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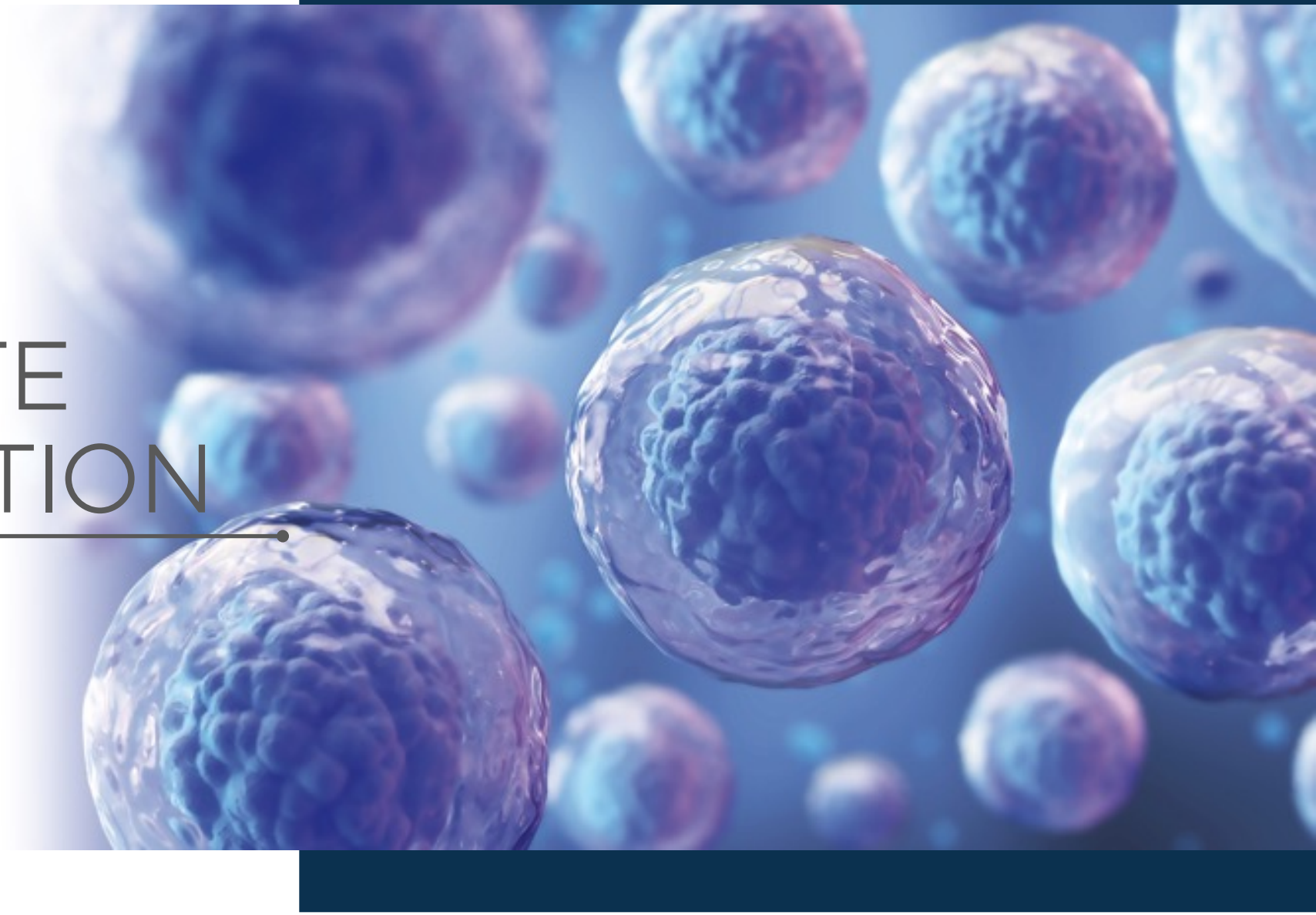

CORPORATE PRESENTATION

NASDAQ: GNTA

April 2024

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Forward-Looking Statement

This presentation contains forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “may,” “will,” “should,” “expects,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “potential” “intends” or “continue,” or the negative of these terms or other comparable terminology. All statements other than statements of historical facts contained in the presentation, such as statements regarding our potential future results of operations and financial position, prospective product candidates, availability of future funding, anticipated clinical trial results, timing of possible product approvals and expected regulatory pathways, future potential collaborations and matters concerning the timing and likelihood of success of plans and objectives of management for future operations, are forward-looking statements. Any such forward-looking statements are based on our current expectations and beliefs, as well as assumptions concerning future events. These statements involve known and unknown risks, uncertainties and other factors that could cause such matters to differ materially from those discussed in such forward-looking statements. We discuss many of these risks in our filings from time to time with the U.S. Securities and Exchange Commission, including under the heading “Risk Factors” in such documents. You should not rely upon forward-looking statements as predictions of future events.

Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance, or achievements. Except as required by law, we are under no duty to update or revise any of the forward-looking statements, whether as a result of new information, future events or otherwise, after the date hereof.

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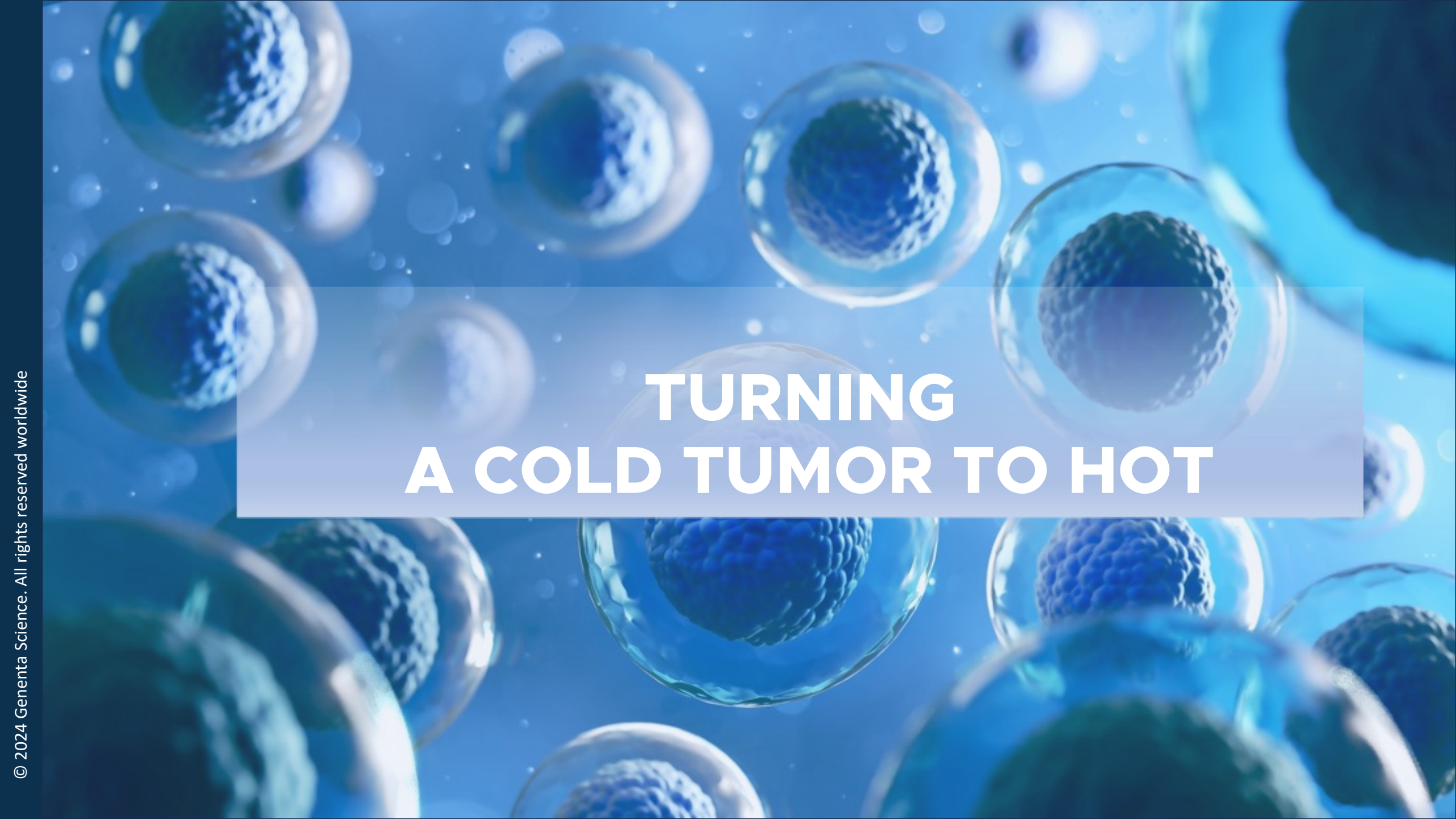

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Leadership

PIERLUIGI PARACCHI
CEO & Co-Founder

- >$200MM raised in Venture Capital (VC); $400MM+ exits
- Co-Founder & Board Member **Altheia Science**, Founder & CEO of **Quantica SGR**, Co-founder of **Axòn Capital** and **AurorA Science**, previously Venture Consultant at **Sofinnova Partners**. Member of the **Assobiotec Executive Committee**, the Italian Association for the development of biotechnology, Moderator of the "Working Table for the Internationalization of Biotechnology Sector" **Ministry of Foreign Policy and Italian Development Cooperation**

LUIGI NALDINI
Professor, M.D., Ph.D.,
Co-Founder & Executive Scientific Board Chairman

- "Father" of Lentiviral Gene Therapy
- Director **SR-Tiget**, Professor of Cell and Gene Therapy at **San Raffaele University**, Milan, Italy
- He developed with Russo, as GSK exe, the **first ever gene therapy product approved** for commercialization, 2017 Strimvelis® for ADA-SCID

CARLO RUSSO
M.D., Chief Medical Officer &
Head of Development

- Former **GSK** head of R&D Rare Disease Unit; Head of Devel. R&D Biopharma Unit
- Former **Merck** Head of Requlatory for New Vaccines, including Gardasil and Rotateg

RICHARD B. SLANSKY
Chief Financial Officer

- 30+ years life science executive experience including at **Biological Dynamics, GenMark** and **CN Bioscience**
- Raised $500MM+ in equity and debt capital in public and and private offerings

STEFANIA MAZZOLENI
Ph.D., Director of Program Development

- 15+ years experience in R&D, oncology and project management, in both academia and industry

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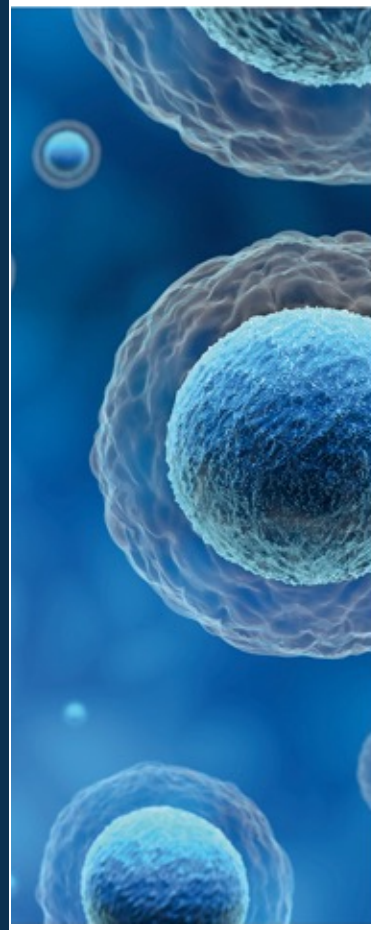
Genenta Built on Strong Foundations



PROPRIETARY PLATFORM TO PROVIDE DURABLE AND SAFE TREATMENTS FOR SOLID TUMORS

GENERATING CLINICAL PROOF OF CONCEPT FOR BREAKING IMMUNE TOLERANCE

ROBUST FUNDING AND PARTNERSHIPS TO TAKE TO NEXT STAGE

- **One-time cell therapy** designed to break tumor-induced immune suppression by enabling sustained targeted expression of **therapeutic payload inside the TME[1] minimizing potential systemic toxicity**
- **Tumor and antigen agnostic**
- Highly synergistic in **combination with I/O**
- Lead product candidate precisely delivers **IFN-α to the tumor microenvironment aiming to break immune tolerance**
- Phase 1/2a clinical data: favorable initial biological data with **no drug limiting toxicities**

- **Expected cash runway to Q2 of 2025**; ~$10M Tax Credit accumulated to date
- Research engine through partnership with **SR-TIGET[2]**

1 TME: tumor microenvironment
2 SR-TIGET is a world leading cell and gene therapy institute founded by San Raffaele Research hospital, a co-founder and key shareholder of Genenta, and non-profit organization Telethon

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Temferon™ Designed to Address Three Major Challenges in I/O Treatment of Solid Tumors

TEMFERON

ACHIEVE DURABLE RESPONSES

ENABLE A DURABLE THERAPEUTIC POTENTIAL

Engineering of hematopoietic stem and progenitor cells (HSPCs) creates a **living drug stable reservoir** that may ensure a persistent response (HSCS ex-vivo Lentiviral strategy).

AGNOSTIC BUT SELECTIVE DELIVERY AND SWITCH COLD TO HOT

DELIVER TREATMENTS TO SOLID TUMOR AND BREAK TUMOR INDUCED TOLERANCE

Tie2+ expressing monocytes (TEMs), naturally recruited by growing tumors, **infiltrate and deliver the payload.**

AVOID SYSTEMIC TOXICITY

LIMIT EXPRESSION OF THERAPEUTIC TO TUMOR MICROENVIRONMENT

Proprietary transgene expression technology designed to ensure **precise intra-tumor expression of payload therapy avoiding systemic toxicity** (microRNA regulation).

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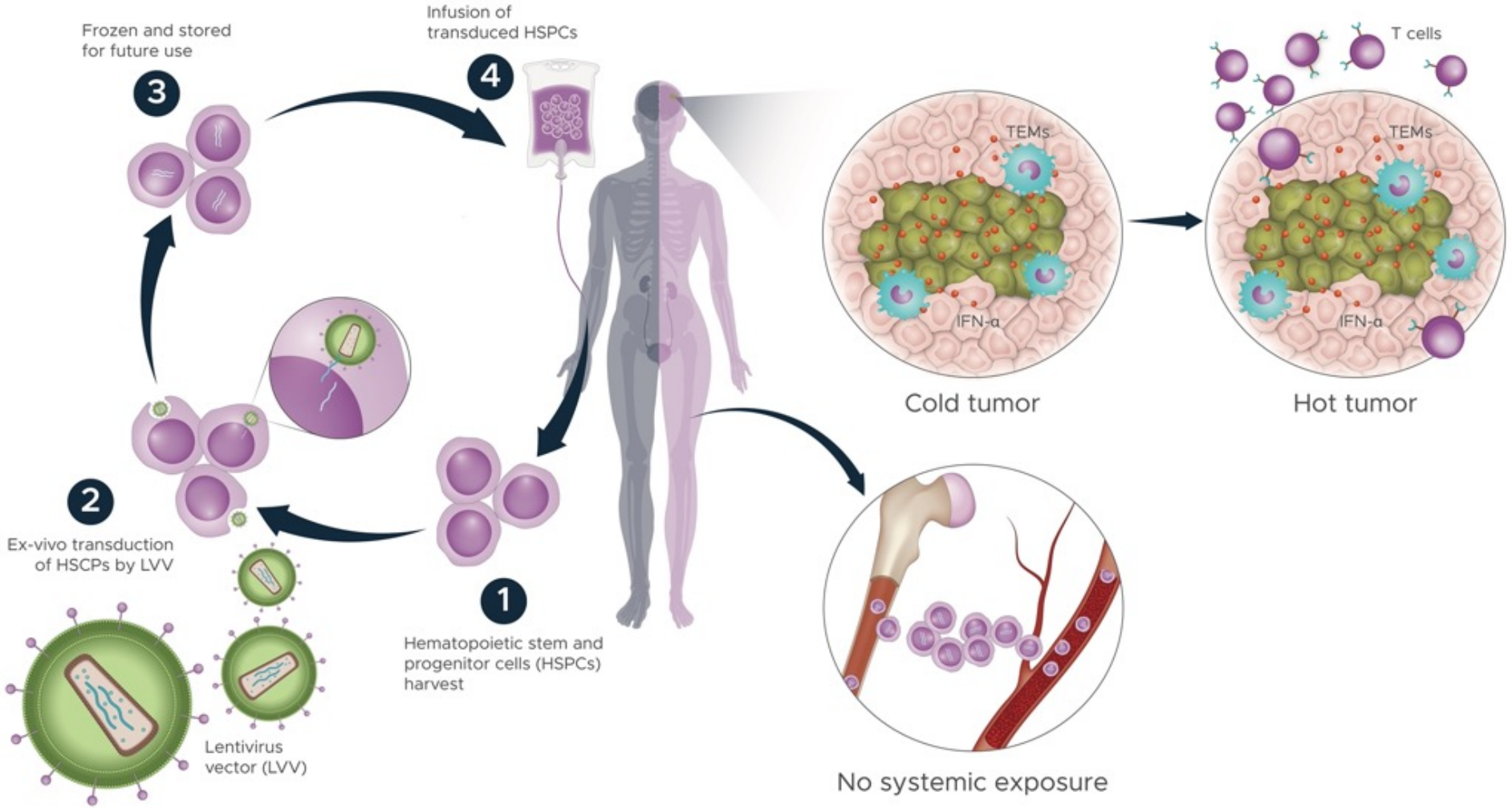
Temferon: Hematopoietic stem cell-based single treatment for solid tumors



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Temferon Agnostic Efficacy Designed to Be Suitable For Treatment of Large Number Of Solid Tumors[1]

INDICATION	MARKET SIZE U.S. INCIDENCE[2]	UNMET NEED 5Y SURVIVAL[3]
Glioblastoma Multiforme	~3,721[4]	8.3%[5]
Renal cell carcinoma	~81,800	78%
Melanoma (Stage 4)	~4,880	35%
High Grade Osteosarcoma	3,970	69%
NSCLC (Stage 4)	~126,320	8%
Breast Cancers (Stage 4)	~17,867	30%
Squamous cell carcinoma (SCC) head and neck: (Stage IV)	~45,000	20-50%
Bladder cancer (Stage 4)	~4,114	8%
Liver & Intrahepatic Bile Duct Cancer	~41,210	22%
Gastroesophageal adenocarcinoma/SCC	~21,560	22%
Mesothelioma	~3,000	12%
Liver metastases (e.g., colorectal, breast, urothelial, melanoma)	~123,000	15% at 1 year
Epithelial ovarian cancer	~19,710	51%

1 – Combo with Immune Checkpoint Inhibitors - I/O, Tie2+ Expressing Monocytes Presence, Tumor Microenvironment access pre- & post-treatment
2 - SEER Database – Estimated new cases in 2023 ; 3 – SEER Database 5-year survival rate 2013-2019;
4 – SEER Estimated New cases in 2023 adjusted on Glioblastoma frequency (15%) over all the primary brain tumor (Omstrom et al., 2019 - https://doi.org/10.1093/neuonc/noz150) ; 5- Stupp et al, 2009 SCC: Squamous Cell Carcinoma

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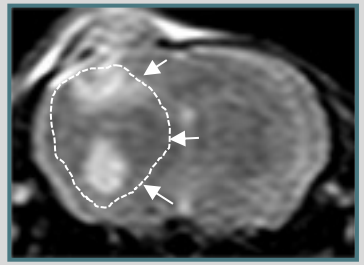
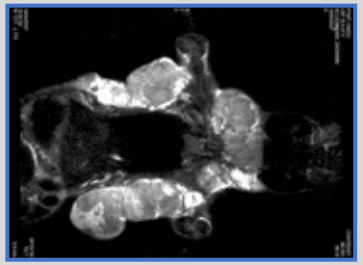
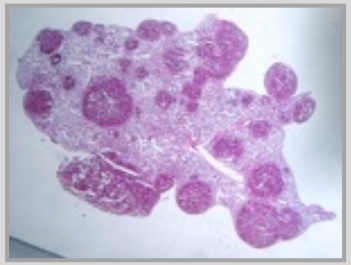
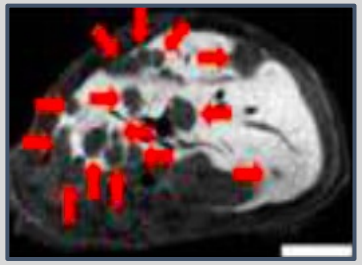
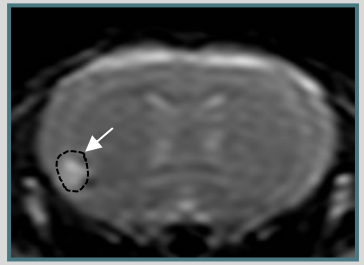
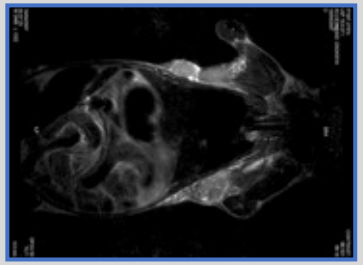
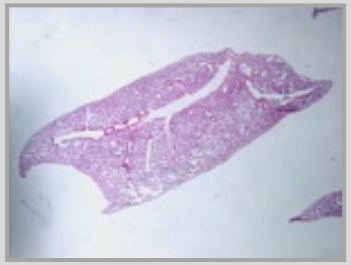
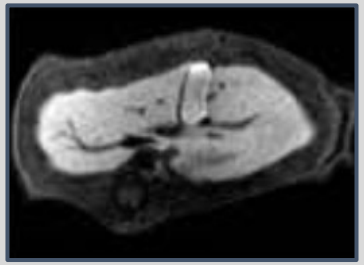
Temferon Agnostic Efficacy in Treating Solid and Hematologic Tumors

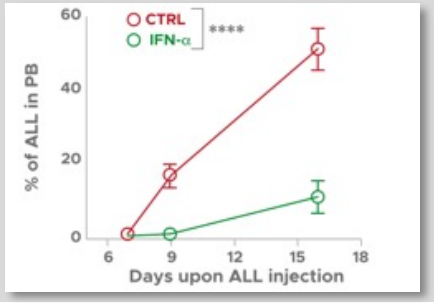
SOLID TUMORS

	GLIOBLASTOMA	BREAST	LUNG METASTASIS	CRC LIVER METASTASIS
CONTROL				
IFN-α IMMUNO-GENE THERAPY				

De Palma et al., Cancer Cell 2008; Escobar et al., Sci Transl Med 2014;
Catarinella et al., EMBO Mol Med 2016; Escobar et al., Nature Communication 2018

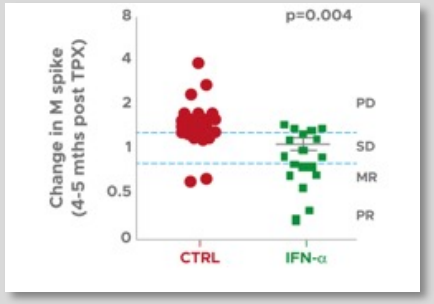
HEMATOLOGICAL MALIGNANCIES

B-ALL
MURINE B-ALL CELLS



Escobar et. al., Nature Communication 2018

MULTIPLE MYELOMA
VK*MYC MICE



B. Gentner Unpublished

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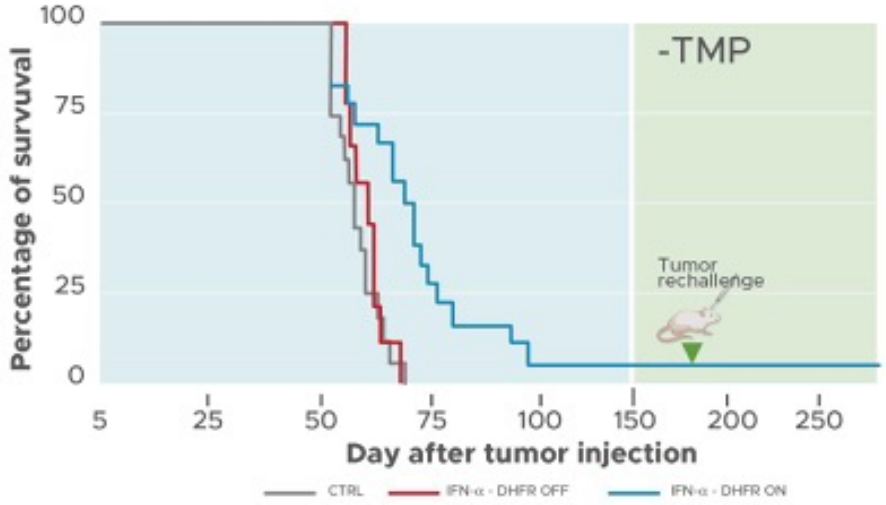
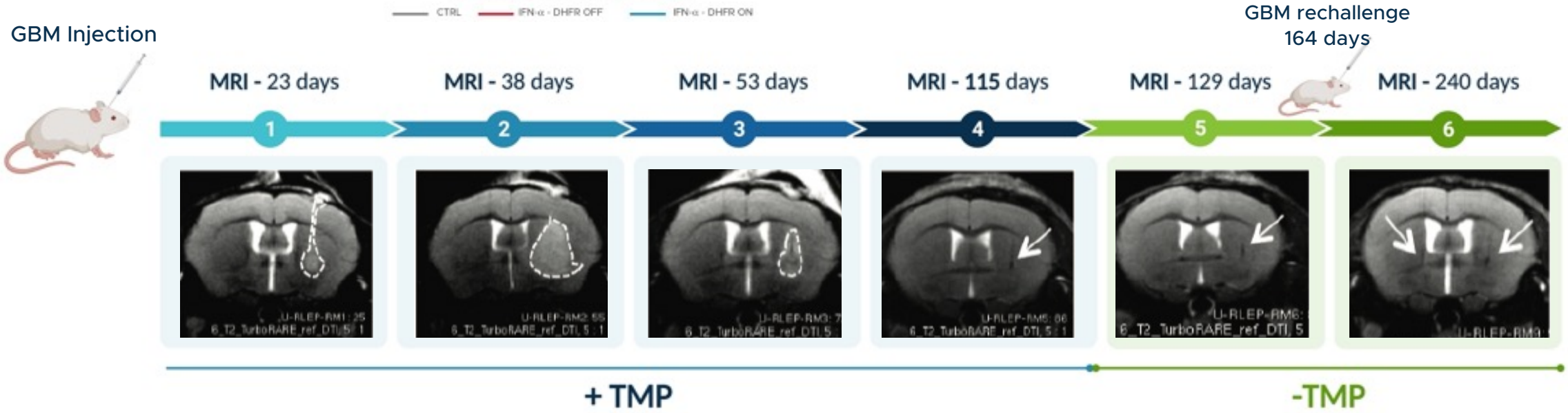
The Temferon Triggered Hot TME Status Results in a Long-Term Immunoprotection



IFN-α cytokine was fused with a destabilizing domain (DD) which cause its proteasome degradation.

Trimethoprim (**TMP**) binds to the DD destabilizing domain and allows IFN-α to be expressed.



Birocchi et al., Science Translational Medicine 2022

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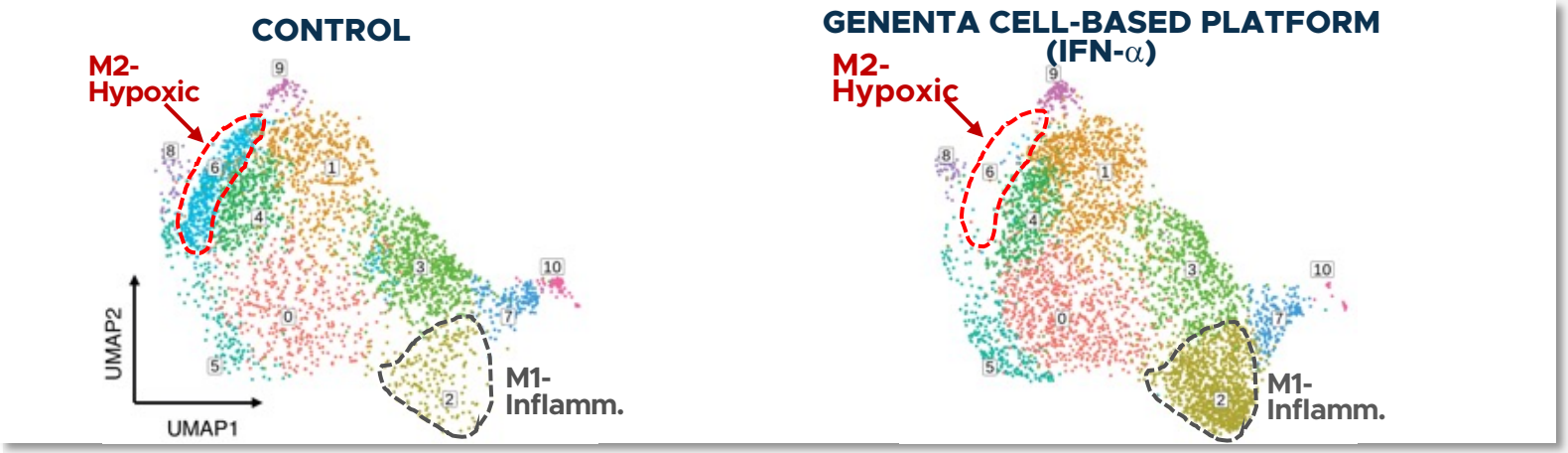
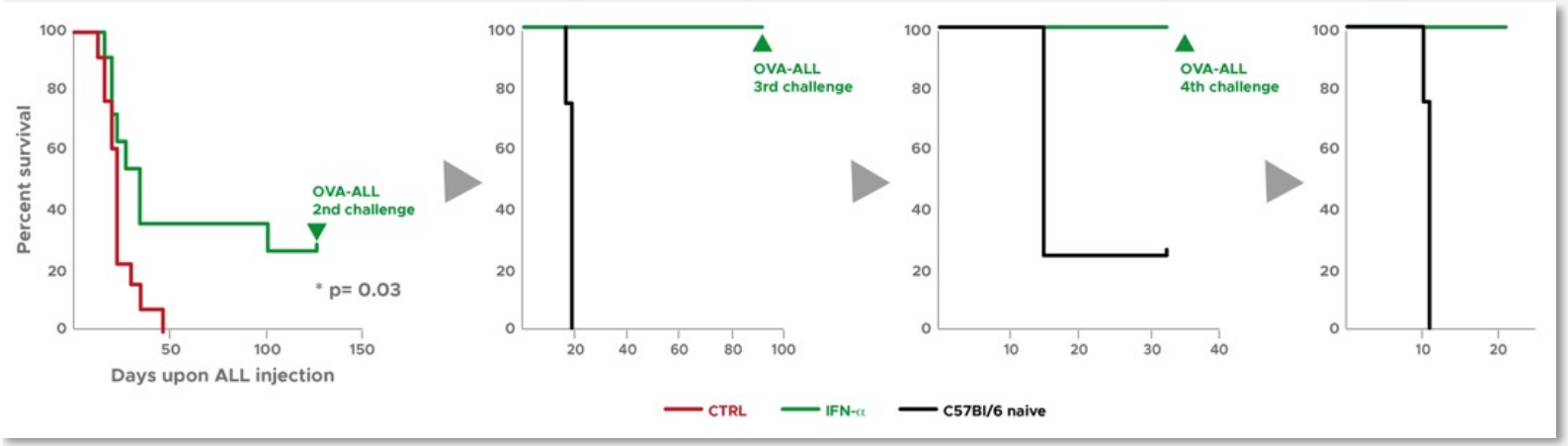
Temferon reprograms the TME and Switches Tumor State from Cold to Hot



SWITCH the TME MYELOID CELL COMPARTMENT…

- imposes an ISG-driven immunostimulatory
- programs to non-classical monocytes associated with M1 skewing of the myeloid populations
- activates tumor-infiltrating DCs



…TO GET a HOT T CELL COMPARTMENT

- increases active CD8+ T cells infiltration
- Induces T cells clonal expansion including cytotoxic CD8+ T cells and tumor-reactive T cell clones
- reduces percentage of exhausted CD8+ T cells
- increases the central memory T cells

Graphs have been faithfully reproduced by the original article

De Palma et al., Cancer Cell, 2008; Escobar et al., Sci Transl Med, 2014; Catarinella et al., EMBO Mol Med, 2016; Escobar et al., Nature Communication 2018; Birocchi et al., Sci Transl Med, 2022

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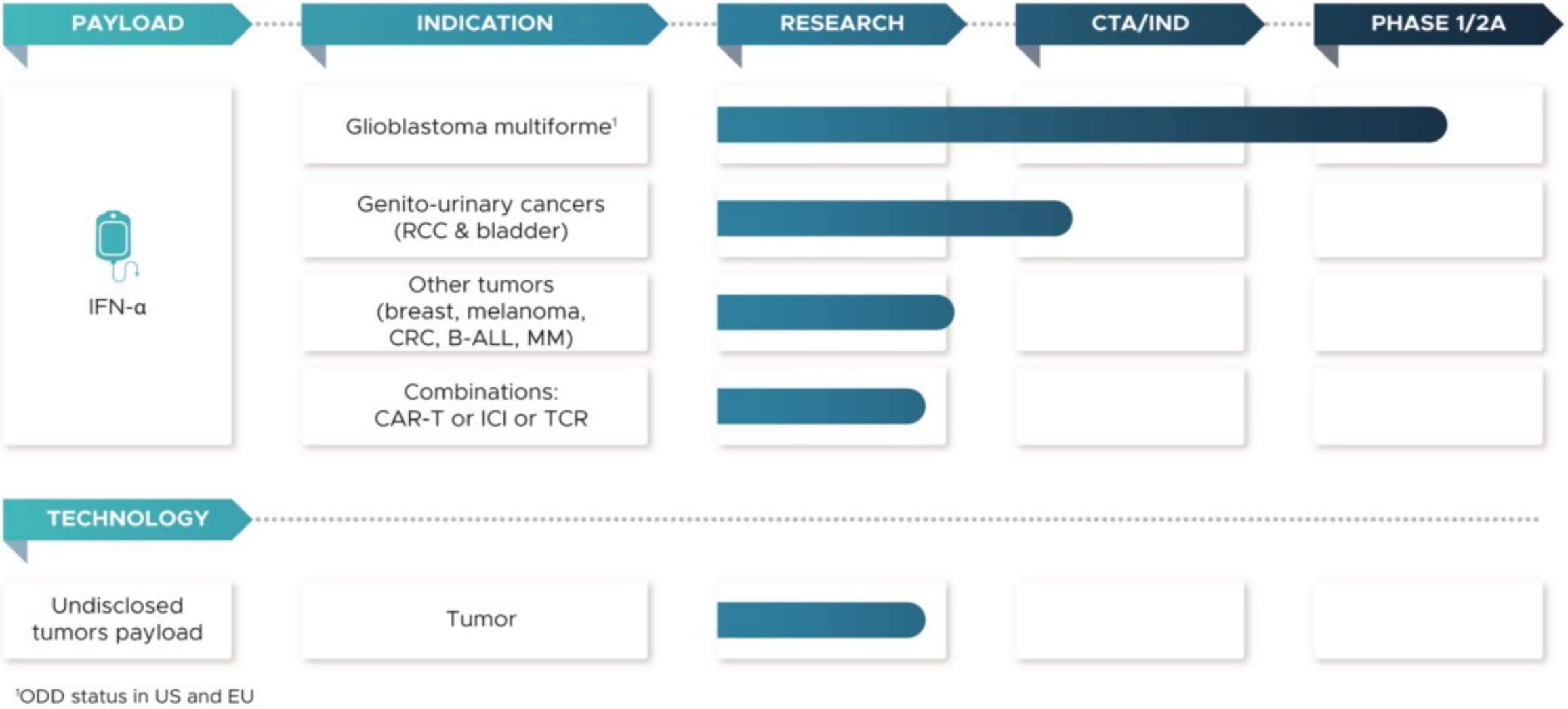
Pipeline



[1]ODD status in US and EU

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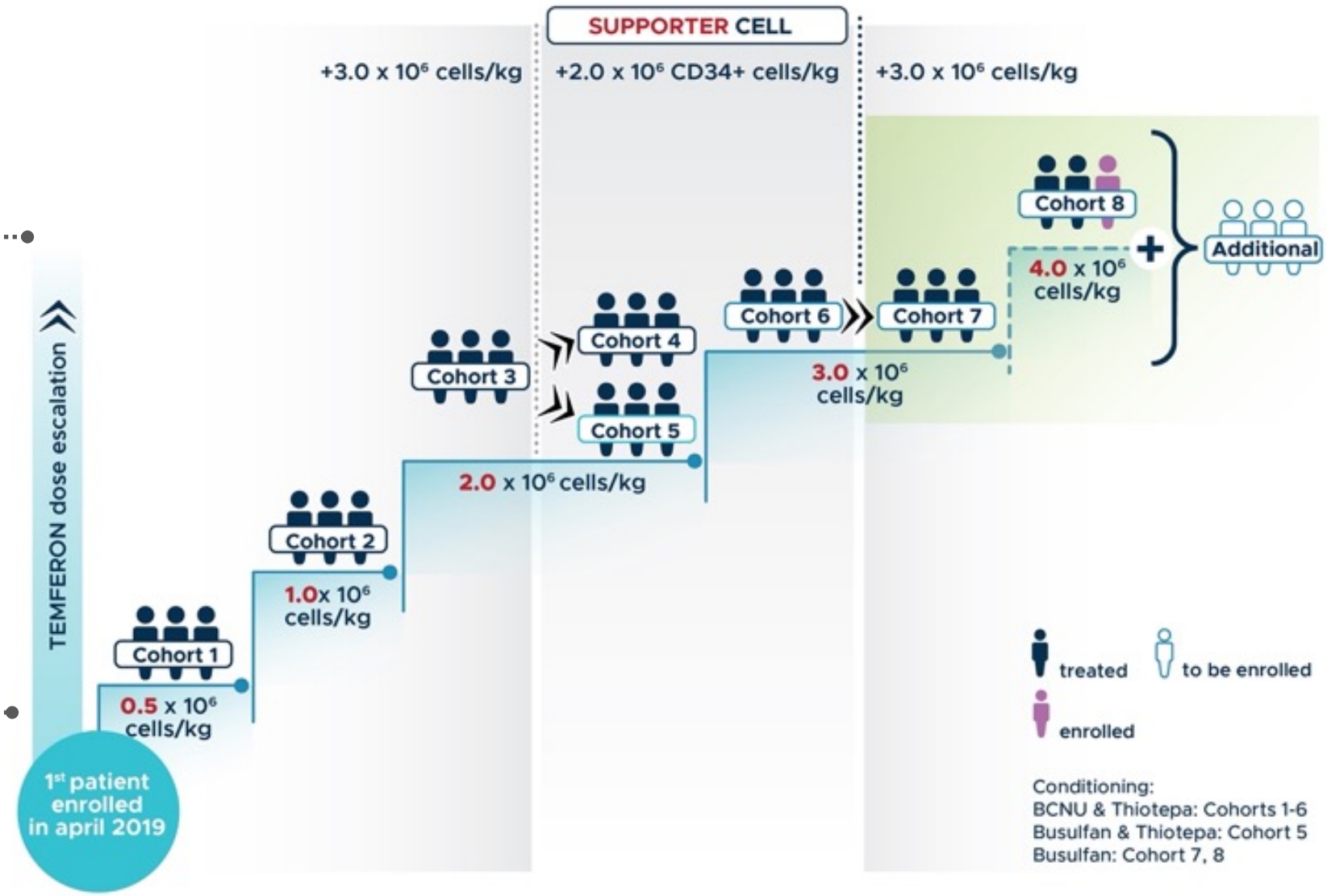
Temferon Dose Ranging Phase 1/2a Trial in uMGMT GBM

A multi-center, open-label, dose escalation & extension study in newly diagnosed GBM patients with unmethylated MGMT promoter following standard of care.
DMC[1] at completion of each cohort

PRIMARY ENDPOINTS:
Tolerability and safety at 90 days

SECONDARY ENDPOINTS:
Long-term tolerability, safety and efficacy including PFS and OS up to 2 years



*1 DMC: Data Monitoring Committee

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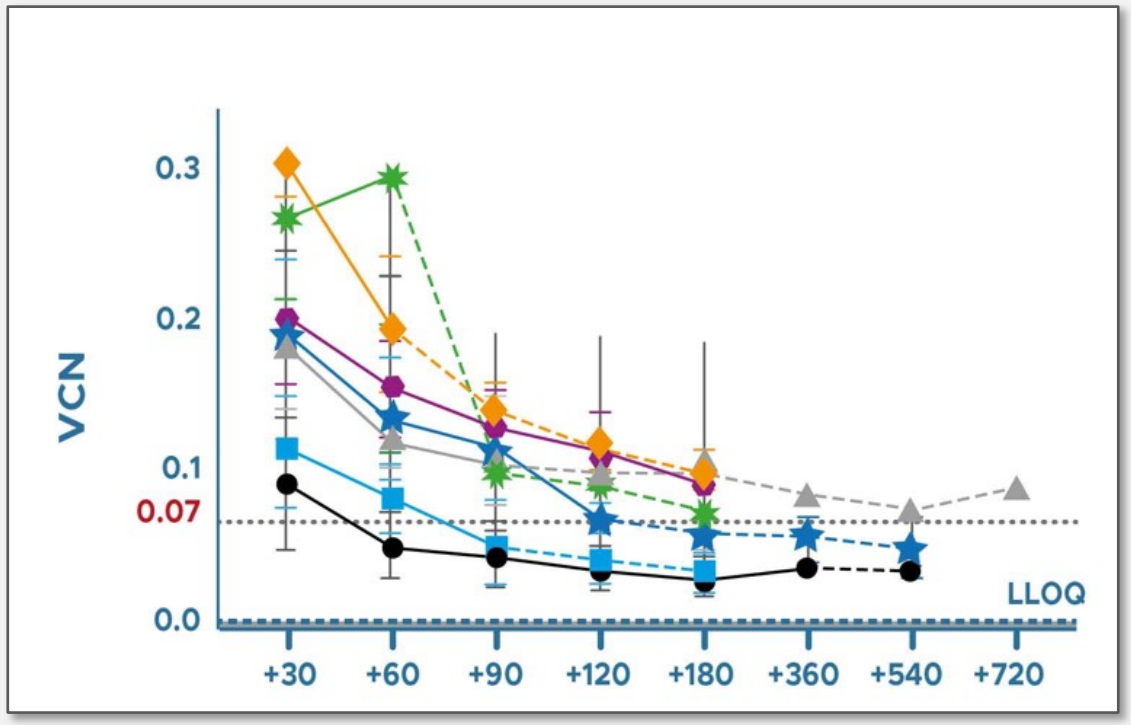
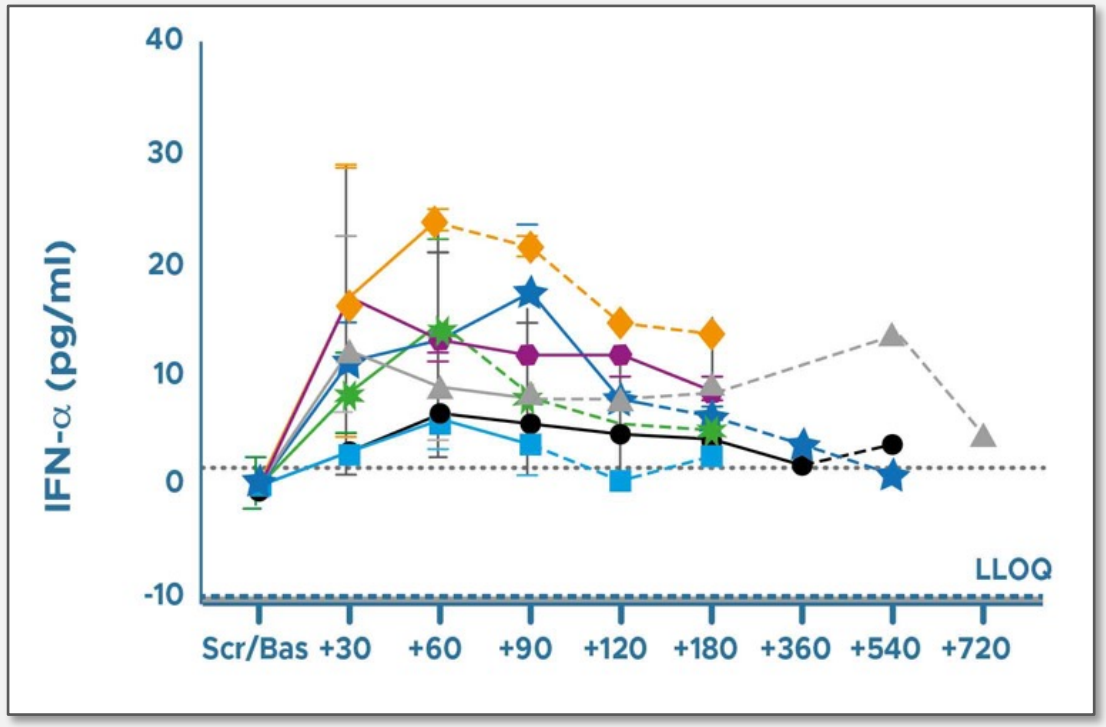
Temferon Single Dose is Durable and Well Tolerated





Cohort 1 Cohort 2 Cohort 3 Cohort 4 Cohort 5 Cohort 6 Cohort 7

Dashes line connect timepoints with less than 3 measurements

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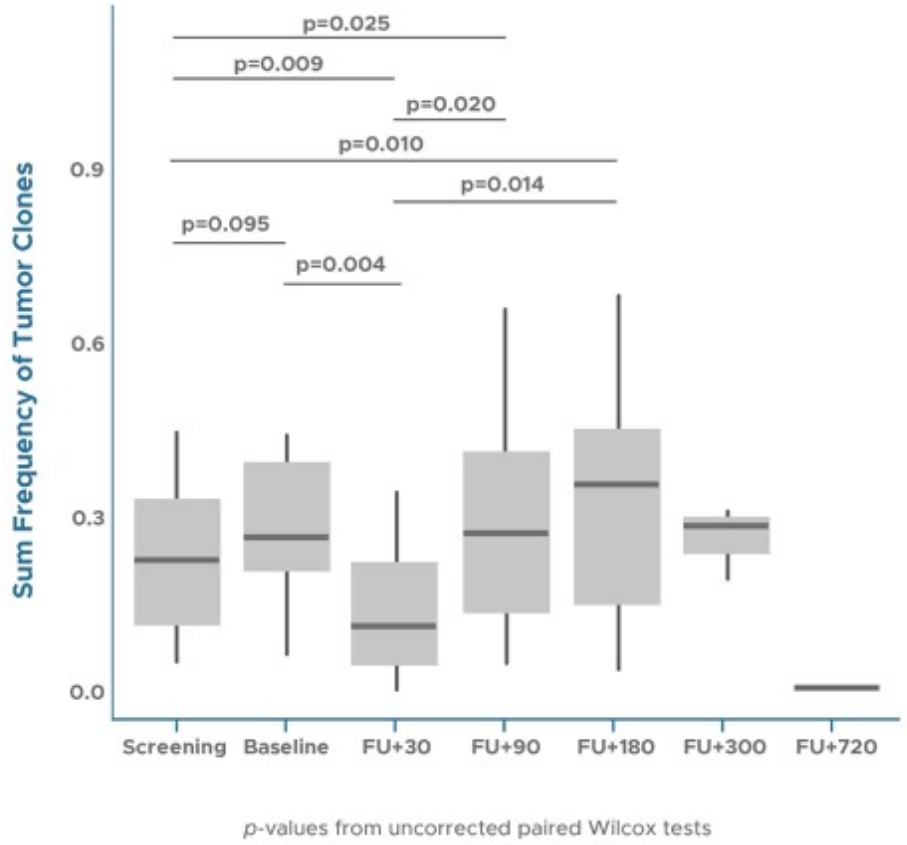
Temferon Breaks Tolerance Allowing Intra Tumor Infiltration of T Cell Clones

T CELL CLONES FROM THE TUMOR CAN OFTEN BE DETECTED IN THE BLOOD

- Contraction at day +30 in the blood (ASCT conditioning)
- Rebound after 3-6 months

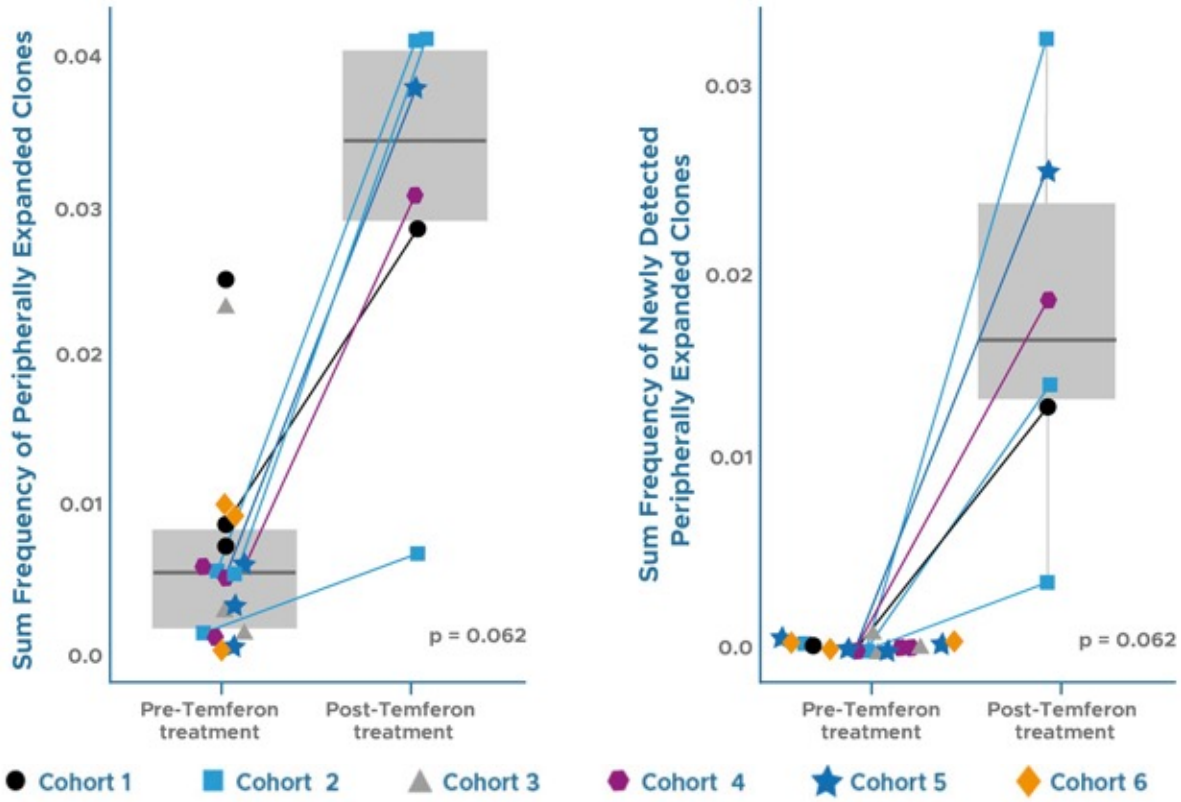


p-values from uncorrected paired Wilcox tests

EXPANDED PERIPHERAL T CELL CLONES ARE INCREASED AT 2nd SURGERY

Pre-existing peripheral T cells clones

Newly-detected peripheral T cells clones



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Preliminary Clinical Data in uMGMT GBM: Safe, Well Tolerated and Biologically Active

SAFETY

Detectable but very **low level of IFN-α** (pg/ml range) in the plasma.
Expected and **manageable** adverse events and serious adverse events[1] associated with autologous stem cell transplantation and glioblastoma.

TOLERABILITY

No dose limiting toxicities to date.
Rapid engraftment and **hematological recovery** observed in all patients treated (n=22).

BIOLOGICAL ACTIVITY

Current data shows median **overall survival of 17** months[2] **with an interim[2] 2-year survival rate higher than what is historically reported.**
Temferon-derived differentiated cells were evident within the peripheral blood 14 days after infusion and were still **detectable at more than 24 months.**
Evidence of a **pro-inflammatory state** in patients that required a second surgery.

1 - The reported serious adverse events (SAEs) for Cohorts 1 to 6 were of the type typically associated with transplant procedures (pneumonia, pulmonary embolism, febrile neutropenia, fatigue, C.diff infection, CMV reactivation, sepsis, anemia due to CMV reactivation) or underlying disease GBM (worsening left hemiparesis, seizure, brain abscess, sudden death). A suspected unexpected serious adverse reaction (SUSAR) of elevated gamma glutamyl transferase was also reported (spontaneously resolved).
2 - Cutoff date – December 21, 2023

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Temferon 2nd Solid Tumor Indication Urinary Cancers

Genenta selected **metastatic clear cell renal cell carcinoma** (mRCC) and **metastatic urothelial carcinoma** (mUC) as additional solid tumor indications for Temferon clinical development

RATIONALE

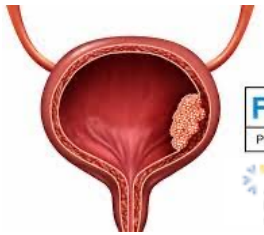
Strong historical evidence to support potential Temferon efficacy

- Until 2005, systemic administration of IFN-α and IL-2 were SOC treatment for mRCC.
- IFN-α in mRCC was associated with a survival benefit compared to controls [644 mRCC pts: OR for death at 1 year=0.56 (95%CI 0.40 to 0.77)[1]]
- Systemic IFN-a use limited in the past by the systemic toxicities
- IFN-α as an intravesical therapy for UC has been evaluated over many decades with variable results.
  Short drug exposure time rather than inherent lack of anti-tumour activity[2]

SOLUTION

Temferon has been designed to attenuate systemic toxicity associated with IFN-α and to achieve greater therapeutic benefit within the TME

Targeted IFN-a delivery as an innovative and clinically relevant approach



FERRING PHARMACEUTICALS

ADSTILADRIN (nadofaragene firadenovec-vncg)

BCG-unresponsive non-muscle invasive bladder

- CR in 51% of patients with *in situ* carcinoma by three months[3]

Temferon reprograms the TME and acts directly on tumors cells and neo-angiogenesis

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1. Coppin et al. 2004; 2. Duplisea 2019; 3. Adstildarin USPI 2023

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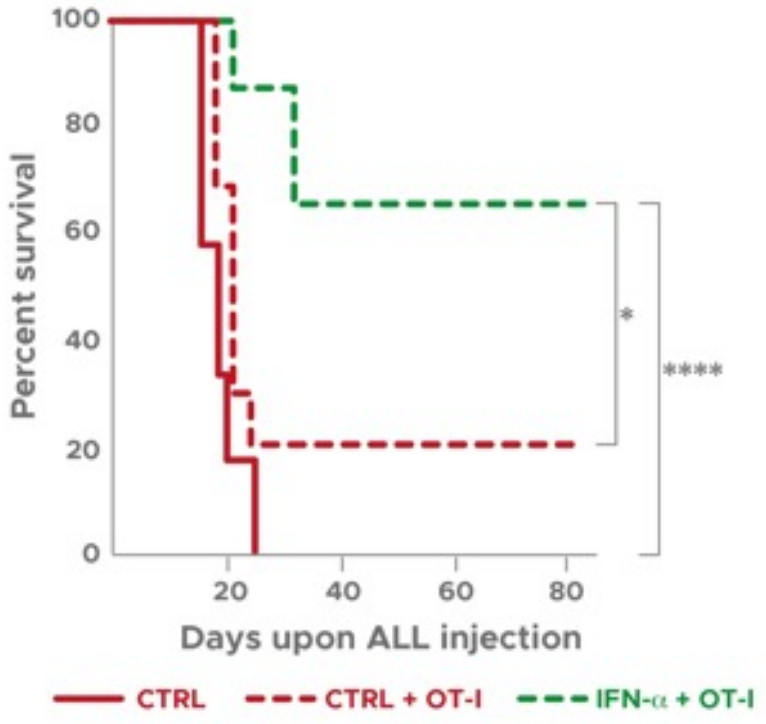
Combination of Temferon with I/O Treatments Increases OS and Tumor Control

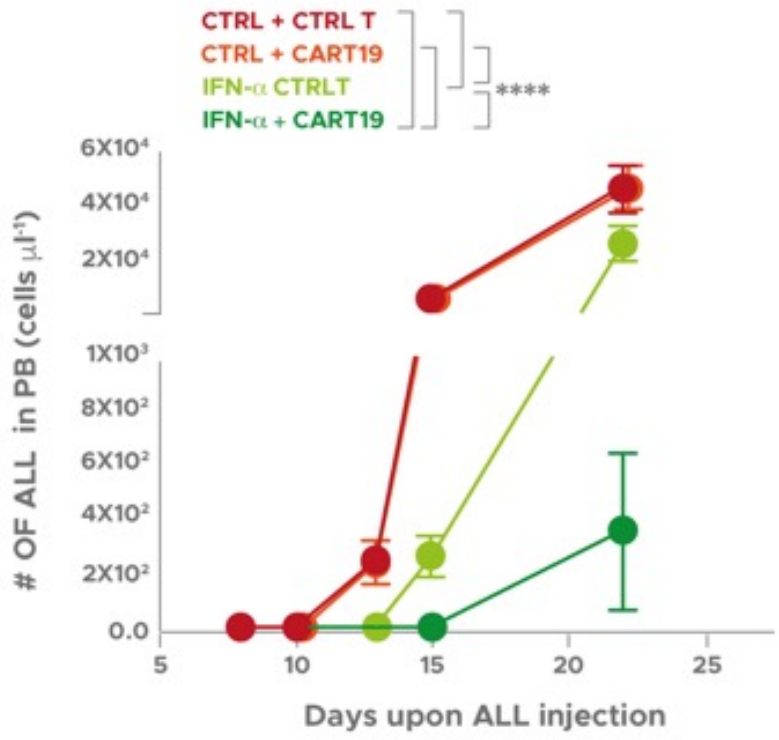
Temferon boosts/rescues other I/O therapies

ADOPTIVE T CELLS TRANSFER



OT-I = Ovalbumin transgenic mice

CAR-T



Escobar et al., Nature Communication 2018

Graphs have been faithfully reproduced by the original articles

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Summary: Working Towards a Transformative Single and Permanent Treatment of a Broad Range of Solid Tumors

- Transformative proprietary platform designed to overcome the challenges of immuno-oncology therapy: infiltrating solid tumors, limiting toxicity and achieving a durable response
- Supported by preclinical and initial clinical data including engineered cells in patients from 14 days until 18 months+ after treatment, and payload expression without systemic toxicity
- Tumor and antigen agnostic; potential for broad combination use
- Combination use with I/O confirmed in preclinical animal models
- Upcoming catalysts:
  - Part 1 of Phase 1/2a for GBM completed enrollment in 1Q'24
  - Amendment Submission for the Phase 2 GBM study in H2'24
- Expected cash runway to Q2 of 2025, with no debt or warrants[1]
- In 1H 2023, the U.S. Food and Drug Administration (FDA) and the European Commission have granted Orphan Drug Designation (ODD) to Temferon for the treatment of glioblastoma multiforme.
- Refractory Advanced Genitourinary Malignancies have been selected as the additional solid tumor indications for Temferon clinical development

1 - Except normal payables, accruals and underwriters' warrants

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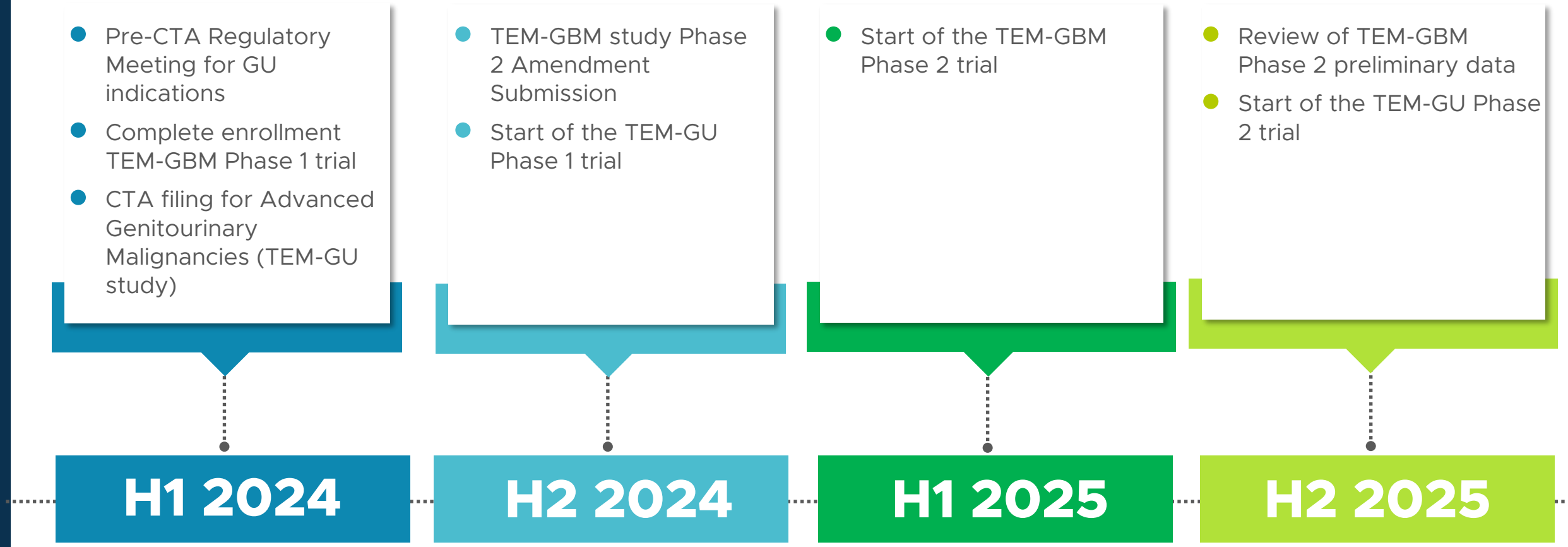
Anticipated Pipeline Development Milestones *



* Our anticipated pipeline development milestones constitute forward-looking statements as discussed in greater detail on slide 2. You should not rely upon forward-looking statements as predictions of future events.

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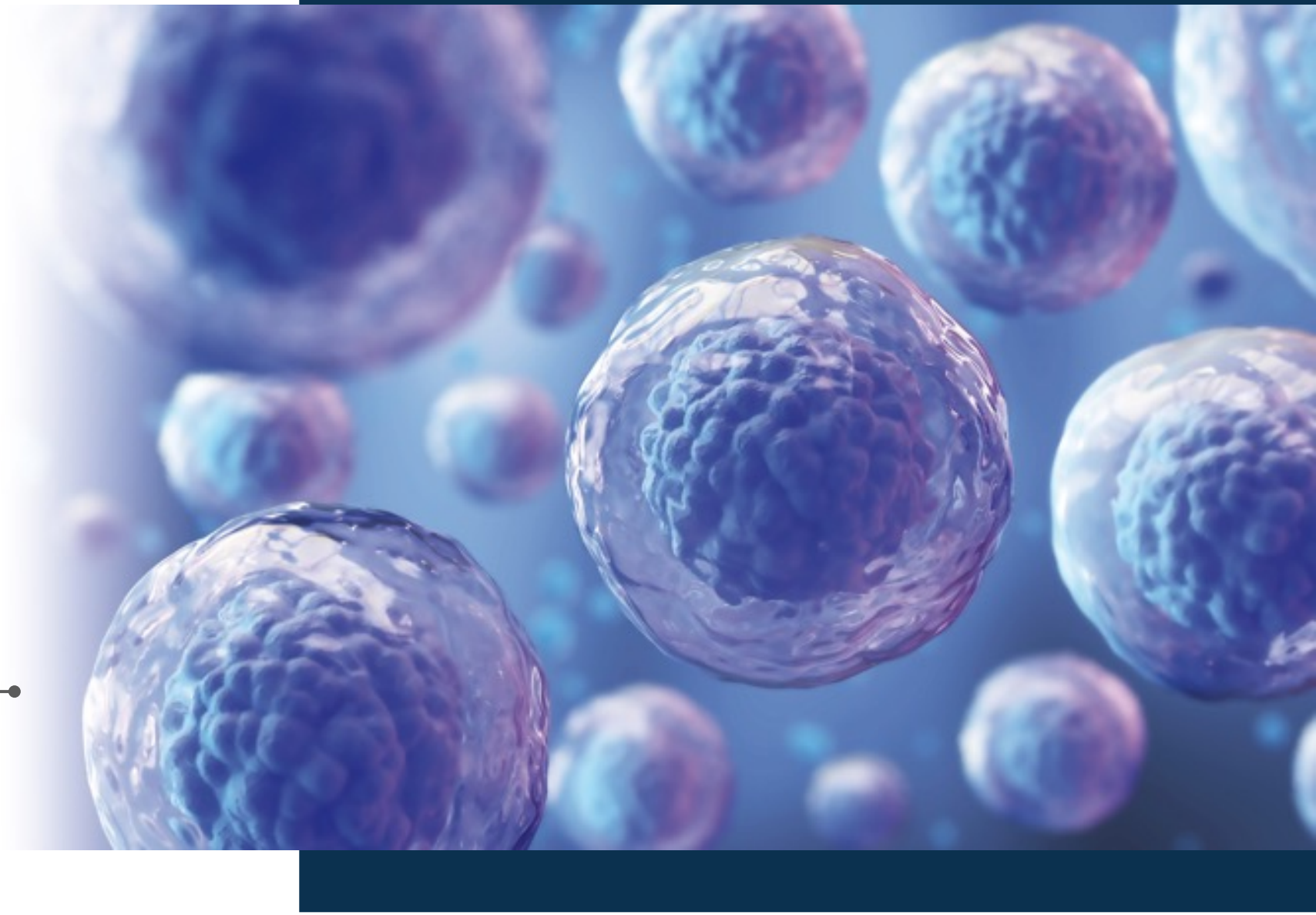

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pierluigi.paracchi@genenta.com

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LaunchLabs - Alexandria Center, 14th Floor - 430 East 29th Street
New York, NY 10016, USA

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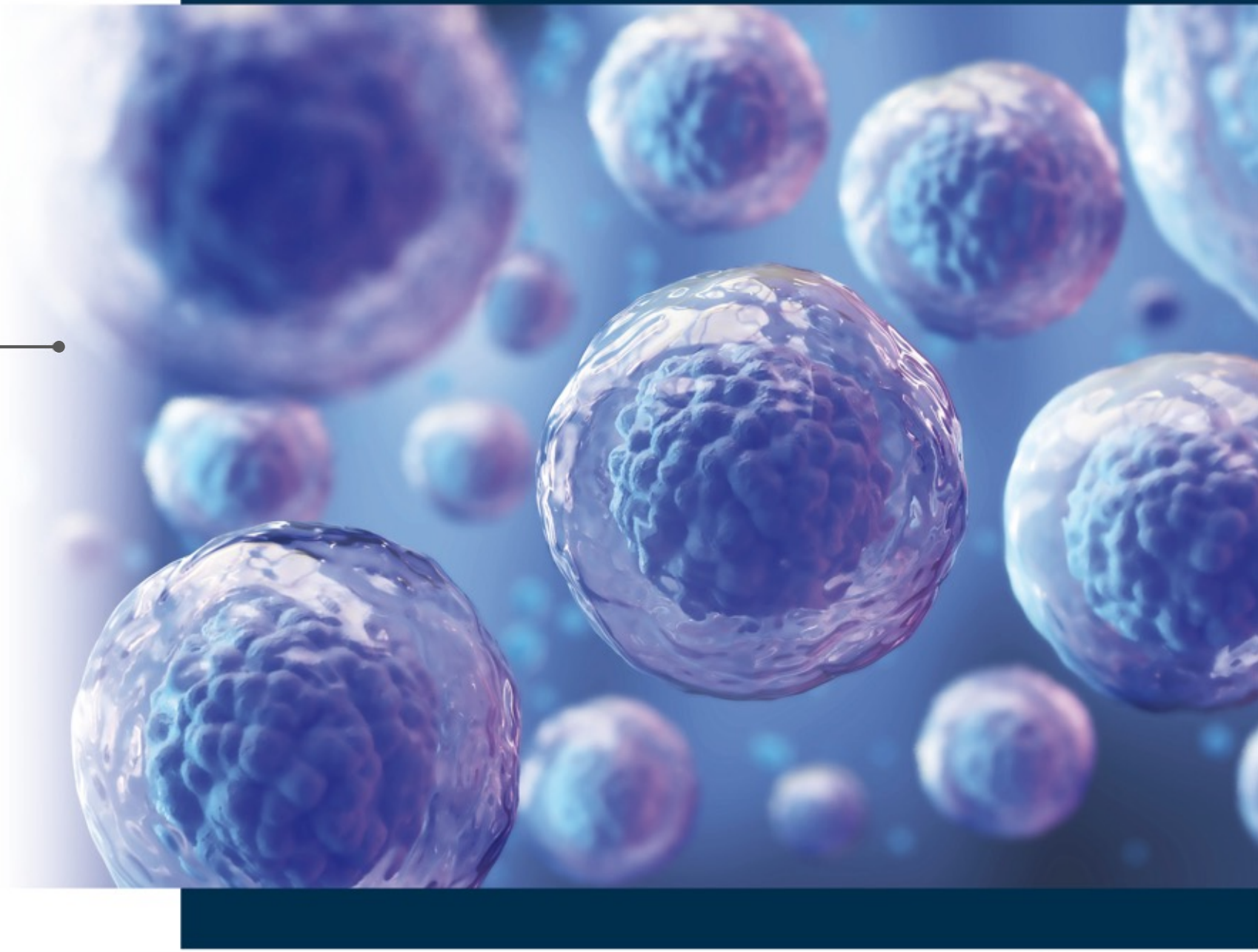
APPENDIX



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MECHANISM OF ACTION

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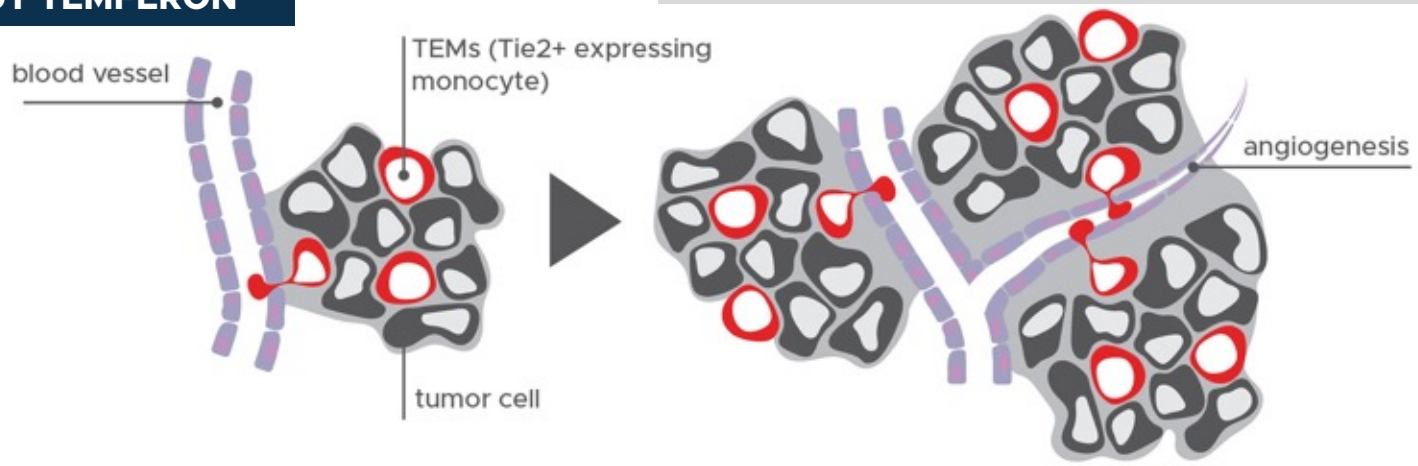
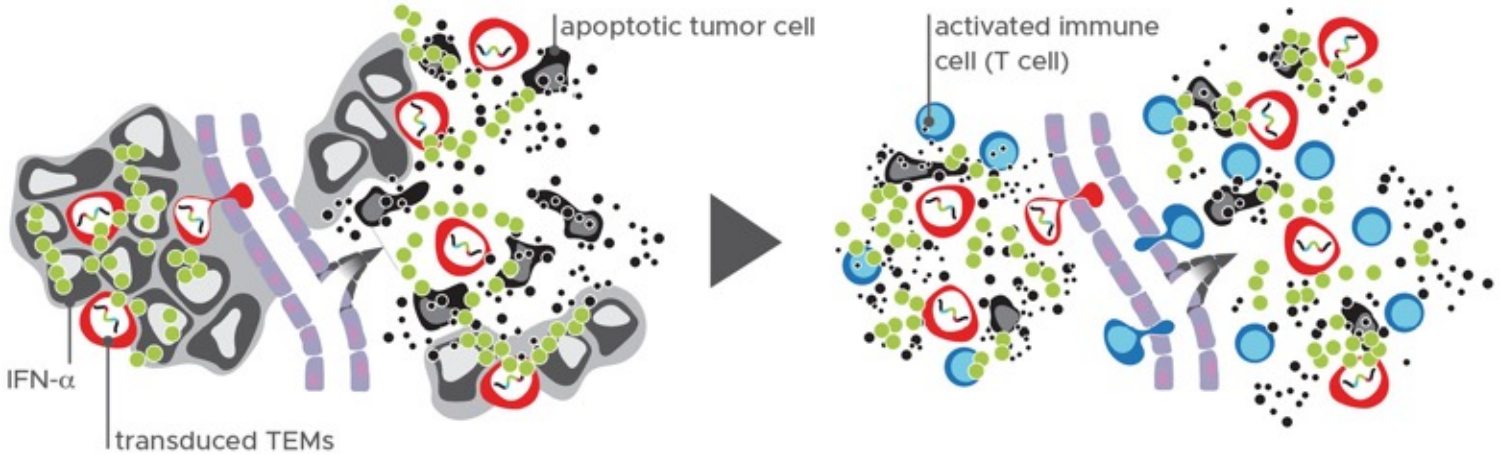
Temferon Designed to Deliver IFN-α in the Tumor Microenvironment to Break Immune Tolerance

WITHOUT TEMFERON



TEMs* are natural tumor infiltrating monocytes associated with angiogenesis in tumors

WITH TEMFERON



IFN-α targets tumor proliferation via anti-angiogenic impact and reprogramming the immune system

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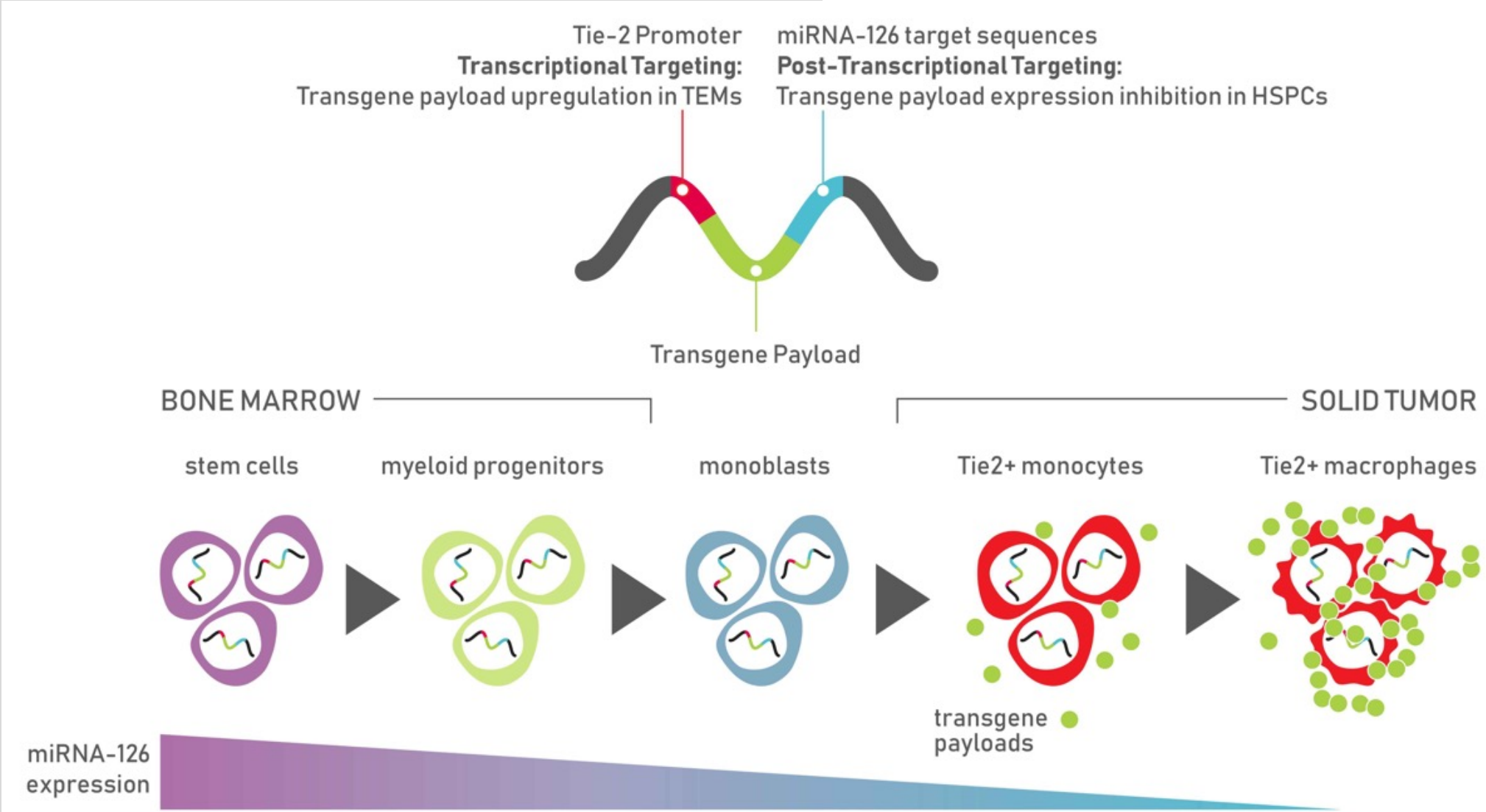
Proprietary mRNA Mediated Control of Payload Expression

Interaction of miRNAs with their miRNA-targets regulates gene expression via mRNA degradation and translational repression



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Clear Development Rationale for Temferon in GBM

ROBUST SCIENTIFIC GROUNDING

- Characterized by **a highly suppressive tumor microenvironment** induced by a subset of tumor associated macrophages
- Temferon is designed **to break immunosuppression**

LIMITED AVAILABLE TREATMENTS

- Temferon may be offered as **1st line monotherapy** after 1st surgery enabling patient's **uncompromised immune system to be harnessed**
- Enables impact of Temferon to be **seen in isolation**
- Temferon **ODD status in US and EU**

FAVORABLE PRECLINICAL DATA

- Temferon demonstrates **control of GBM** pathology despite its aggressive nature
- T emferon creates **a pro-inflammatory state** that induces an immune system reset, **breaking tumor tolerance**

ABOUT GBM

Estimated market size by 2032: $3.4B[1]

Annual incidence: 3 per 100,000 adults[2], ~60% with uMGMT promoter status[3] (target population)

Median survival: ~≤ 15 months[3]; 5-year survival: 5.5%[4]

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1- Glioblastoma Multiforme (GBM) Market Insight, Epidemiology and Market Forecast-2032; 2 - https://www.ncbi.nlm.nih.gov/books/NBK470003/; 3 - https://www.futuremedicine.com/doi/10.2217/cns-2021-0007; 4 - https://www.statpearls.com/ArticleLibrary/viewarticle/22272

Intellectual Property

- Potential 12-year market exclusivity for new biological products (U.S.)
- Key patents already granted

	US	EU	China	Japan	ROW	Expiration
Gene vector comprising mi-RNA	✓	✓	✓	✓	✓	4/30/2030
mi-RNA regulated vectors	✓	✓	✓	✓	✓	5/26/2026*
Monocyte cell (Tie-2) activation process	✓	✓	✓	✓	✓	10/5/2027
Method for Genetic Modification	✓	✓	✓	✓	✓	10/24/2034*
Vector Production	✓	pending	pending	✓	pending	7/13/2035
Type 1 IFN gene therapy	pending	pending	pending	pending	pending	4/20/2038**

*Later expiration for certain U.S. patents pursuant to patent term adjustment (35 U.S.C. §154(b))
** Application pending, anticipated expiration based on 20 years patent term.

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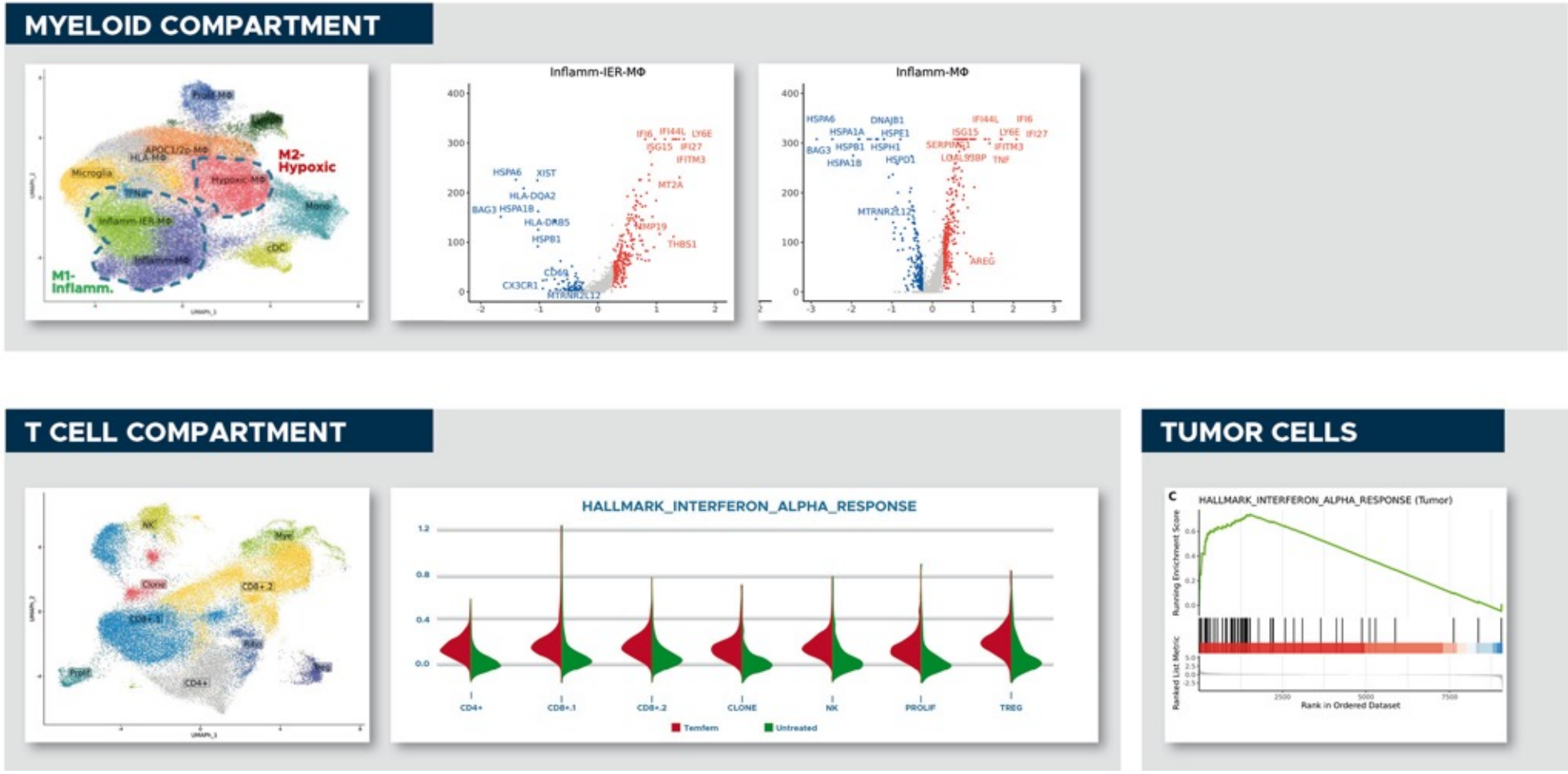
scRNAseq of GBM TME in Temferon and SOC Treated Patients

scRNAseq of GBM TME: Comparison of **5 Temferon patients** and **6 SOC control relapses pts**

- Temferon patients who underwent second were compared to six recurrent glioblastoma patients treated as per the current first line standard of care (SOC – Temozolomide + Radiotherapy).
- Patients who received Temferon showed a general upregulation of IFN-α response hallmarks in the myeloid and T cells compartment of hematopoietic origin (CD45+ cells) and in the tumor cells (CD45-).



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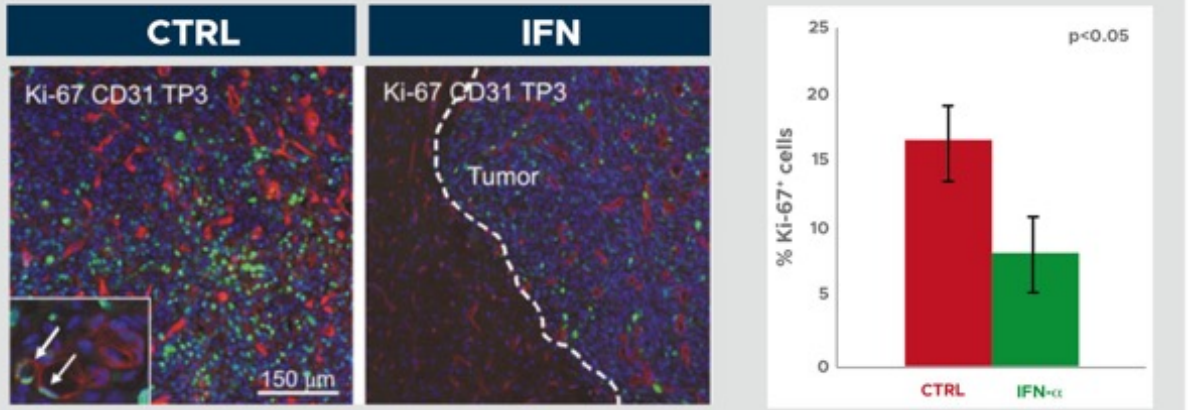
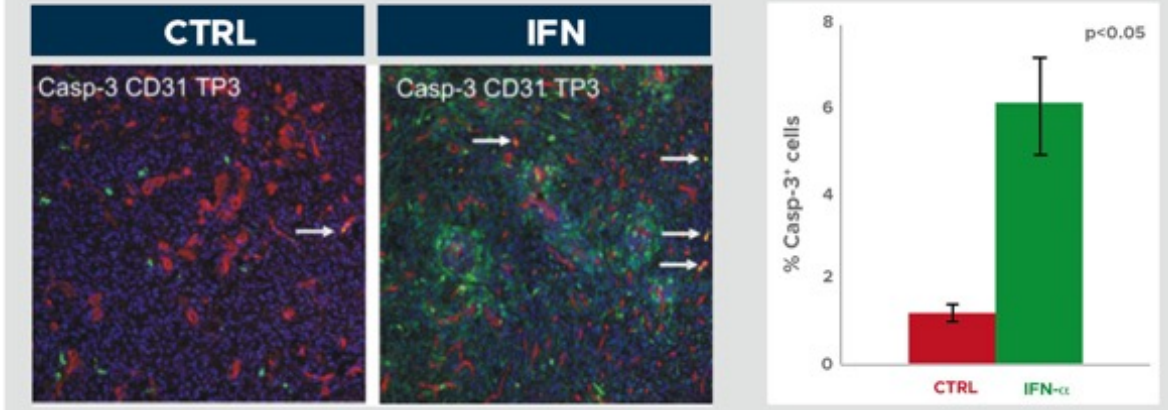
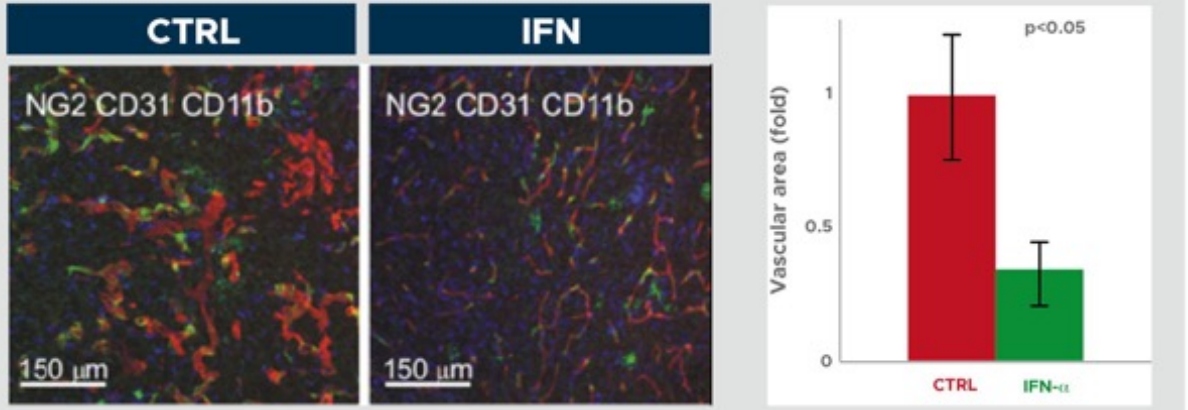
TEMs Cells Therapy Counteract Tumor Growth by Acting on Proliferation and on Vascularization

Tumor growth inhibition by TEMs IFN cell therapy in immunocompromised mice demonstrated the direct targeting at host-derived components like tumor cells and vessels







- Reduction of proliferative index (Ki67)
- Reduction of vascularization and vessels normalization (CD31)
- Increase apoptosis (Casp-3)

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Scientific Advisory Board

LUIGI NALDINI
Professor, M.D., Ph.D.

He has pioneered the development of lentiviral vectors for gene therapy. With over 280 scientific papers, he has a SCOPUS Author h-index of 101. He has won numerous awards: the Outstanding Achievement Award from the American Society of Gene and Cell Therapy (ASGCT) in 2014, President of ESGCT in 2015, the Beutler Prize from the American Society of Hematology (ASH) in 2017, the Jeantet-Collen Prize for Translational Medicine in 2019. He was nominated as "Grande Ufficiale" dell'Ordine "Al Merito della Repubblica Italiana", one of the highest ranking honors in Italy, by the President of the Republic in 2019 and he is "Socio Corrispondente – Classe di Scienze Fisiche, Matematiche e Naturali" at Accademia Nazionale dei Lincei.

BERNHARD GENTNER
Professor, M.D., Ph.D.

Co-Founder. He is Professor in Immuno-Oncology, attending physician in the Oncology Department at Lausanne University Hospital, Medical Director for the T cell therapy platform and heads of HSC engineering within the Lausanne branch of the Ludwig Institute. He was Group Leader at SR-TIGET and Staff Hematologist at the San Raffaele Hospital. Received a MD from the University of Heidelberg and trained at MD Anderson Cancer Center and Baylor College of Medicine, Houston, Erlangen University Hospital and at San Raffaele Vita-Salute University. He is Author of more than 60 scientific publications and the recipient of the Young Investigator Award of ESGCT.

KENNETH C. ANDERSON
Professor, M.D.

Kraft Family Professor of Medicine at Harvard Medical School and Director of the Lebow Institute for Myeloma Therapeutics and Jerome Lipper Multiple Myeloma Center at Dana-Farber Cancer Institute. He is a Doris Duke Distinguished Clinical Research Scientist and American Cancer Society Clinical Research Professor.

LISA COUSSENS
Professor, M.D., Ph.D., FAACR

Professor and Chairwoman, Cell, Developmental & Cancer Biology Department at Oregon Health & Science University. She also serves as Hildegard Lamfrom Endowed Chair in Basic Science and Associate Director for Basic Science, Knight Cancer Institute.

MICHELE DE PALMA
Professor, Ph.D.

Professor at EPFL (École Polytechnique Federal de Lausanne). He is known for his work on the role of macrophages in cancer progression and the discovery of Tie2-expressing angiogenic monocytes.

RICHARD FLAVELL
Professor, Ph.D., FRS

Sterling Professor of Immunobiology at Yale University School of Medicine, and an Investigator of the Howard Hughes Medical Institute.

WOLF-HERVÉ FRIDMAN
Professor, M.D., Ph.D.

Professor Emeritus of Immunology at the Paris Descartes University Medical School in Paris, France. Former head of the Immunology Lab. of European.

MIRIAM MERAD
Professor, M.D., Ph.D.

Director of the Precision Immunology Institute at Mount Sinai School of Medicine NYC and Director of the Mount Sinai Human Immune Monitoring Center. Elected member of the American Society of Clinical Investigation and the recipient of the William B. Coley Award for Distinguished Research in Basic and Tumor Immunology.

TRICK Y. WEN
Professor, M.D.

Professor, Neurology, Harvard Medical School Director, Center for Neuro-Oncology, Dana-Farber Cancer Institute, Boston.

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Financial Profile

Cash & cash equivalents and marketable securities[1]	€ 18.8 MM
Expected cash runway	Q2 of 2025
Debt and warrant[2]	0
Number of shares outstanding[3]	€ 18.3 MM
Average volume[3]	~ 4K shares

1 - As of December 31, 2023
2 - Except normal payables, accruals and underwriters' warrants
3 - As of March 31, 2024

Stock Ownership Info

Founders and Leadership	29%
San Raffaele Hospital[1]	10%
Institutions/Large FOs/Sovereign Fund	19%

1 - San Raffaele Research hospital is a co-founder and key shareholder of Genenta; ongoing relationship through service contract for clinical research.
San Raffaele in alliance with non-profit organization Telethon runs the leading gene therapy institute SR-TIGET

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