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NOX-A12 for Treatment of Brain Cancer – Potential for Transformational Activity in Glioblastoma

November 2026

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Forward Looking Statements

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TME Pharma Key Asset NOX-A12 (INN: Olaptesed Pegol)

NOX-A12 combination in oncology

- Statistically significant survival benefit in chemotherapy-resistant (MGMT-unmethylated), newly diagnosed glioblastoma vs. internal standard of care histology-matched cohort in clinical Phase 1/2 study: p=0.003, HR: 0.17
- Median overall survival (mOS) internal standard of care histology-matched cohort doubled from 9.5 to 19.9 months
- RANO Overall Response Rate of 83.3% (5/6): one confirmed complete response (CR), four partial responses (PR) and one stable disease (SD)
- Combination treatment safe and well tolerated and resulted in reduced tumor perfusion and delayed tumor regrowth
- Fast Track (FDA) and Orphan Drug Designation granted (US & EU)
- Open IND in the US and Phase 2 study approved and open in Germany with clinical trial supply in place to start treatment

Ready-to-go randomized controlled clinical Phase 2 study to confirm survival benefit signal at different NOX-A12 dose levels and to address contribution of components of the combination treatment

Experienced Biopharma Team and Board

MANAGEMENT



Diede van den Ouden
Chief Executive Officer
- 20+ years professional investor experience
- Executive and advisory roles in EU listed companies
- Track record of corporate reorganization



Aram Mangasarian
Chief Scientific Officer
- 25 years in Biotech - Business Development, R&D + IP Management
- M&A and Out-licencing: $505m Astrazeneca acquisition, €150m Forest Labs license, $30m Allergan alliance



Dirk Eulberg
Chief Operating Officer
- 25 years in Biotech – Non-clinical and Clinical R&D, Project Management & IP Management
- Development of 3 drugs from discovery to clinic
- Lead role in big pharma and academic collaborations

SUPERVISORY BOARD



Chairman of the Board
Maurizio Petitbon

- 25+ years of healthcare venture and growth credit investments



Oscar Izeboud
Scenic Biotech
CEO
- 25+ years experience in biotech, including 14 years in investment banking



Lee Schalop
LSWorks
Founder
- 35+ years in banking & biotech incl. successful sale of a brain cancer company

Corporate Information

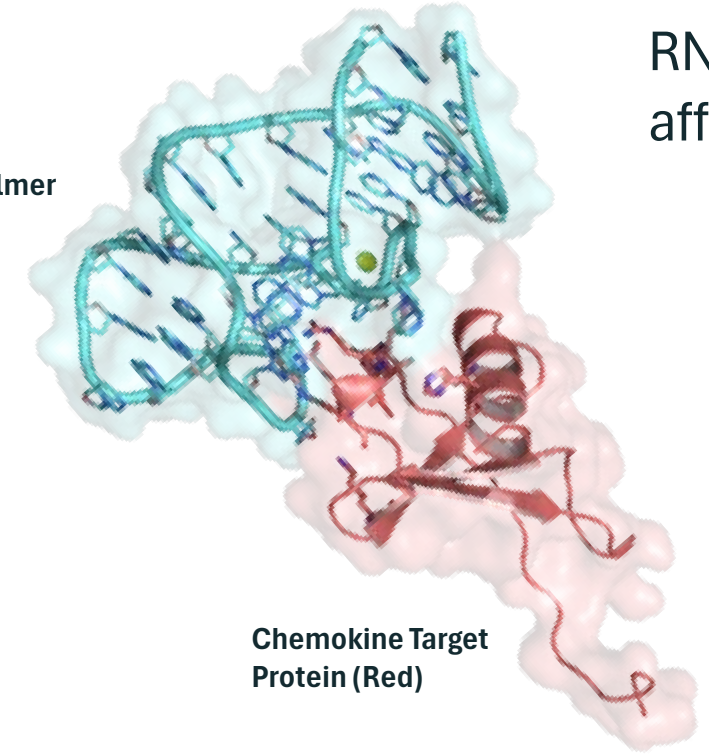
TME PHARMA NV IS PUBLICLY TRADED

Listed since	2016
ISIN code	NL0015000YE1
Ticker	ALTME
Market	Euronext Growth Paris
Market cap*	€10.3 M
Shares outstanding*	96,688,981

*As of close on November 16, 2026

Financial visibility into Q2 2028

Spiegelmer Platform: Next-Generation RNA Aptamers



Spiegelmer (Blue)

Chemokine Target Protein (Red)

RNA aptamers made with L-stereoisomer bind their targets with affinity similar or higher than antibodies and come with key benefits:

- Natural resistance to nuclease degradation - no chemical modification of backbone needed
- Large interaction surface enables complete inhibition of both key chemokine domains: receptor activation & anchoring for location

Chemokines are like street-signs in the body for moving cells, they are anchored (location information) and display instructions e.g. ('enter here') for moving cells that can 'see' them with the appropriate receptors.

FDA Approved RNA Aptamers

izervay (avacincaptad pegol intravitreal solution)

MACUGEN® PEGAPTANIB SODIUM INJECTION

Iveric bought by Astellas for $5.9b

Source: Oberthür (2015), Nature Commun 6:6923, crystal structure of the Spiegelmer NOX-E36 bound to chemokine CCL2.

Glioblastoma is a Devastating Orphan Brain Cancer

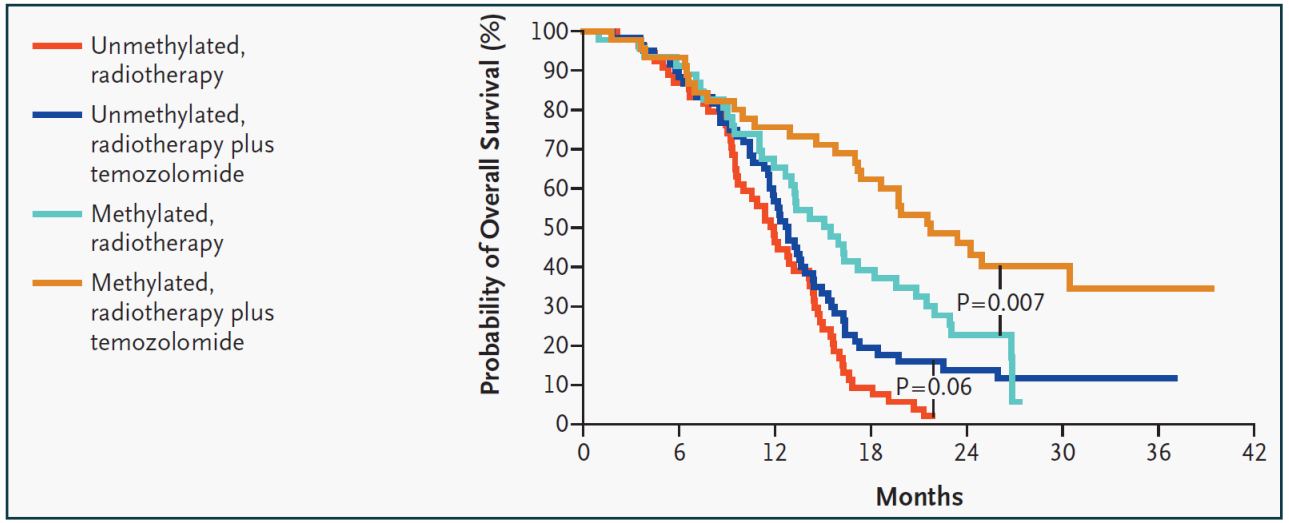
LACK OF EFFECTIVE THERAPIES & LOW OVERALL SURVIVAL

Orphan Status

29,000 New Cases per year US + Eur-5 [1]

5-year Survival 7.0% [2]

≈ 250 active clinical trials [3]



NOX-A12 OFFERS CHEMO-FREE REGIMEN FOR HIGH UNMET NEED PATIENTS WHO ARE:

CHEMO-RESISTANT

- >50% of GBM patients have **unmethylated MGMT**[4] promoter leading to **no significant benefit from chemotherapy** and worse prognosis
- **NOX-A12 trial omits chemotherapy** improving overall safety profile and offers immune-friendly regimen

PARTIAL TUMOR RESECTION

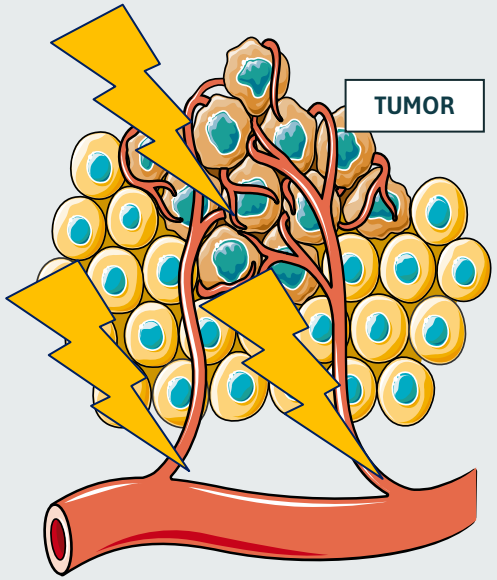
- Patients with **measurable tumor remaining** after maximal safe surgical removal of cancer have worse prognosis vs. patients with complete tumor resection

The NOX-A12 GLORIA study focuses on patients with tumor detectable after surgery that is chemotherapy resistant – the most difficult to treat patient population in GBM whose expected median survival is approx. 10 months

Sources: 1) In the US, UK, FR, ES, DE & IT, Global Data April 2022; 2) Price (2025), Neuro-Oncology 27 suppl_4:iv1; 3) Clinicaltrials.gov database (Phase 1 – 4 interventional trials whose status is either "recruiting" or "not yet recruiting"); 4) Hegi (2018), Clin Cancer Res 25:1809. Graph from Hegi (2005), New Engl J Med 352:997.

NOX-A12's Mode of Action is Relevant to GBM: Attacking Key Survival Mechanisms Following Radiotherapy

RADIOTHERAPY



RADIOTHERAPY kills many tumor cells and destroys blood vessels in irradiated zone leading to lack of oxygen (hypoxia) in the tumor making a more hostile environment for the tumor

Vessel destruction triggers **HYPOXIA**

SUPERIOR NOX-A12 PHARMACOLOGY
Direct targeting of CXCL12 provides more complete inhibition of axis than CXCR4 or CXCR7 antagonists

VASCULOGENESIS
One of two pathways activated in distinct zones of brain tumors to rebuild blood vessels[1]. CXCL12-driven and blocked by NOX-A12

HIF-1

HIF-1 triggers the two main pathways to re-grow blood vessels: **Vasculogenesis & Angiogenesis.**

CXCL12 chemokine

NOX-A12

Attraction to CXCL12

Monocytes

Endothelial cells

CXCR4 receptor

CXCR7 receptor

VEGF

ANGIOGENESIS
One of two pathways activated in distinct zones of brain tumors to rebuild blood vessels in brain cancer[1]

Although anti-VEGF monotherapy (bevacizumab) improved PFS it had no survival benefit in GBM[2]

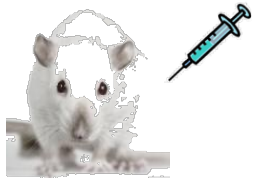
Inhibition of the CXCL12/CXCR4/CXCR7 axis can block tumor vasculogenesis

Sources: 1) Giordano (2026), Nature Commun 17:3405; 2) Gilbert (2014), New Engl J Med 370:699 & Chinot (2014), New Engl J Med 370:709.
Figure adapted from Liu (2014), Neuro-Oncology 16:21 and Kioi (2010), J Clin Invest 120:694.

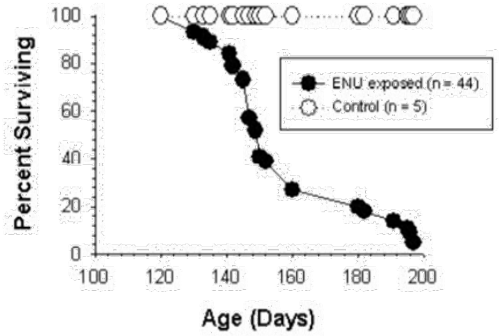
NOX-A12 + Radiotherapy Increases Survival and Demonstrates Complete Regression of Brain Tumors in Animal Models

Autochthonous brain tumor model in rats

- Spontaneous tumor development in immuno-competent host
- Diversity of tumor cell types with therapeutic resistance comparable to human situation
- Refractory to standard therapies

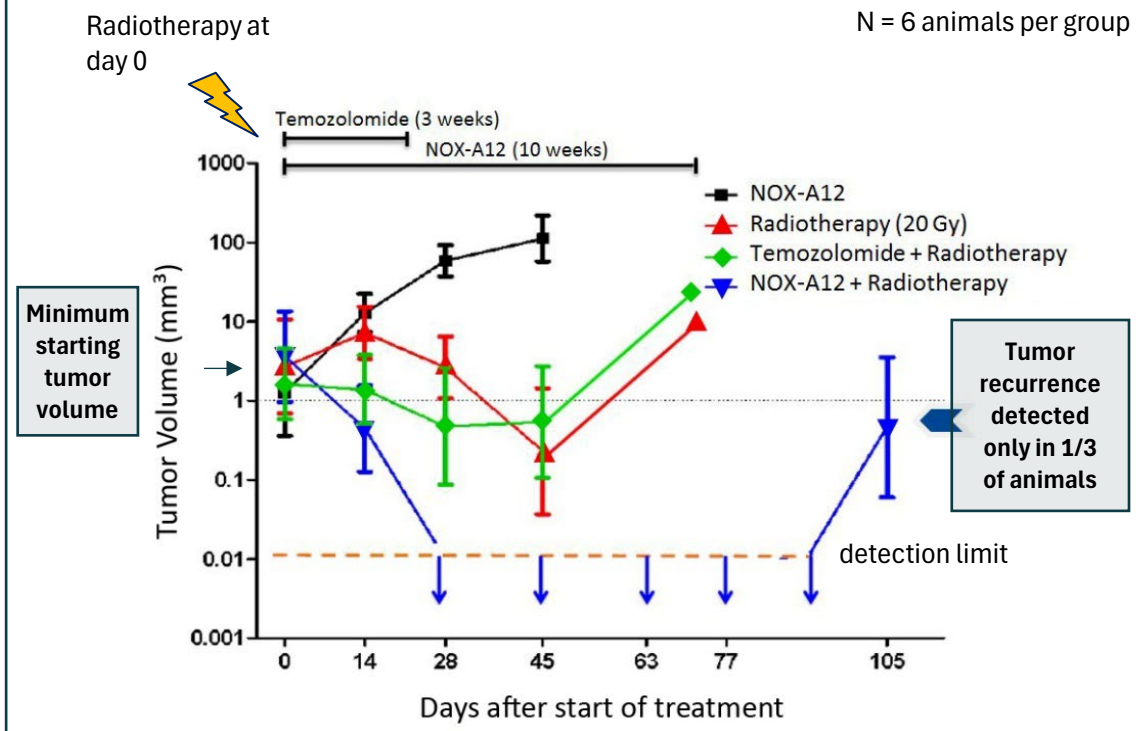


Pregnant rats:
ENU (carcinogen) on gestational age day 17 - 18



EFFECTS OF TREATMENTS

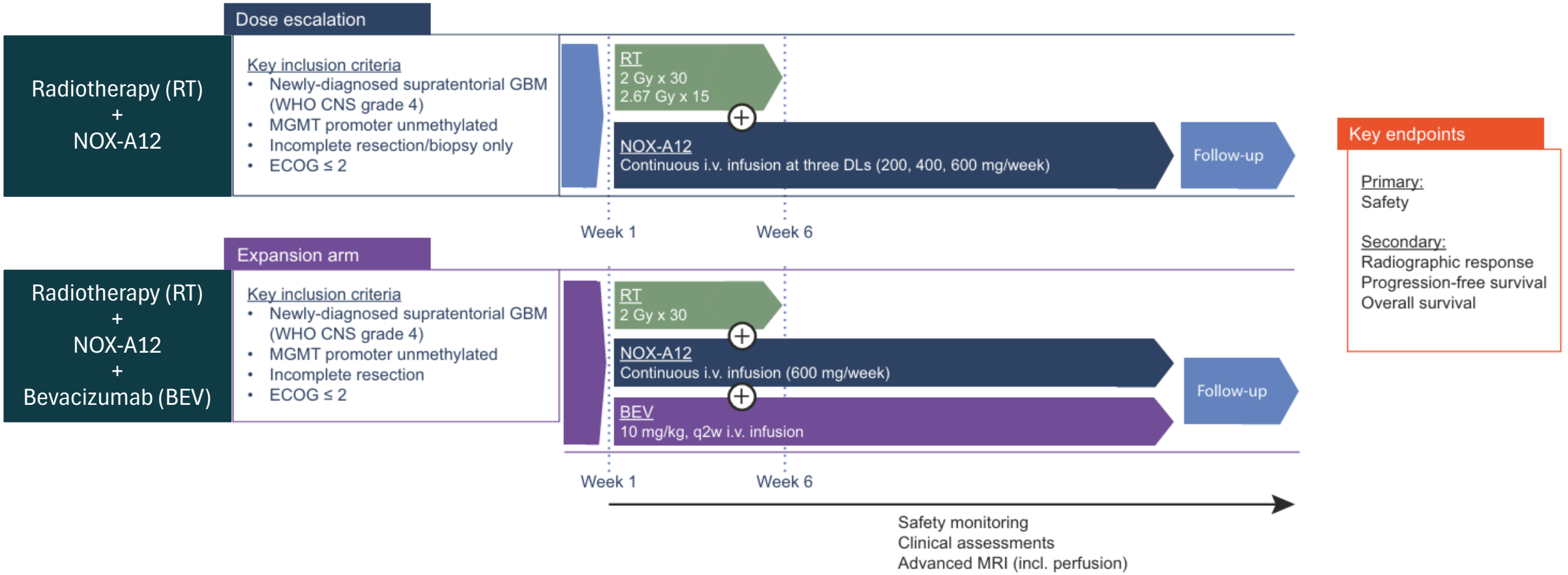
N = 6 animals per group



NOX-A12 + radiotherapy resulted in 100% complete response (67% durable) in brain cancer rat model

Source: Liu (2014), Neuro-Oncology 16:21; ENU: N-ethyl-N-nitrosourea, RT: radiotherapy, TMZ: temozolomide, Gy: Gray.

GLORIA Phase 1/2 Dose Escalation Study & Expansion Arm

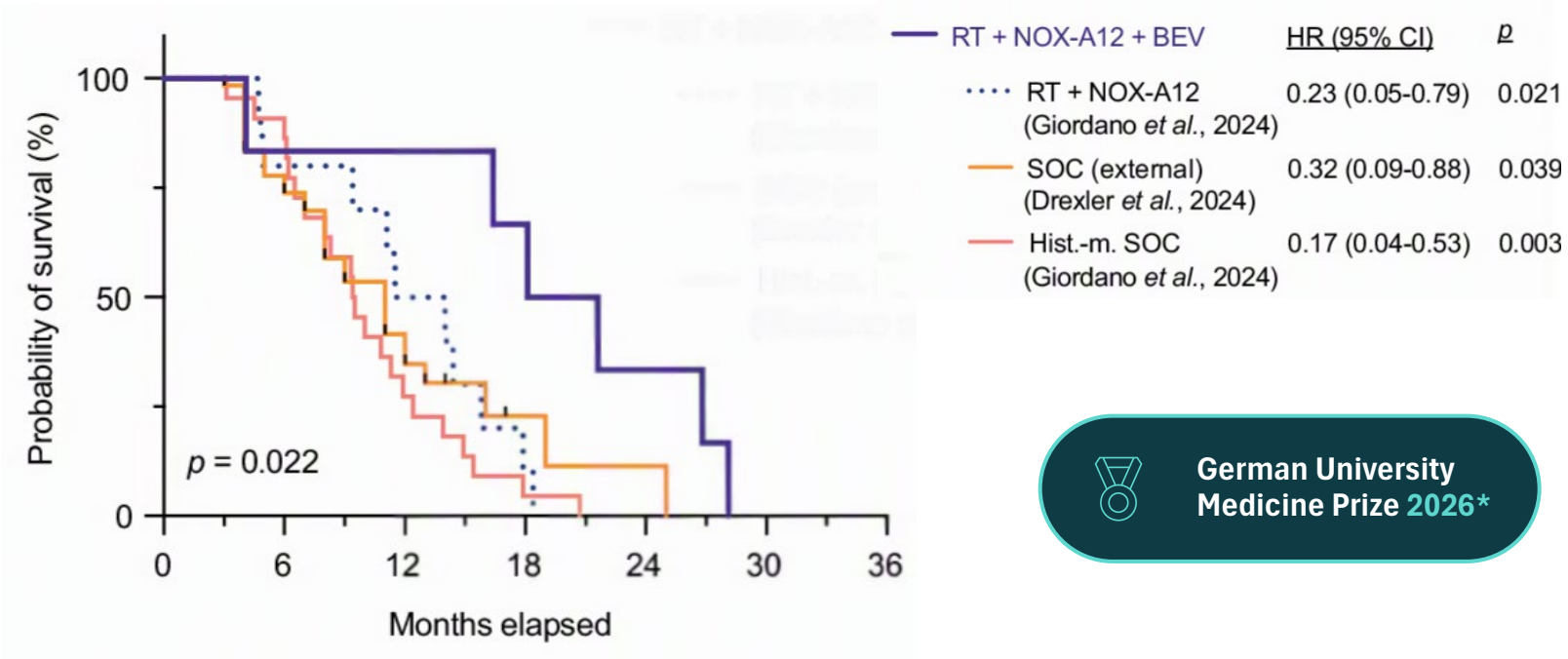


Expected median survival in this population receiving standard of care is approx. 10 months[1]

Source: 1) Giordano (2026), Nature Commun 17:3405, Standard of care data from internal Standard of care histology-matched reference cohort.
MGMT promoter unmethylated: patients resistant to standard of care chemotherapy.

NOX-A12 Therapy in Combination with Bevacizumab and Radiotherapy Prolongs Survival of Glioblastoma Patients

Overall Survival



German University Medicine Prize 2026*

Data published in

Giordano (2026), Nature Commun 17:3405

nature communications

Article https://doi.org/10.1038/s41467-026-71362-7

L-RNA aptamer-based CXCL12 inhibition combined with radiotherapy and bevacizumab in newly-diagnosed glioblastoma: expansion of the phase I/II GLORIA trial

Giordano (2024), Nature Commun 15:4210

nature communications

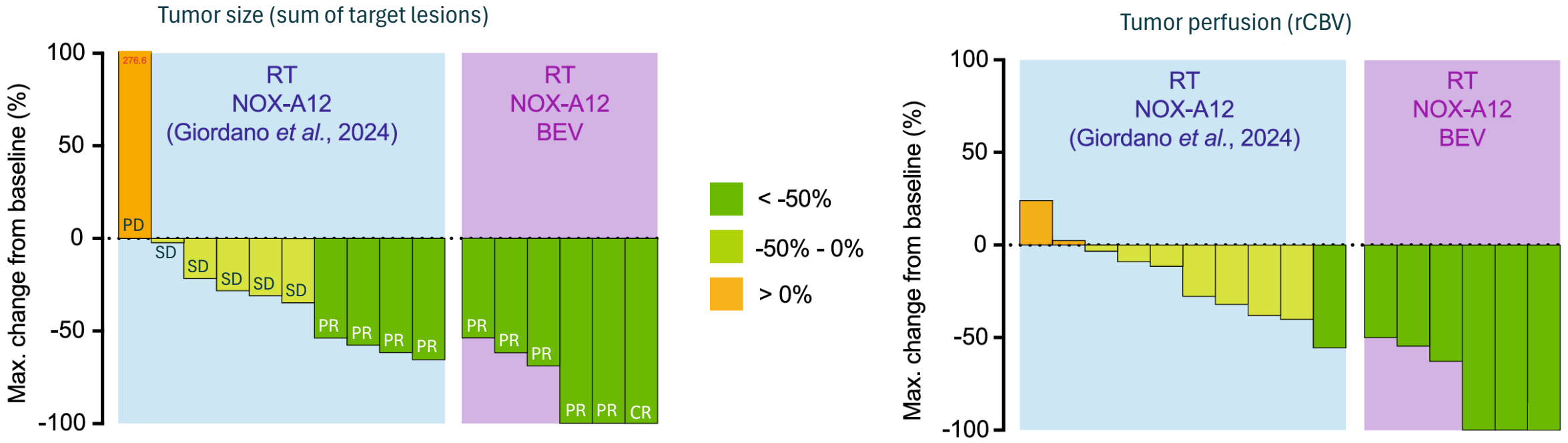
Article https://doi.org/10.1038/s41467-024-48416-9

L-RNA aptamer-based CXCL12 inhibition combined with radiotherapy in newly-diagnosed glioblastoma: dose escalation of the phase I/II GLORIA trial

- **19.9 months mOS for NOX-A12 + RT + bevacizumab** combination and 12.7 months for NOX-A12 + RT
- 9.5 months mOS for internal histology-matched SOC and 11.0 months for external SOC cohort

* TME Pharma Press Release, November 3, 2026.

NOX-A12 Combination Improves Best Radiographic Response and Reduces Tumor Blood Perfusion



- NOX-A12 combination with bevacizumab **improves response and depth of tumor shrinkage**
- Tumor shrinkage **correlates with reduced tumor blood perfusion**

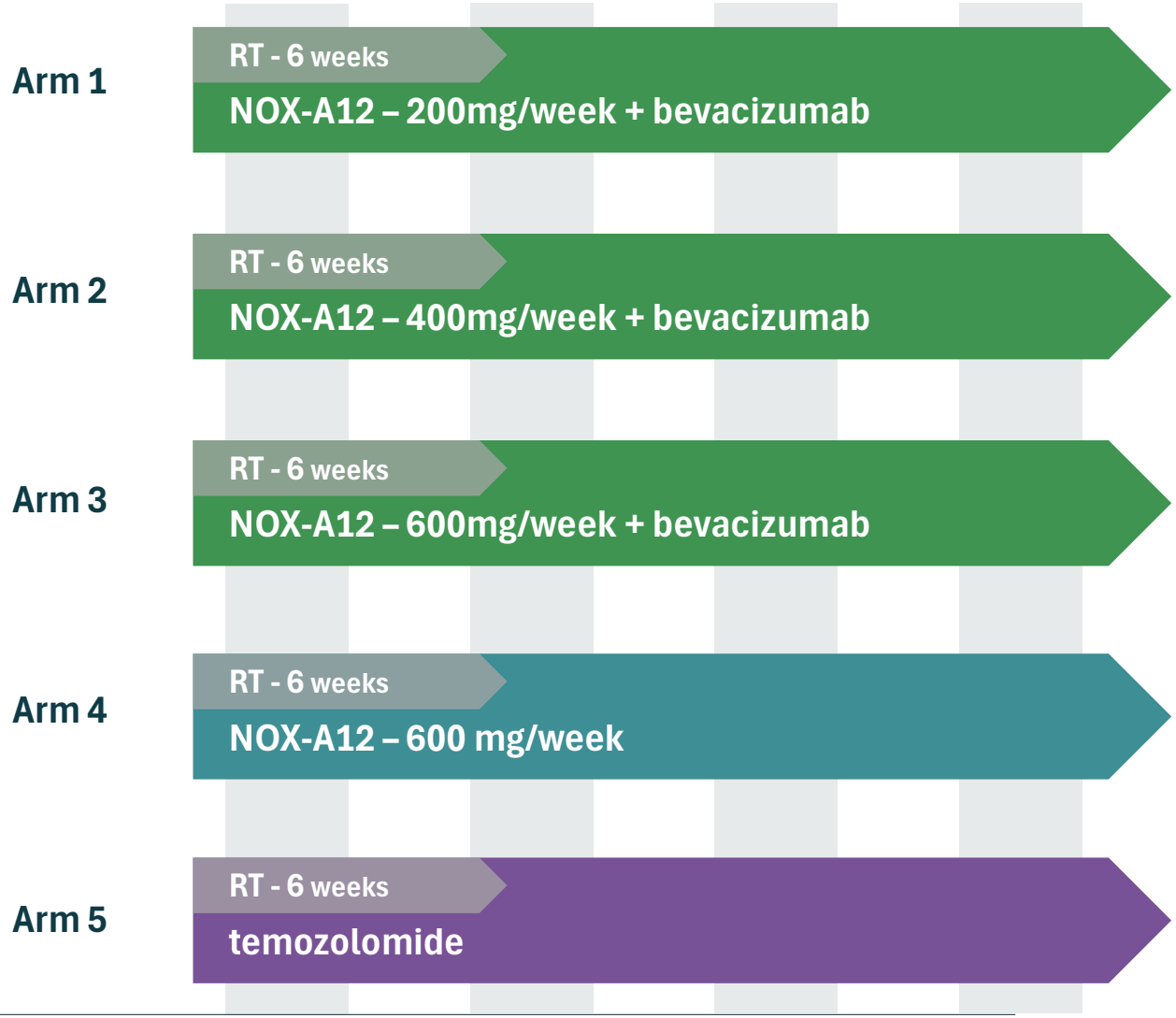
Source: Giordano (2026), Nature Commun 17:3405.
PD: progressive disease; SD: stable disease; PR: partial response; CR: complete response; rCBV: relative cerebral blood volume.

Approved Phase 2 Study Design in GBM in US and Germany: 5-arm Randomized Controlled Study, n=100 (20 Patients per Arm)

- Newly diagnosed glioblastoma patients with extremely poor prognosis:
  - Incomplete surgical resection
  - MGMT promoter unmethylated: chemotherapy ineffective
- Randomized-controlled enrollment
- Treatment duration 1 to 2 years

Expected survival in this population receiving standard of care[1]:
- mOS of approx. 10 months

Orphan Drug and Fast Track Designations awarded by FDA



Source: 1) Giordano (2026), Nature Commun 17:3405, Standard of care data from internal SoC histology-matched reference cohort.

Current Development Status

Regulatory

- Orphan Drug Designation in US & EU
- Open IND and Fast Track Designation in US
- Approved Phase 2 study in Germany and US

Clinical development

- Phase 2 study ready to recruit: clinical study sites open in Germany
  ClinicalTrials.gov: NCT04121455
- NOX-A12 clinical trial supply on stock, ready to be shipped to study sites

CMC

- GMP processes established at two CMOs, supply of raw materials secured

➢ Recruitment of patients into Phase 2 study possible within short timeframe

Relevant Benchmark Studies in Chemotherapy Resistant Glioblastoma from US and EU

Experimental Agent (Company)	Surgical removal of detectable tumor (T=total; P=partial; B=biopsy only)	Patient number	Response criteria	Overall Response Rate (ORR)	Median Overall Survival (mOS) in months	Status	Reference
NOX-A12 + Radiotherapy + bevacizumab (TME Pharma)	**0% T; 100% P**	**6**	**RANO**	**83%**	**19.9**	**Ph 1/2 ongoing, Orphan Drug Designation & Fast Track Designation granted**	**Giordano (2026), Nat Commun**
Tumor Treating Fields (TTF) + Radiotherapy + Temozolomide (Novocure)	53% T; 34% P; 13% B	209	Macdonald	n.a.	16.9	Approved	Stupp R (2017), JAMA
Val-083 after Radiotherapy + Temozolomide chemotherapy) (Kintara)	information not provided	36	RANO	n.a.	16.5	Failed pre-defined criteria for GBM AGILE trial Ph 2/3	O'Brien (2021), Soc Neuro-Oncology Ann Meeting
Paxalisib + Radiotherapy (Kazia)	77% T; 17% P; 10% B	30	RANO	3%	15.7	Failed pre-defined criteria for GBM AGILE trial Ph 2/3	Wen P (2022), J Clin Oncol
Enzastaurin + Radiotherapy (Denovo)	43.9% T; 40.4% P; 15.8 B	57	Macdonald	7%	15	Orphan Drug Designation & Fast Track Designation granted; Ph 3 ongoing	Wick W (2013), Neuro-Oncology
Temozolomide chemotherapy + Radiotherapy + bevacizumab (Roche)	63% T; 34% P; 3% B #	215	Macdonald	n.a.	14.3	Failed in Ph 3	Gilbert MR (2014), New Engl J Med
Regorafenib + Radiotherapy (Bayer)	57% T; 14% P; 16% B; 12% other	49	RANO	n.a.	14.3	Failed pre-defined criteria for GBM AGILE trial Ph 2/3	Wen PY (2026), J Clin Oncol
Nivolumab anti-PD-1 immunotherapy + Radiotherapy (BMS)	54% T; 46% P	280	RANO	7.8%	13.4	Failed in Ph 3	Omuro A (2022), Neuro-Oncology
Temozolomide chemotherapy + Radiotherapy	information not provided	60	n.a.	n.a.	12.7	Approved (current standard of care)	Hegi ME (2005), New Engl J Med

Brain Cancer is an Area of Active Pharma Interest

- **Servier** received **FDA approval** for VORANIGO/vorasidenib in **low grade, IDH mutant glioma** in Aug 2024 following its **$2 billion** acquisition of **Agios'** oncology business in 2021[1]. EMA approval obtained September 2025
- **Royalty Pharma** acquired a stake in Agios' royalty payments for VORANIGO in 2024 and projected the **drug could reach more than $1 billion in annual peak sales** in the U.S. **based on around 1,500 new diagnoses per year and prevalence of approximately 10,000 in the US**[1]
- **Day One Biopharmaceuticals** out-licensed ex-U.S. rights for its BRAF-mutant pediatric low-grade glioma drug OJEMDA/tovorafenib to **Ipsen in a $461 million deal** including $111 million upfront and $350 million in milestone payments and double-digit tiered royalties[2]. Accelerated FDA approval obtained in April 2024
- **Servier** acquired **Day One Biopharmaceuticals** in April 2026 for **$2.5 billion**, expanding the rare cancer / pediatric glioma position[7]
- **GSK** is investing in the development for **glioblastoma as one of two focus indications** for their PARP inhibitor ZEJULA/niraparib which is listed as "in Phase 3/Registration" in the pipeline[3]
- **MSD/Merck** acquired **Modifi Biosciences** in October 2024 for **$30 million upfront** and **up to $1.3 billion** with potential future payments for development of MOD-246 a "precision chemotherapy" which was developed to target glioblastoma[4]
- **Jazz Pharmaceuticals** announced acquisition of **Chimerix** in March 2025 for a total consideration of **$935 million,** adding the Phase 3 MODEYSO/dordaviprone program in **H3 K27M-mutant diffuse glioma to their pipeline**[5]. FDA approval was granted in August 2025[6]

Sources: 1) Fierce Pharma, Aug 6 2024 and Royalty Pharma press release of 28 May 2024; 2) Day One Biopharmaceuticals Press Release, 25 July 2024; 3) GSK Presentation 17 June 2024 , Getting Ahead of Cancer, pages 43-44 Link: getting-ahead-of-oncology-presentation.pdf (gsk.com) and GSK Pipeline Q2 2026; 4) https://modifibio.com/wp-content/uploads/2024/10/Modifi-Biosciences-Acquired-by-Merck-FINAL.pdf; 5) Jazz Pharmaceuticals to Acquire Chimerix, Further Diversifying Oncology Portfolio | Jazz Pharmaceuticals plc; 6) FDA grants accelerated approval to dordaviprone for diffuse midline glioma | FDA; 7) Servier Press Release, April 23, 2026.

Commercial Patent Protection Projected to Expire in 2040's

Patents

- **Core Method of Use claims** on NOX-A12 + irradiation + bevacizumab for glioblastoma will **expire in 2043** (before any extension), if granted
- Granted patent covering use of NOX-A12 for therapy of cancer expiring 2031 (before extension)

Regulatory

- **Orphan Drug Exclusivity as second layer of commercial protection would provide**
  - 10+2 years in EU (granted for NOX-A12 in glioma)
  - 7 years from approval in US (granted for NOX-A12 in glioblastoma)
  - 10 years in Japan
  - 7 years in China (glioblastoma validated as orphan since Sept 2023)

NOX-A12 Potential to Transform GBM Clinical Practice

- Unprecedented activity in chemotherapy-resistant (MGMT-unmethylated) glioblastoma patients: **statistically significant improvement in survival** and **doubling of mOS**[1]
- **Excellent safety and tolerability** in a chemotherapy-free regimen[1]
- **Commercial exclusivity** in glioblastoma market, estimated by TME to be €2.5 billion/yr in 2027[2], will be protected by **foundational method of use claims to at least** 2043 (before any extension) if granted, and **Orphan Drug protection** as second layer of protection in major markets[3]
- **Fast Track** (FDA) and **Orphan Drug Designation granted** (US & EU)
- **Open IND** in the US and **Phase 2 study approved in Germany**
- **Randomized controlled clinical Phase 2 study ready-to-go** to confirm survival benefit signal
- **Commercial and scientific rationale to expand into other CNS indications** with high unmet need where radiotherapy is routinely used and there are only limited good options available

Sources: 1) Giordano (2026), Nature Commun 17:3405 & Giordano (2024), Nature Commun 15:4210; 2) Based on US + EU 27 geography, potential pricing aligned with atezolizumab when sold with VEGF (US: Medicare payment limit, Europe average of DE, ES , FR, IT and UK pricing), peak market share 55% of MGMT unmethylated tumor patients; 3) PCT filing WO2023247651A1 and data on file at TME Pharma.



Thank you.

Contact us:

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