient that drives further influx of melflufen into the cell, resulting in intracellular peak of alkylating agents

5 Melflufen and alkylating metabolites cause irreversible nuclear and mitochondrial damage by linking DNA strands which induces apoptosis.

6 Melflufen is able to overcome del(17p)/p53-deficiency-mediated resistance seen with conventional alkylators.



Del, deletion; PDC, peptide-drug conjugate; pFPhe, p-L fluoro-phenylalanine ethyl ester; melflufen, melphalan flufenamide; p53, tumor suppressor protein 53.

1. Chauhan D, et al. *Clin Cancer Res*. 2013;19(11):3019-31. 2. Wickström M, et al. *Oncotarget*. 2017;8(39):66641-66655. 3. Kumari R, et al. *Br J Cancer*. 2021;124(8):1428-1436.
4. Miettinen JJ, et al. *Cancers (Basel)*. 2021;13(7):1527. 5. Westermark U, et al. *Biochem Biophys Res Commun*. 2023;656:122-130. 6. Ray A, et al. *Br J Haematol*. 2016;174(3):397-409.
7. Mateos MV, et al. ASH 2020. Poster 3237.

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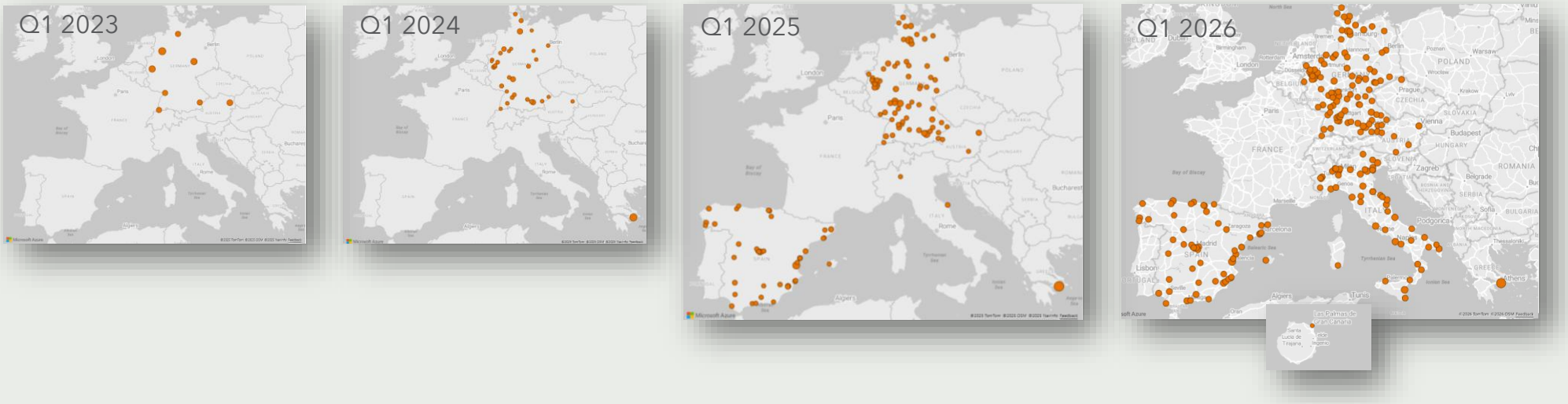
European sales trajectory

Revenue, European sales, million SEK

European sales



≈800 patients* treated since EMA approval in 2022

Inclusion in updated EHA/EMN guidelines, in our wanted position with 1B recommendation, is driving awareness, advocacy and clarifying the Pepaxti position which all are key success factors for the launch

Positive clinical experience triggers RWD publication to support peer-to-peer recommendations

Overall European number of patients is an estimated number based on insights and sales data.

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Independent data from real-world studies of melflufen

These studies confirm the findings from our clinical program – melflufen is effective and has a manageable safety profile, with adverse events primarily being hematological.

USA [1]
- 12 patients
- Median 5.5 prior lines of therapy
- ORR: 55%
- Hematological AEs, all manageable with supportive care.
- No instances of mucositis, alopecia, or secondary malignancies.

Germany [2]
- 2 patient cases
- Severe renal insufficiency
- >6 cycles of melflufen
- Well-tolerated therapy in patients with severely reduced renal function

Italy [3]
- 8 patients
- ORR: 37.5%
- Hematological AEs, all manageable with dose delays, dose reductions and supportive care.

Italy [4]
- 17 patients
- ORR: 41%
- Manageable safety profile
- Response to subsequent immuno-therapy treatment, with the majority achieving VGPR or better
- First published case of melflufen as bridging to CAR T (with a complete response as outcome)

Spain [5]
- 19 patients
- Median 5 prior lines of therapy, 74% with prior immunotherapy
- ORR 28%
- A useful therapeutic option also in patients with prior immunotherapy.

Spain [6]
- 60 patients (33 with prior immunotherapy)
- ORR 40%, 45% in patients with prior immunotherapy
- 2 patients with bridging to CAR T (with a partial response)
- Melflufen is a feasible and active option in heavily pretreated RRMM, including patients with prior immunotherapy.

Long-term responders [7]
- 3 patient cases (IT, CZ, GR)
- Number of melflufen cycles: 46, 57and 83
- Well-tolerated therapy

Ongoing Non-Interventional studies: **HARBOUR** [8] (in Germany) and **LAGOON** [9] (in Spain)

AEs, adverse events; BCMA, B-cell maturation antigen; CAR T, chimeric antigen receptor T; CZ, Czech Republic; GR, Greece; IT, Italy; ORR, overall response rate; VGPR, very good partial response.

1. Hossain S. et al. *Eur J Haematol.* 2025; 114(6): 982-989. 2. Fenchel K. et al. *Blood*. 2025;146(Suppl 1):7521-7522. 3. Giunta G. et al. European Myeloma Network (EMN) Meeting, 10-12 Apr 2025. 4. Mancuso K. et al. *Eur J Haematol*. 2026; in press. 5. Martínez-Campuzano D. et al. International Myeloma Society (IMS) Annual Meeting, 2025, Poster PA-493. 6. Alegre A. et al. Poster at COMy, 14-17 May 2026. 7. Talarico M. et al. *J Cancer Res Clin Oncol.* 2025; 151(11): 288. 8. Waldschmidt J. et al. *Oncol Res Treat.* 2024; 47(Suppl 2):285. 9. REEC. https://reec.aemps.es/reec/public/eo_detail.html

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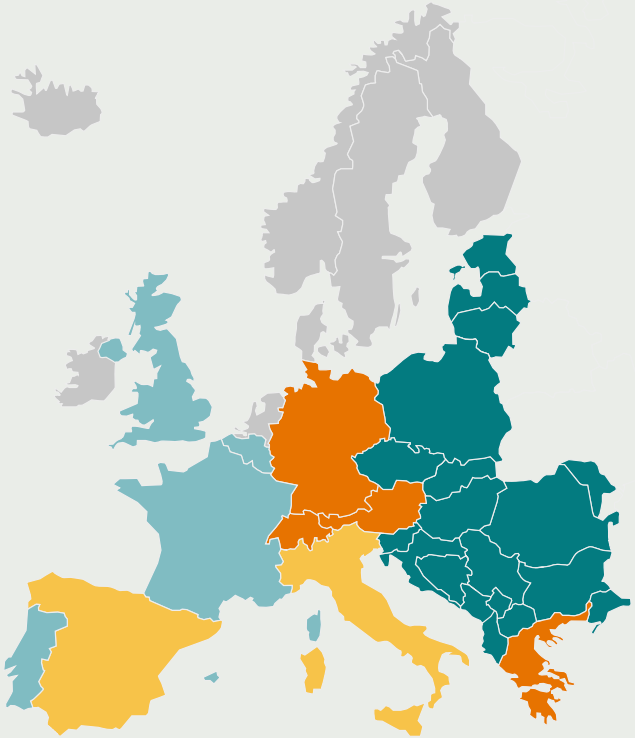
European commercialization

≈55%
Phase I – completed
Phase II – completed
Phase II – pending
≈35%
Phase III
≈10%
Phase IV

Market exclusivity until 2037



% of market potential per phase out of SEK ≈1.5 billion estimated annual market potential.

Germany
Austria
Switzerland
Greece
Spain
Italy
Nordics
Netherlands
Ireland
France
United Kingdom
Central/ Eastern Europe

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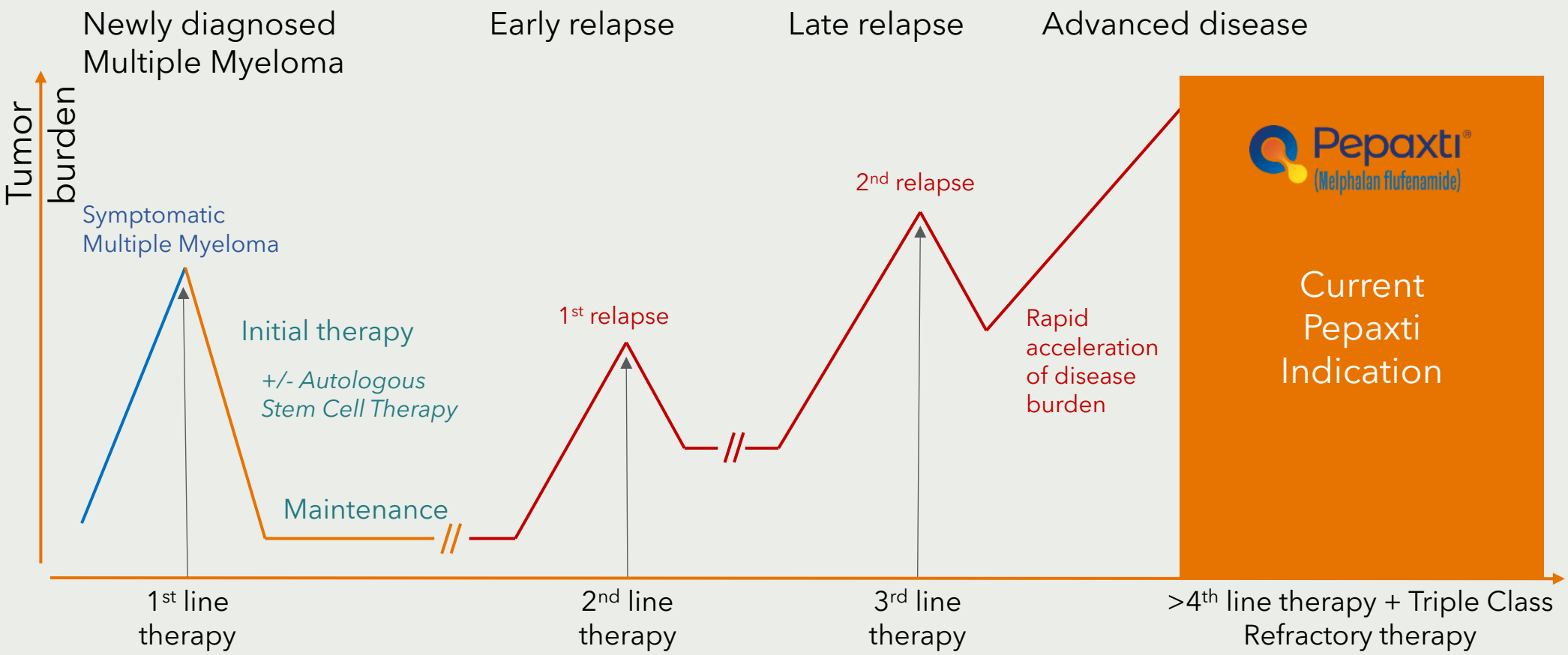
Oncopeptides intends to expand Pepaxti into third line therapy



Adapted from Borrello, Leuk Res, 2012; Richardson et al., Blood Cancer J, 2018

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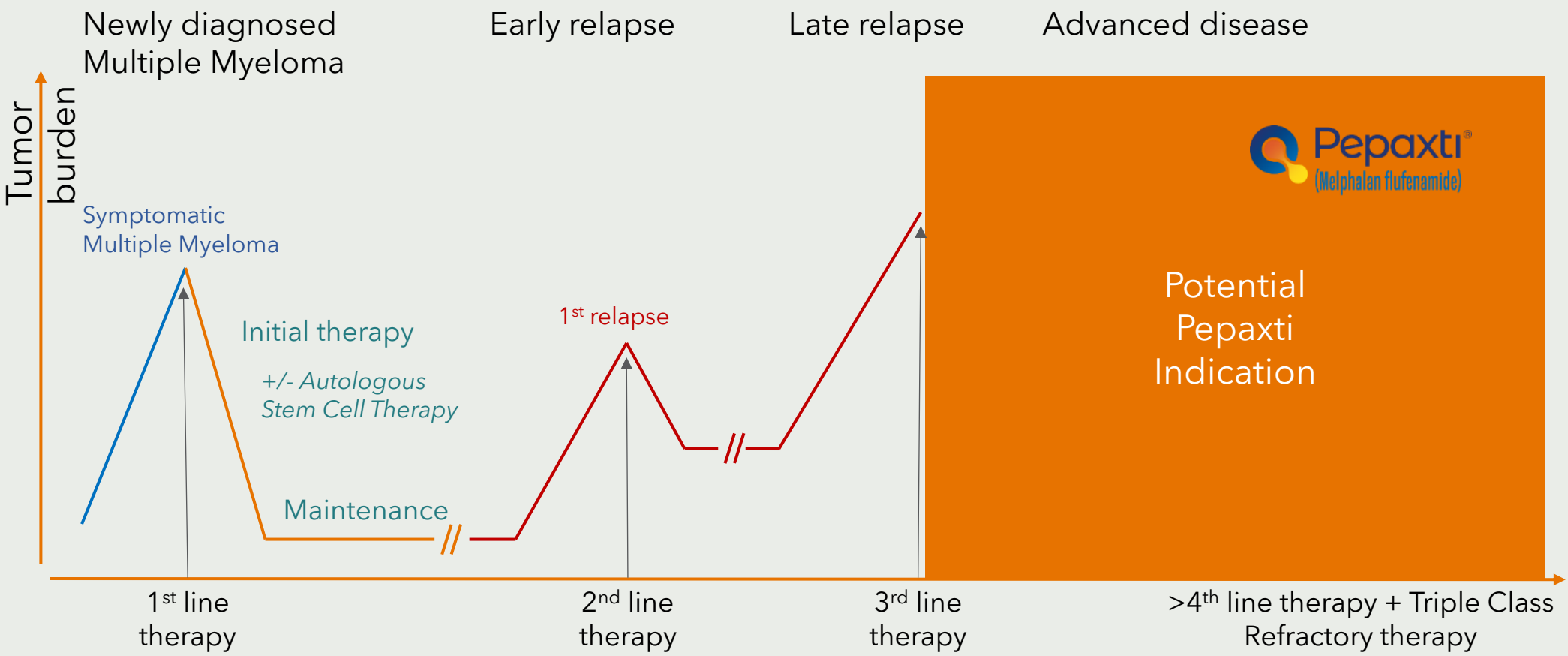
Multiple Myeloma treatment course – a marathon, not a sprint



Adapted from Borrello, Leuk Res, 2012; Richardson et al., Blood Cancer J, 2018

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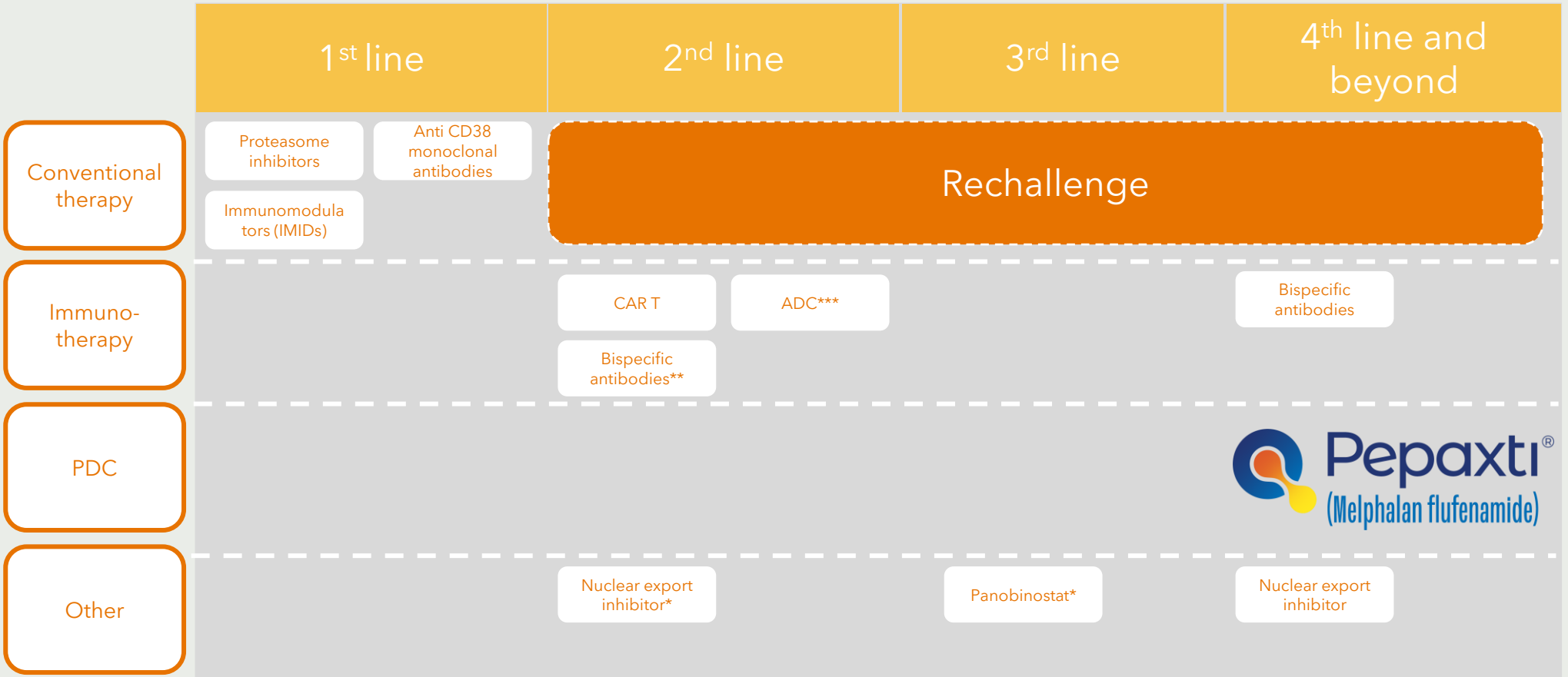
Broadening the therapeutic reach

- Current indication
  - 4th Line+ treatment
  - Adult patients with RRMM who have received at least 3 prior lines of therapies
  - Refractory to at least 1 PI, 1 IMiD, and 1 anti-CD38 mAb
- Future potential indication
  - 3rd line+ treatment
  - Adult patients with RRMM who have received at least 2 prior lines of therapies
  - Refractory to Lenalidomide and the last line of therapy

Removal of the "Triple Class Refractory" requirement facilitates **earlier and more frequent** patient identification

Multiple Myeloma treatment landscape



*In combination with bortezomib
**In combination, teclistamab+daratumumab (approved by FDA, filed with EMA; expected approval Q3 2026)
***In combination with bortezomib or pomalidomide

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Execution timeline and milestones

May-July 2026

Type II Variation Submission to EMA

H2 2026

Initial Regulatory Feedback expected

H1 2027

European Commission Final Decision

2027

Market Access & Price negotiations

Bringing hope to patients

If approved and price negotiations are successful, this indication expansion represents a **significant milestone** for Oncopeptides, the patients we serve, and our shareholders.

Third line approval and market access

- Increases total European sales potential
- Efficient use of current commercial infrastructure
- New complementary Mode of Action for third line patients

Potential added opportunities

- Focus on key markets remain – for now
- Approval and market access would change business case for Pepaxti and could open doors to new markets – in Europe and beyond – through own commercialization, partnerships or a combination

Financial impact

- 2x number of addressable patients
  and
  2x average number of treatment cycles
- Market Access and price in third line remaining unknown factor
- Our assessment of the current therapeutic and pricing landscape supports a move into third line with a maintained innovative price level

Rest of World partnerships

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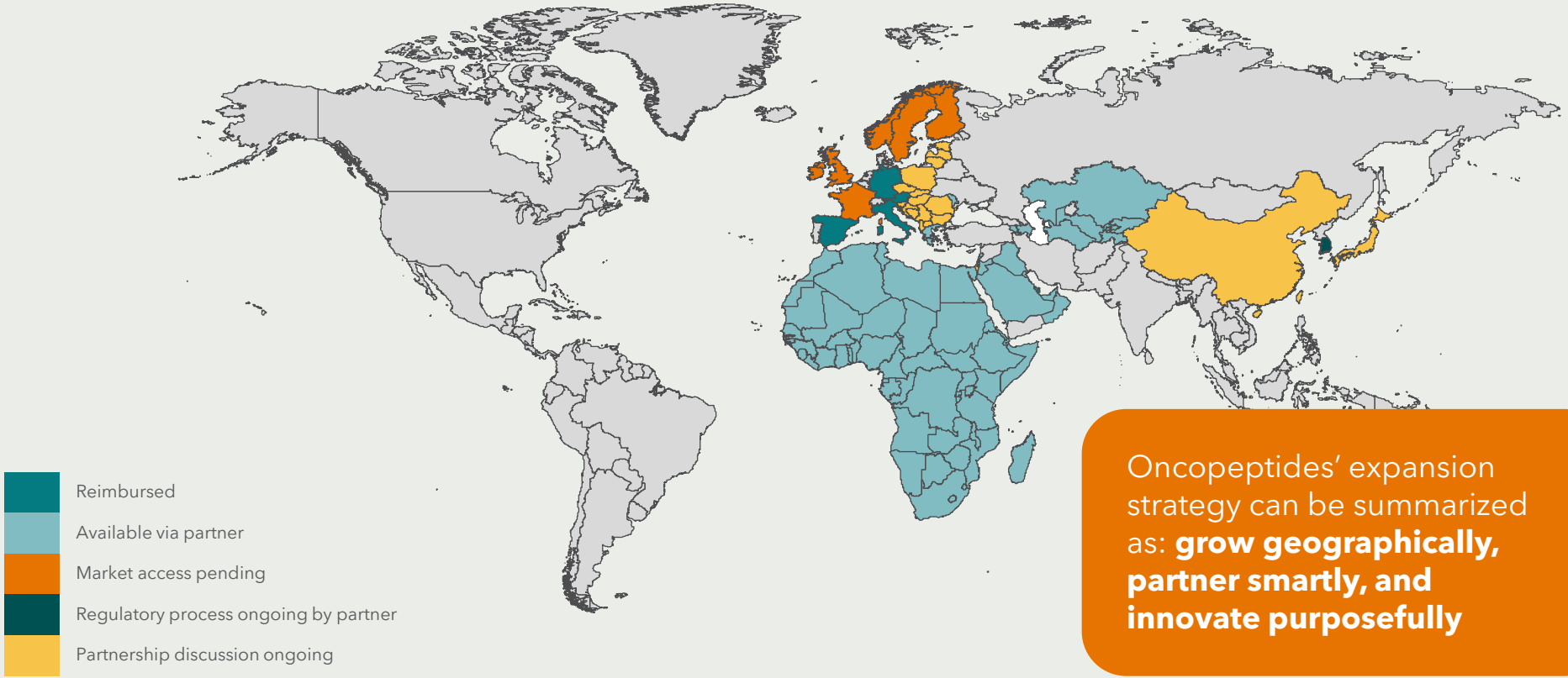
Pepaxti commercialization and partnership landscape



Oncopeptides' expansion strategy can be summarized as: **grow geographically, partner smartly, and innovate purposefully**

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Pipeline

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Pipeline assets

PDC: A global, multi-indication opportunity building onto our existing innovation

OPD5 – Global opportunity with potential for additional indications

OPDC3 – Designed for enhanced selectivity, global opportunity with potential in solid tumors

SPiKE: A platform with exciting potential globally and in multiple disease areas

OPSP1 - A differentiated innovative immunotherapy

Our PDC Platform:

validated science**, limitless** potential

Validated scientific breakthrough

Our proprietary technology is a "smart" system designed to bypass healthy tissue and concentrate cancer-killing power directly inside cancer cells

Overcoming treatment resistance

Our platform is engineered to overcome common resistance pathways (such as p53 mutations) that often stop traditional drugs from working

Real-world proof-of-concept

With over SEK 25.6 million in Q1-26 sales and ~800 patients treated since launch, Pepaxti has proven that this science delivers results in clinical practice

Growth beyond myeloma

We are deploying this same validated mechanism to target multi-billion dollar markets like Glioblastoma, evolving from a niche player into a pioneer in difficult-to-treat cancers

Glioblastoma

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Glioblastoma

A brain tumor with high unmet need and growing market potential

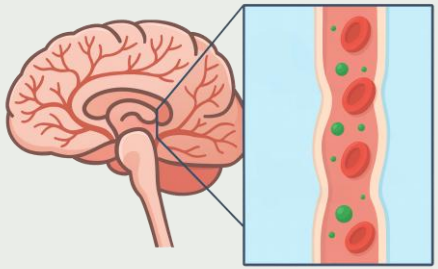
Most aggressive brain cancer – grows fast, invariably relapses, and has no cure.

Rare but severe – affects about 3-4 people per 100,000 each year, usually above the age of 60.

Poor survival – even with treatment, patients live only about 12–15 months after diagnosis.

New, brain-penetrating therapies are urgently needed.

Glioblastoma



Blood brain barrier

The barrier

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The challenge

No major **therapeutic breakthrough** since TMZ approval in 2005

	Sturdy Tumour	Blood Brain Barrier	Therapy Resistance	Cold Tumour
BARRIER				
CLINICAL GAP	Most agents exhibit no anti-tumor activity at pharmacological concentrations	Limited drug distribution from plasma (CNS bioavailability)	Reduction of therapeutic effect e.g., MGMT	Limited anti-tumor activity from immune dependent strategies

Current standard of care: temozolomide (TMZ)

	Sturdy Tumour	Blood Brain Barrier	Therapy Resistance	Cold Tumour
BARRIER				
CLINICAL GAP	Most agents exhibit no anti-tumor activity at pharmacological concentrations	Limited drug distribution from plasma (CNS bioavailability)	Reduction of therapeutic effect e.g., MGMT	Limited anti-tumor activity from immune dependent strategies
TMZ	Low glioblastoma cytotoxicity	~30% CNS bioavailability (CNS/plasma ratio)	Monofunctional alkylator; highly sensitive to DNA repair upregulation (MGMT)	TMZ does not have immune-dependent activity

Our answer

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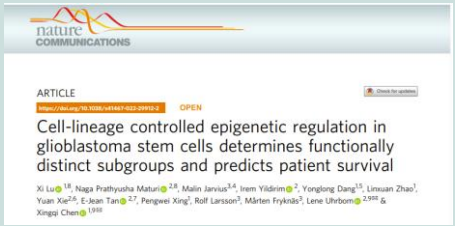
Why Glioblastoma?

An external finding in 2020, published in 2022, was followed by a **grant to the GlioPep Project** in 2023

Prof L Uhrbom, Institution for Immunology, Genetics and Pathology reached out

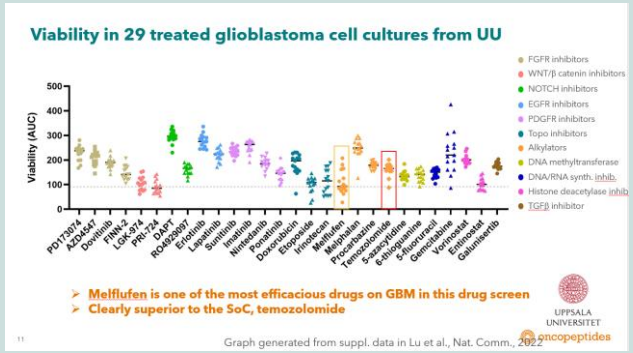

nature COMMUNICATIONS

ARTICLE

OPEN

Cell-lineage controlled epigenetic regulation in glioblastoma stem cells determines functionally distinct subgroups and predicts patient survival

Xi Lu[1,8], Naga Prathyusha Maturi[2,8], Malin Jarvius[3,4], Irem Yildirim[2], Yongfeng Dang[1,5], Linxuan Zhao[1], Yuan Xie[2,6], E-Jean Tan[2,7], Pengwei Xing[1], Rolf Larsson[3], Mårten Fryknäs[3], Lene Uhrbom[2,9✉] & Xingqi Chen[1,9✉]

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Co-funded by the European Union

Oncopeptides receives a research grant from Sweden´s Innovation Agency to explore the PDC platform in solid tumors

Oncopeptides AB (publ.) (Nasdaq Stockholm: ONCO), a biotech company focused on research, development and commercialization of therapies for difficult-to-treat hematological diseases, today announced that the company has received a research grant of 3 MSEK from Sweden´s Innovation Agency (Vinnova), to explore the development of new treatment options for glioblastoma, an aggressive and incurable form of brain cancer. The grant enables exploratory research to better understand the potential of the PDC platform in solid tumors such as glioblastoma.

Grant from Swedish innovation agency Vinnova to the GlioPep project with a research consortium incl. Oncopeptides, Uppsala University, Pharmatest and Xenopath during Mar-23 until Mar-26

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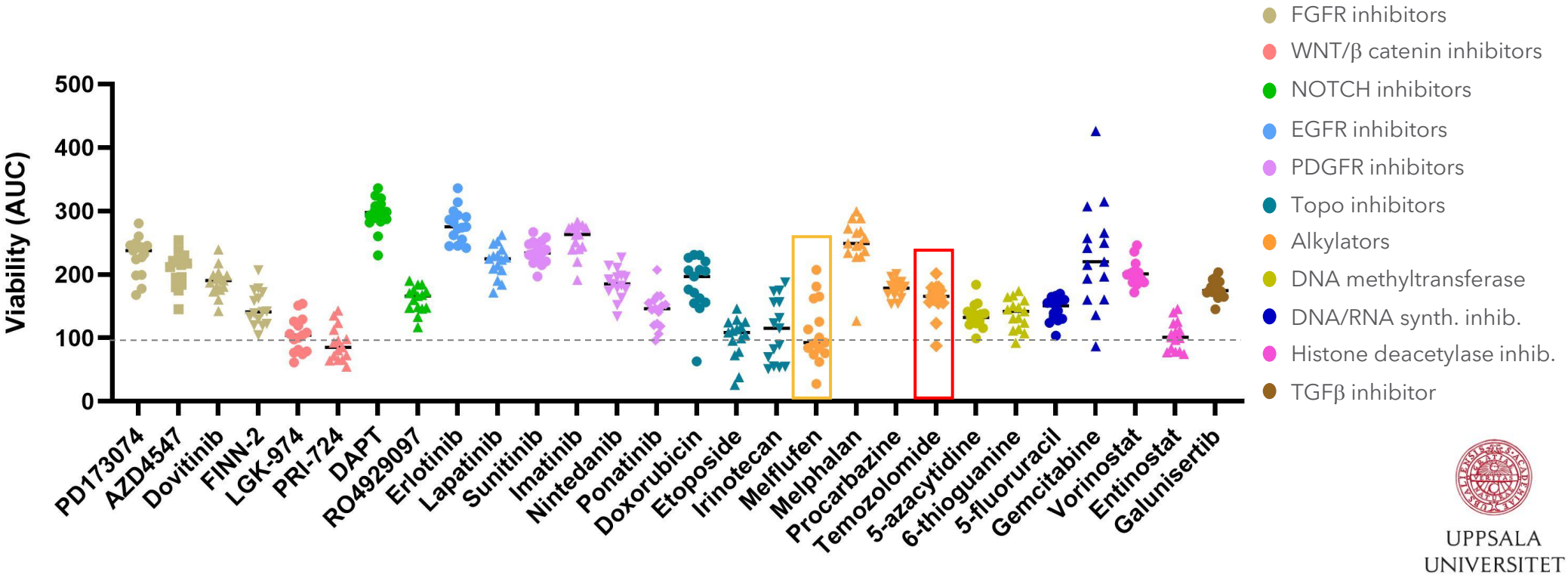
Viability in 29 treated glioblastoma cell cultures



UPPSALA UNIVERSITET

Melflufen is one of the **most efficacious drugs** on glioblastoma in this drug screen. **Clearly superior** to the standard of care: temozolomide.

Graph generated from suppl. data in Lu et al., Nat. Comm., 2022

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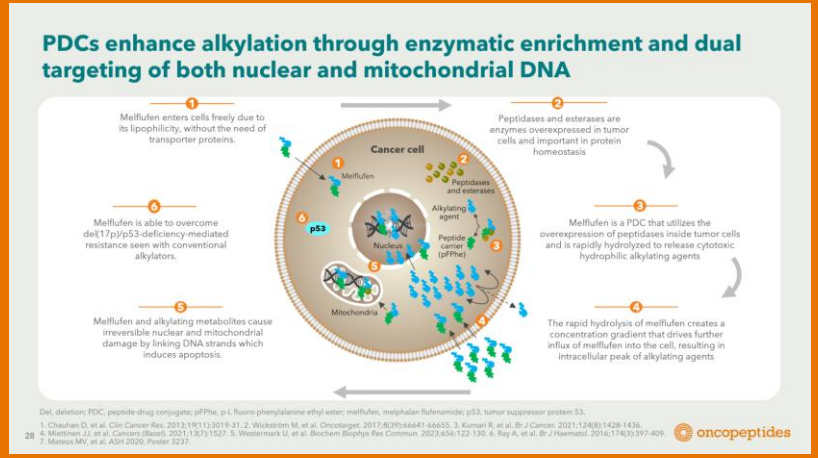
Potential of PDCs

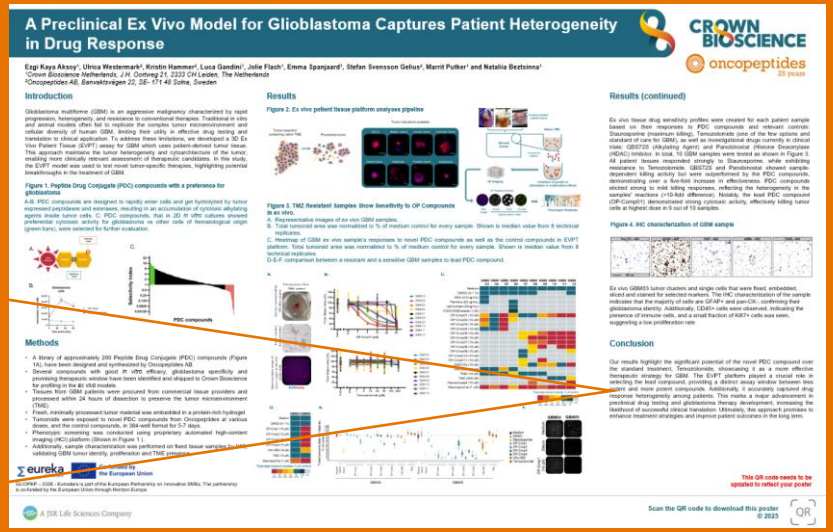
Critical BBB passage confirmed

- OPD5 has shown promising preclinical data with good activity at pharmacological concentrations
- OPD5 has shown an efficient blood-brain barrier penetration and strong tumor reduction in preclinical models

Conclusion

Our results highlight the significant potential of the novel PDC compound over the standard treatment, Temozolomide, showcasing it as a more effective therapeutic strategy for GBM. The EVPT platform played a crucial role in selecting the lead compound, providing a distinct assay window between less potent and more potent compounds. Additionally, it accurately captured drug response heterogeneity among patients. This marks a major advancement in preclinical drug testing and glioblastoma therapy development, increasing the likelihood of successful clinical translation. Ultimately, this approach promises to enhance treatment strategies and improve patient outcomes in the long term.





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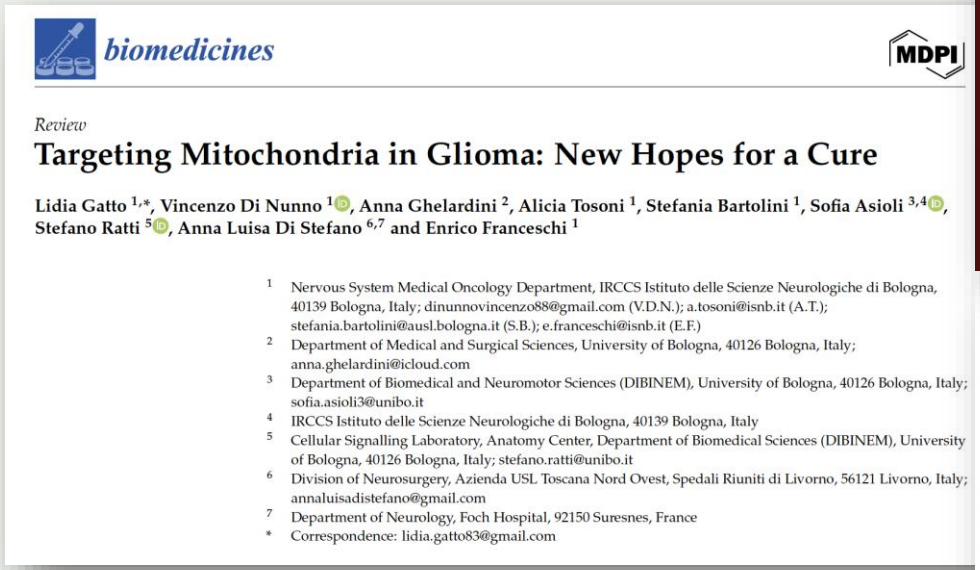
Mitochondrial function critical



biomedicines

MDPI

Review

Targeting Mitochondria in Glioma: New Hopes for a Cure

Lidia Gatto [1,*], Vincenzo Di Nunno [1], Anna Ghelardini [2], Alicia Tosoni [1], Stefania Bartolini [1], Sofia Asioli [3,4], Stefano Ratti [5], Anna Luisa Di Stefano [6,7] and Enrico Franceschi [1]

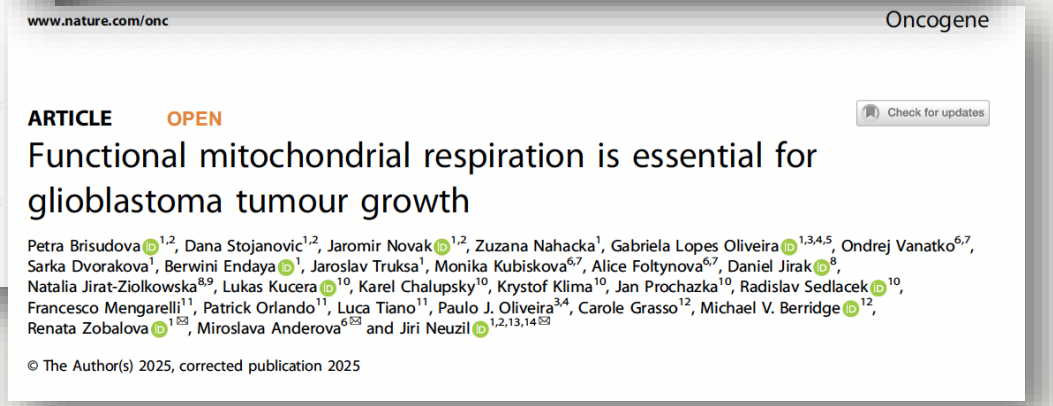
1 Nervous System Medical Oncology Department, IRCCS Istituto delle Scienze Neurologiche di Bologna, 40139 Bologna, Italy; dinunnovincenzo88@gmail.com (V.D.N.); a.tosoni@isnb.it (A.T.); stefania.bartolini@ausl.bologna.it (S.B.); e.franceschi@isnb.it (E.F.)
2 Department of Medical and Surgical Sciences, University of Bologna, 40126 Bologna, Italy; anna.ghelardini@icloud.com
3 Department of Biomedical and Neuromotor Sciences (DIBINEM), University of Bologna, 40126 Bologna, Italy; sofia.asioli3@unibo.it
4 IRCCS Istituto delle Scienze Neurologiche di Bologna, 40139 Bologna, Italy
5 Cellular Signalling Laboratory, Anatomy Center, Department of Biomedical Sciences (DIBINEM), University of Bologna, 40126 Bologna, Italy; stefano.ratti@unibo.it
6 Division of Neurosurgery, Azienda USL Toscana Nord Ovest, Spedali Riuniti di Livorno, 56121 Livorno, Italy; annaluisadistefano@gmail.com
7 Department of Neurology, Foch Hospital, 92150 Suresnes, France
* Correspondence: lidia.gatto83@gmail.com

Home > Discover Oncology > Article

The promise of mitochondria in the treatment of glioblastoma: a brief review

Review | Open access | Published: 09 February 2025

Volume 16, article number 142, (2025) Cite this article



www.nature.com/onc Oncogene

ARTICLE OPEN

Check for updates

Functional mitochondrial respiration is essential for glioblastoma tumour growth

Petra Brisudova [1,2], Dana Stojanovic [1,2], Jaromir Novak [1,2], Zuzana Nahacka [1], Gabriela Lopes Oliveira [1,3,4,5], Ondrej Vanatko [6,7], Sarka Dvorakova [1], Berwini Endaya [1], Jaroslav Truksa [1], Monika Kubiskova [6,7], Alice Foltynova [6,7], Daniel Jirak [8], Natalia Jirat-Ziolkowska [8,9], Lukas Kucera [10], Karel Chalupsky [10], Krystof Klima [10], Jan Prochazka [10], Radislav Sedlacek [10], Francesco Mengarelli [11], Patrick Orlando [11], Luca Tiano [11], Paulo J. Oliveira [3,4], Carole Grasso [12], Michael V. Berridge [12], Renata Zobalova [1] ✉, Miroslava Anderova [6] ✉ and Jiri Neuzil [1,2,13,14] ✉

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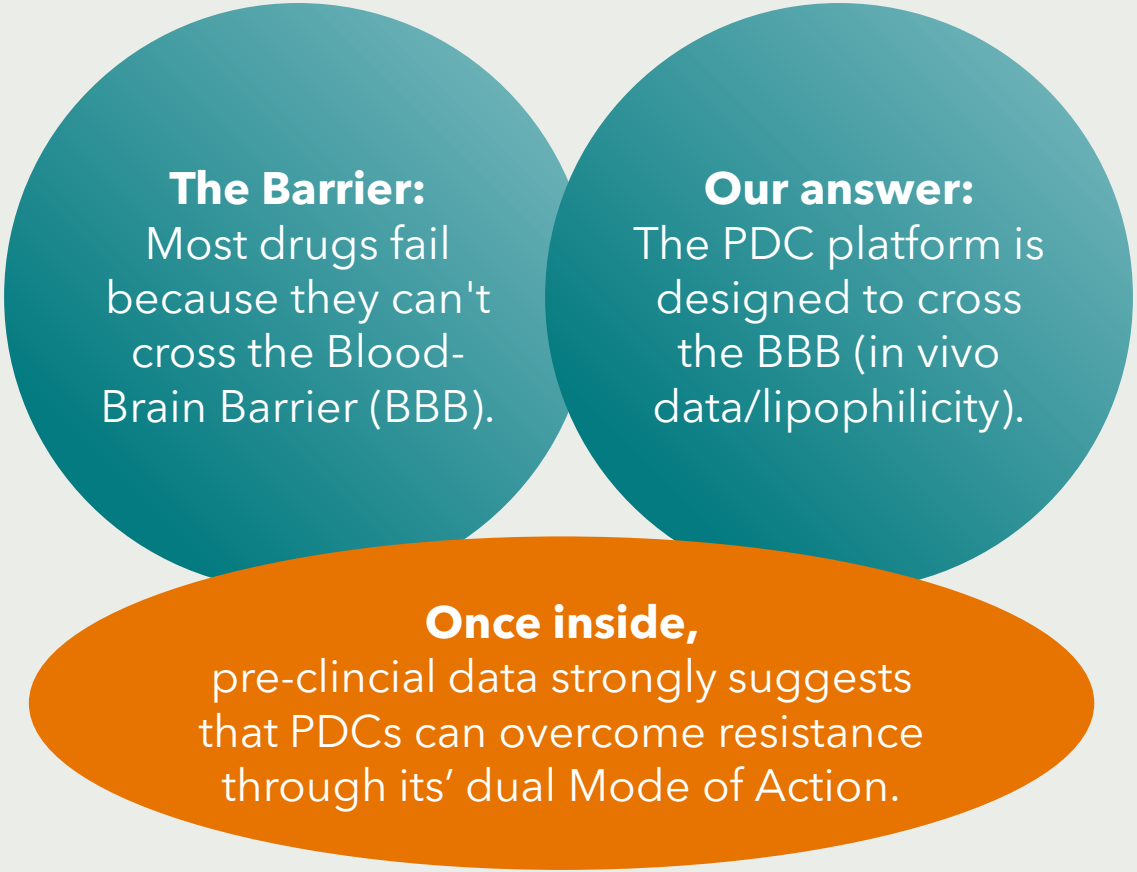
Alkylating PDCs (Pepaxti, OPD5, OPDC3)

BARRIER	Sturdy Tumour	Blood Brain Barrier	Therapy Resistance	Cold Tumour
CLINICAL GAP	Most agents exhibit no anti-tumor activity at pharmacological concentrations	Limited drug distribution from plasma (CNS bioavailability)	Reduction of therapeutic effect e.g., MGMT	Limited anti-tumor activity from immune dependent strategies
TMZ	Low glioblastoma cytotoxicity	~30% CNS bioavailability (CNS/plasma ratio)	Monofunctional alkylator; highly sensitive to DNA repair upregulation (MGMT)	TMZ does not have immune-dependent activity
PDCs	High glioblastoma cytotoxicity	100% CNS bioavailability (CNS/plasma ratio)	Bifunctional alkylator with low sensitivity to DNA repair upregulation (MGMT)	Alkylating PDCs do not have immune-dependent activity

In summary


The Barrier:
Most drugs fail because they can't cross the Blood-Brain Barrier (BBB).
Our answer:
The PDC platform is designed to cross the BBB (in vivo data/lipophilicity).
Once inside,
pre-clincial data strongly suggests that PDCs can overcome resistance through its' dual Mode of Action.

The Glioblastoma "Window of Opportunity”:

a **high reward** leap

Solving the #1 challenge

The "blood-brain barrier" prevents most drugs from reaching brain tumors; our PDCs have shown a unique ability to cross this barrier in preclinical models

A smarter way to test

Launching a focused study of approx. 10 patients using our approved drug as a "clinical probe" to prove human brain penetration quickly and efficiently

Low cost, massive impact

For a relatively low investment, we expect to generate human proof-of-concept data needed to validate our next-generation assets for an $8B market

Company transformation

Our glioblastoma program drives PDC platform expansion, transforming Oncopeptides into a multi-indication global player

In closing

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Our potential

Pipeline
Transformative potential

Unique opportunity: Targeting the $8B+ Glioblastoma market with cost-efficient "Window of Opportunity" study as next step

Smart leverage: Using melflufen as a clinical probe allows us to validate the mechanism at a low cost before committing to larger OPD5 trials

Additional opportunities: Potential in other indications down the line

Rest of World partnerships
Licensing upside

High-margin licensing model: Unlocking global value without operational overhead or infrastructure costs

Pure upside: Milestones and royalties provide additional capital to fuel further innovation

Pepaxti in Europe
Commercial base

Growth momentum: Delivering strong sales growth (+91% Q1-26 vs Q1-25), expected to establish a self-sustaining financial base in 2027
Market validation: Approx 800 patients treated since approval, with inclusion in EHA/EMN guidelines driving standard-of-care adoption
3rd line opportunity: Approval to treat patients in third treatment line would mean 2x patients and 2x treatments cycles

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Thank you for listening

Bringing hope through science

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Appendix: Glioblastoma

Glioblastoma

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Glioblastoma

A brain tumor with high unmet need and growing market potential

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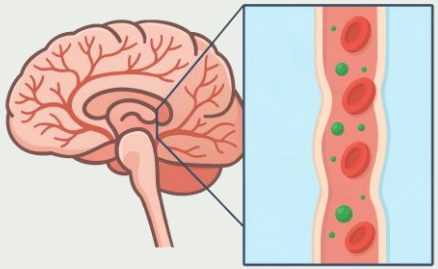
Rare but severe – affects about 3-4 people per 100,000 each year, usually above the age of 60.

Poor survival – even with treatment, patients live only about 12–15 months after diagnosis.

New, brain-penetrating therapies are urgently needed.

Glioblastoma



Blood brain barrier

The barrier

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The challenge

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	Sturdy Tumour	Blood Brain Barrier	Therapy Resistance	Cold Tumour
BARRIER				
CLINICAL GAP	Most agents exhibit no anti-tumor activity at pharmacological concentrations	Limited drug distribution from plasma (CNS bioavailability)	Reduction of therapeutic effect e.g., MGMT	Limited anti-tumor activity from immune dependent strategies

Current standard of care: temozolomide (TMZ)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Radiotherapy plus Concomitant and Adjuvant Temozolomide for Glioblastoma

Roger Stupp, M.D., Warren P. Mason, M.D., Martin J. van den Bent, M.D., Michael Weller, M.D., Barbara Fisher, M.D., Martin J.B. Taphoorn, M.D., Karl Belanger, M.D., Alba A. Brandes, M.D., Christine Marosi, M.D., Ulrich Bogdahn, M.D., Jürgen Curschmann, M.D., Robert C. Janzer, M.D., Samuel K. Ludwin, M.D., Thierry Gorlia, M.Sc., Anouk Allgeier, Ph.D., Denis Lacombe, M.D., J. Gregory Cairncross, M.D., Elizabeth Eisenhauer, M.D., and René O. Mirimanoff, M.D., for the European Organisation for Research and Treatment of Cancer Brain Tumor and Radiotherapy Groups and the National Cancer Institute of Canada Clinical Trials Group*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

MGMT Gene Silencing and Benefit from Temozolomide in Glioblastoma

Monika E. Hegi, Ph.D., Annie-Claire Diserens, M.Sc., Thierry Gorlia, M.Sc., Marie-France Hamou, Nicolas de Tribolet, M.D., Michael Weller, M.D., Johan M. Kros, M.D., Johannes A. Hainfellner, M.D., Warren Mason, M.D., Luigi Mariani, M.D., Jacoline E.C. Bromberg, M.D., Peter Hau, M.D., René O. Mirimanoff, M.D., J. Gregory Cairncross, M.D., Robert C. Janzer, M.D., and Roger Stupp, M.D.

Temozolomide is standard of care. But has **no efficacy** in patients with upregulated DNA repair (**MGMT**)

Current standard of care: temozolomide (TMZ)

	Sturdy Tumour	Blood Brain Barrier	Therapy Resistance	Cold Tumour
BARRIER				
CLINICAL GAP	Most agents exhibit no anti-tumor activity at pharmacological concentrations	Limited drug distribution from plasma (CNS bioavailability)	Reduction of therapeutic effect e.g., MGMT	Limited anti-tumor activity from immune dependent strategies
TMZ	Low glioblastoma cytotoxicity	~30% CNS bioavailability (CNS/plasma ratio)	Monofunctional alkylator; highly sensitive to DNA repair upregulation (MGMT)	TMZ does not have immune-dependent activity

Our answer

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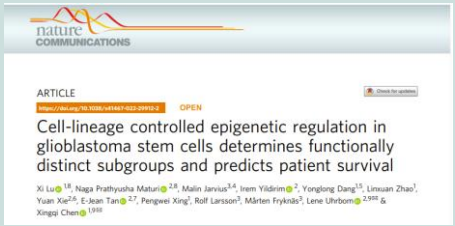
Why Glioblastoma?

An external finding in 2020, published in 2022, was followed by a **grant to the GlioPep Project** in 2023

Prof L Uhrbom, Institution for Immunology, Genetics and Pathology reached out

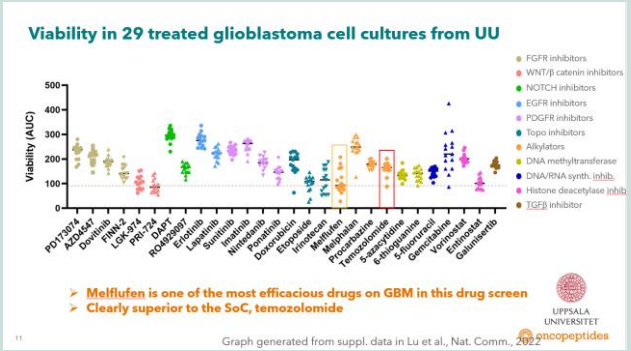

nature COMMUNICATIONS

ARTICLE

OPEN

Cell-lineage controlled epigenetic regulation in glioblastoma stem cells determines functionally distinct subgroups and predicts patient survival

Xi Lu[1,8], Naga Prathyusha Maturi[2,8], Malin Jarvius[3,4], Irem Yildirim[2], Yongfeng Dang[1,5], Linxuan Zhao[1], Yuan Xie[2,6], E-Jean Tan[2,7], Pengwei Xing[1], Rolf Larsson[3], Mårten Fryknäs[3], Lene Uhrbom[2,9✉] & Xingqi Chen[1,9✉]

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Co-funded by the European Union

Oncopeptides receives a research grant from Sweden´s Innovation Agency to explore the PDC platform in solid tumors

Oncopeptides AB (publ.) (Nasdaq Stockholm: ONCO), a biotech company focused on research, development and commercialization of therapies for difficult-to-treat hematological diseases, today announced that the company has received a research grant of 3 MSEK from Sweden´s Innovation Agency (Vinnova), to explore the development of new treatment options for glioblastoma, an aggressive and incurable form of brain cancer. The grant enables exploratory research to better understand the potential of the PDC platform in solid tumors such as glioblastoma.

Grant from Swedish innovation agency Vinnova to the GlioPep project with a research consortium incl. Oncopeptides, Uppsala University, Pharmatest and Xenopath during Mar-23 until Mar-26

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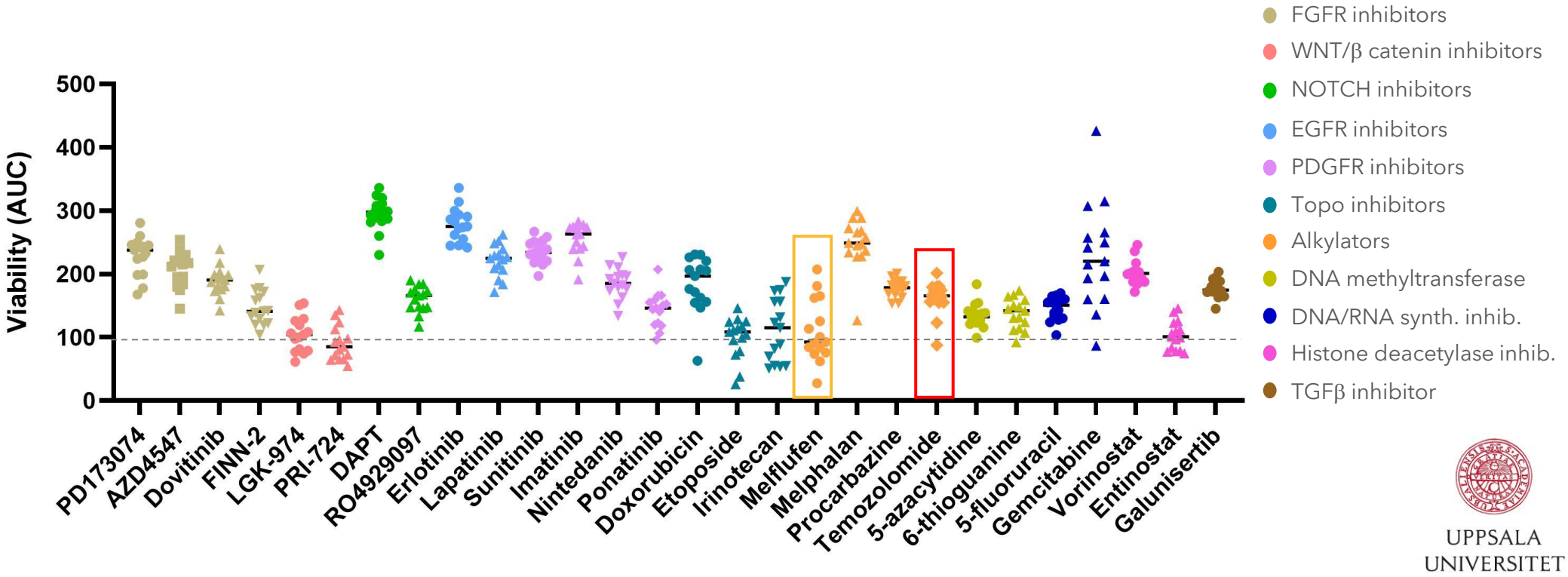
Viability in 29 treated glioblastoma cell cultures



UPPSALA UNIVERSITET

Melflufen is one of the **most efficacious drugs** on glioblastoma in this drug screen. **Clearly superior** to the standard of care: temozolomide.

Graph generated from suppl. data in Lu et al., Nat. Comm., 2022

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Gliopep project

GLIOPEP project: March 2023 – March 2026

eurostars™

EUREKA
innovation across borders

oncopeptides

- Drug development expertise
- Compound development
- Lead optimization
- Candidate drug selection

UPPSALA UNIVERSITET

- Glioblastoma expertise
- *Ex vivo* mouse model development
- Compound profiling

CROWN BIOSCIENCE

- High-throughput drug screening
- Patient *ex vivo* model development
- Compound profiling

XENOPAT

- PDOX model expertise
- *In vivo* model development
- Compound efficacy *in vivo*

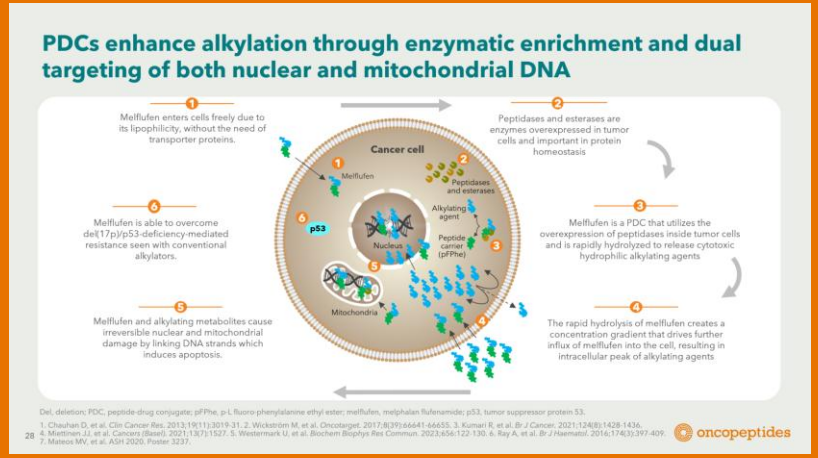
Potential of PDCs

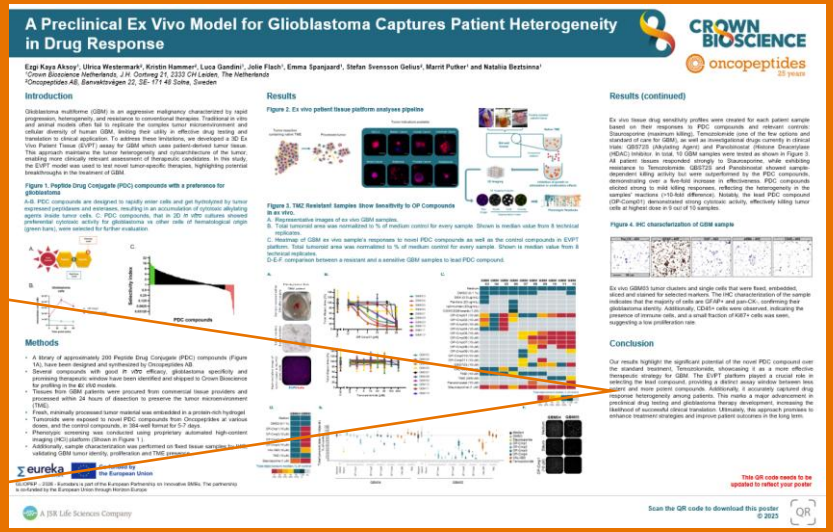
Critical BBB passage confirmed

- OPD5 has shown promising preclinical data with good activity at pharmacological concentrations
- OPD5 has shown an efficient blood-brain barrier penetration and strong tumor reduction in preclinical models

Conclusion

Our results highlight the significant potential of the novel PDC compound over the standard treatment, Temozolomide, showcasing it as a more effective therapeutic strategy for GBM. The EVPT platform played a crucial role in selecting the lead compound, providing a distinct assay window between less potent and more potent compounds. Additionally, it accurately captured drug response heterogeneity among patients. This marks a major advancement in preclinical drug testing and glioblastoma therapy development, increasing the likelihood of successful clinical translation. Ultimately, this approach promises to enhance treatment strategies and improve patient outcomes in the long term.





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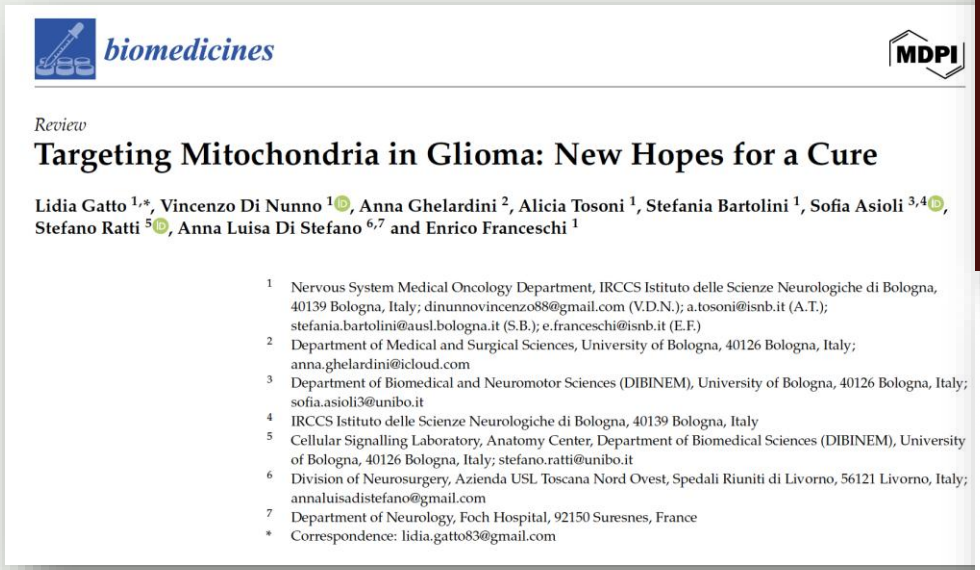
Mitochondrial function critical



biomedicines

MDPI

Review

Targeting Mitochondria in Glioma: New Hopes for a Cure

Lidia Gatto [1,*], Vincenzo Di Nunno [1], Anna Ghelardini [2], Alicia Tosoni [1], Stefania Bartolini [1], Sofia Asioli [3,4], Stefano Ratti [5], Anna Luisa Di Stefano [6,7] and Enrico Franceschi [1]

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4 IRCCS Istituto delle Scienze Neurologiche di Bologna, 40139 Bologna, Italy
5 Cellular Signalling Laboratory, Anatomy Center, Department of Biomedical Sciences (DIBINEM), University of Bologna, 40126 Bologna, Italy; stefano.ratti@unibo.it
6 Division of Neurosurgery, Azienda USL Toscana Nord Ovest, Spedali Riuniti di Livorno, 56121 Livorno, Italy; annaluisadistefano@gmail.com
7 Department of Neurology, Foch Hospital, 92150 Suresnes, France
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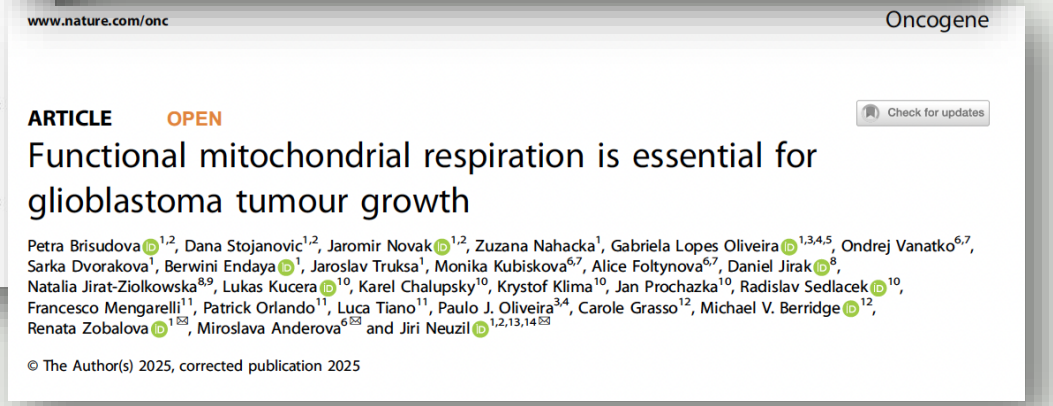
The promise of mitochondria in the treatment of glioblastoma: a brief review

Review | Open access | Published: 09 February 2025

Volume 16, article number 142, (2025) Cite this article



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ARTICLE OPEN

Check for updates

Functional mitochondrial respiration is essential for glioblastoma tumour growth

Petra Brisudova [1,2], Dana Stojanovic [1,2], Jaromir Novak [1,2], Zuzana Nahacka [1], Gabriela Lopes Oliveira [1,3,4,5], Ondrej Vanatko [6,7], Sarka Dvorakova [1], Berwini Endaya [1], Jaroslav Truksa [1], Monika Kubiskova [6,7], Alice Foltynova [6,7], Daniel Jirak [8], Natalia Jirat-Ziolkowska [8,9], Lukas Kucera [10], Karel Chalupsky [10], Krystof Klima [10], Jan Prochazka [10], Radislav Sedlacek [10], Francesco Mengarelli [11], Patrick Orlando [11], Luca Tiano [11], Paulo J. Oliveira [3,4], Carole Grasso [12], Michael V. Berridge [12], Renata Zobalova [1], Miroslava Anderova [6] and Jiri Neuzil [1,2,13,14]

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Alkylating PDCs (Pepaxti, OPD5, OPDC3)

BARRIER	Sturdy Tumour	Blood Brain Barrier	Therapy Resistance	Cold Tumour
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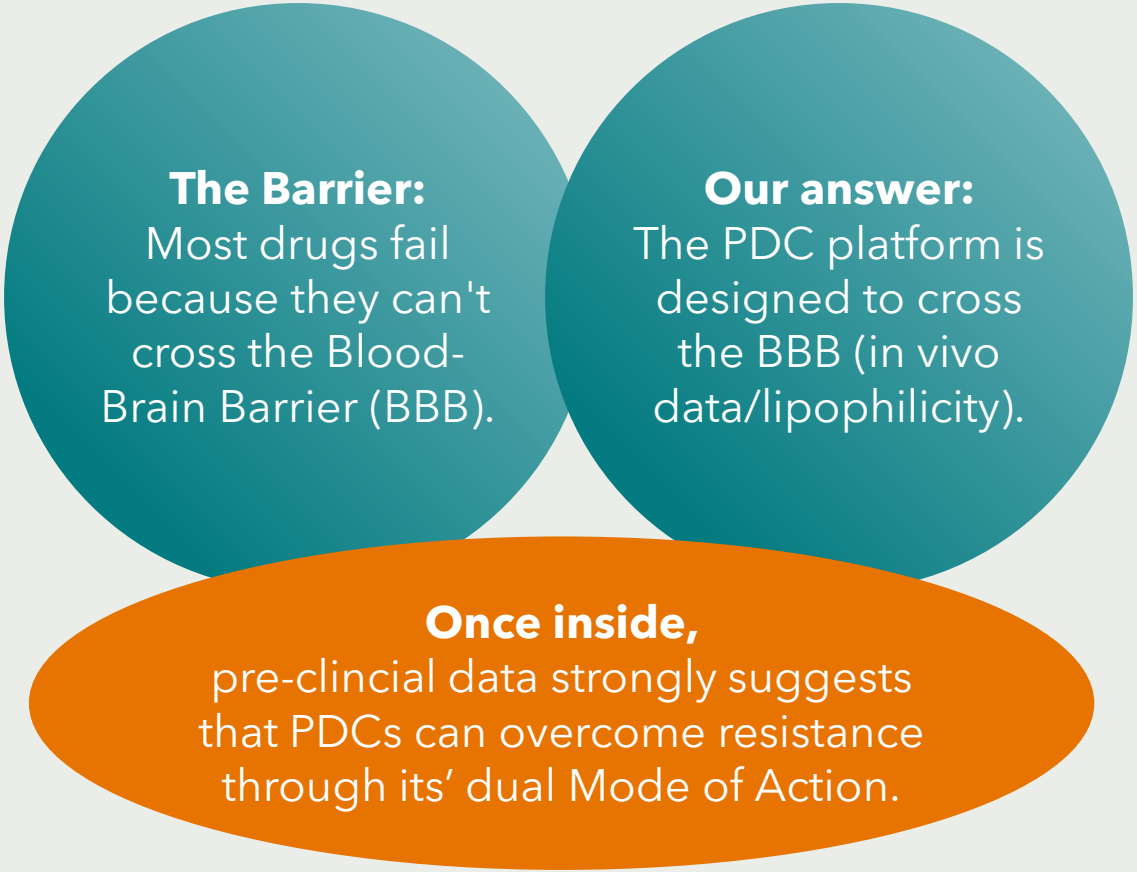
TMZ	Low glioblastoma cytotoxicity	~30% CNS bioavailability (CNS/plasma ratio)	Monofunctional alkylator; highly sensitive to DNA repair upregulation (MGMT)	TMZ does not have immune-dependent activity
PDCs	High glioblastoma cytotoxicity	100% CNS bioavailability (CNS/plasma ratio)	Bifunctional alkylator with low sensitivity to DNA repair upregulation (MGMT)	Alkylating PDCs do not have immune-dependent activity

In summary


The Barrier:
Most drugs fail because they can't cross the Blood-Brain Barrier (BBB).
Our answer:
The PDC platform is designed to cross the BBB (in vivo data/lipophilicity).
Once inside,
pre-clincial data strongly suggests that PDCs can overcome resistance through its' dual Mode of Action.

Next steps

oncopeptides

The overall success rate for bringing a glioblastoma therapy to approval is ~1–2%[1], reflecting a historically poor development track record, partly due to blood–brain barrier (BBB) delivery constraints[2].

What is the most clever approach to enter clinic with a promising candidate in an indication like Glioblastoma?

Glioblastoma "Window of Opportunity" study

a **high reward** leap

Solving the #1 Challenge

The "blood-brain barrier" prevents most drugs from reaching brain tumors; our PDCs have shown a unique ability to cross this barrier in preclinical models.

A Smarter Way to Test

Launching a focused study of approx. 10 patients using our approved drug as a "clinical probe" to prove human brain penetration quickly and efficiently.

Low Cost, Massive Impact

For a relatively low investment, we expect to generate human proof-of-concept data needed to validate our next-generation assets for an $8B market.

Company Transformation

With 125% sales growth in 2025, our glioblastoma program drives PDC platform expansion, transforming Oncopeptides into a multi-indication global player.

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