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A New Wave in Radiopharmaceutical Treatment for Recurrent Glioblastoma

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Therapeutic Modality

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Blue Wave's Targeted Alpha Therapy

- Blue Wave's platform leverages **biopolymer (alginate) nanoparticles**, functionalized with **targeting peptides**, to selectively deliver **radionuclide payloads** directly to tumor cells.

- Its proprietary portfolio covers the use of alginate nanoparticles with a **variety** of peptide sequences and radionuclide payloads, enabling a **highly scalable approach** for treating multiple solid tumor types.

- The lead product candidate, **^{225}Ac-RGD-Alginate nanospheres** (ARAspheres), is currently in preclinical development to establish proof of concept (PoC) for treating GBM.

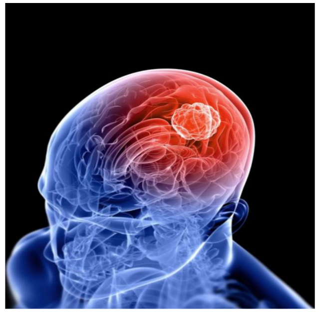
- ARAspheres can be defined as a **Targeted Alpha Therapy.**

Target Indication / Unmet Medical Need

Why Glioblastoma (GBM)?

- One of the **most urgent** and underserved **medical needs** in oncology.
- A strategically compelling opportunity for a **novel, locally administered** radiopharmaceutical like ARAspheres.
- A **rare disease**, qualifying for **orphan drug designation** in both the U.S. and Europe (accelerated regulatory pathways and premium pricing).
- **Reduced development timelines** due to the short mOS and clear clinical endpoints, in particular for recurrent GBM.

Glioblastoma: a Highly Unmet Medical Need

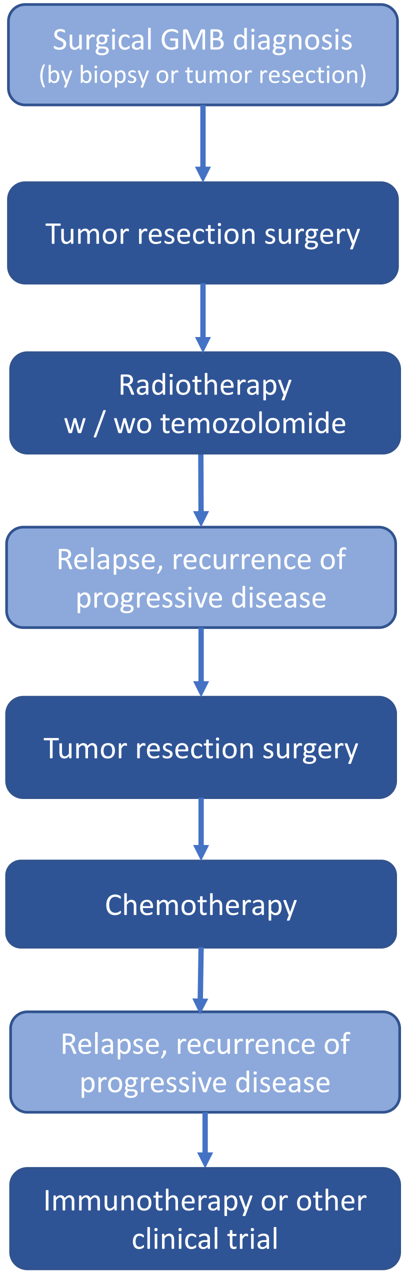


- Glioblastoma multiforme is an **infiltrative** tumor, which metastasizes **locally** in the brain, surrounding the primary lesion
- The tumor grows **quickly** and can double size in 10 days
- More than **79,000** incident cases in 2023, expected to exceeed 86,900 cases by 2028*
- Only 30% of patients are alive 2 years after diagnosis
- Patients with glioblastoma have **limited** therapeutic options; 98 % die of the disease

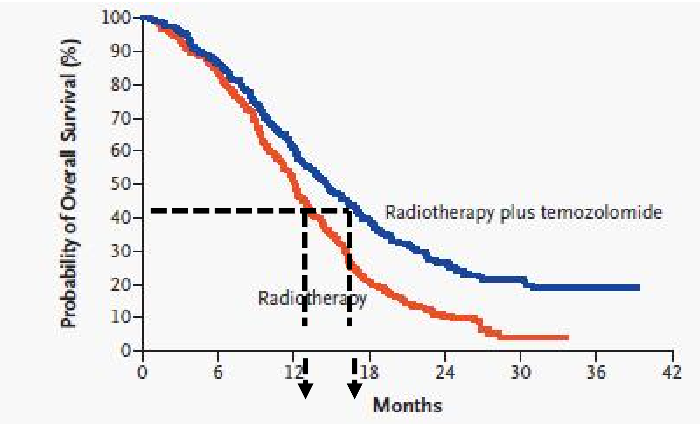
* Source: Global Data; epidemiology data refer to the following countries: Australia, Brazil, Canada, China, France, Germany, India, Italy, Japan, Mexico, Russia, South Africa, South Korea, Spain, UK, US

GBM: Current Standard of Care Overview

- **Standard treatment guidelines** are followed globally for GBM
- Approx. **90%** of newly diagnosed GBM patients undergo **surgery**, followed after 6-8 weeks later by **radiation therapy** and **chemotherapy**
- The majority of patients experience treatment failure as glioblastoma often recurs
- Approx. **40-50%** of GBM patients undergo a **second** surgical **resection,** followed by **chemotherapy**
- The current standard of care is suboptimal: the average **survival rate** for relapsed GBM patients is only **4-6** months
- As a result, patients are actively searching for **alternative** treatment options



Understanding Limitations of Current GBM Therapies



Stupp et al., Engl J Med 2005; 352, pp. 987-996
DOI: 10.1056/NEJMoa043330

- Surgical resection will by default leave **remaining** tumor cells
  - it may not be possible to give high enough dose to all remaining tumor cells with **external beam radiation**
  - **chemotherapy** may not be effective on remaining cells, due to resistance
- Moreover, both treatments are started **4-8 weeks after** surgery, so residual tumor cells can **re-grow**
- These treatments do not differentiate between healthy and tumor cells, resulting in **severe side-effects**

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Mechanism of Action / TPP

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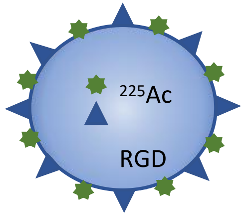
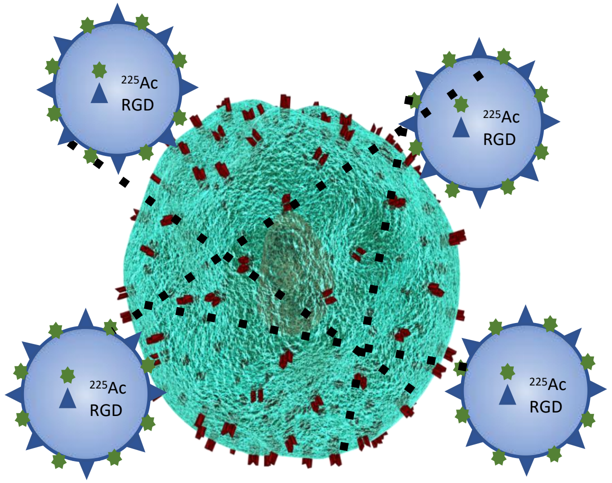
ARAspheres Has Potential to Improve the Lives of GBM Patients



Carrier: **nanometer-sized** alginate nanoparticles which can diffuse in the brain

- The nanoparticles carry **RGD, a clinically validated targeting peptide,** which binds to specific tumor cell receptors (αVβ3 integrins), highly expressed on glioblastoma cells
- Alginate is an excellent **chelator**



Payload: alpha particle radiation emitting radionuclide (**Actinium-225**), with a **T1/2 of 10 days**

- **Range:** a few cell diameters
- **Mechanism of action:** cell death by **alpha** radiation-induced unrepairable **DNA damage** to tumor cells

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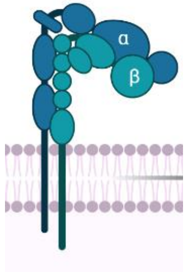
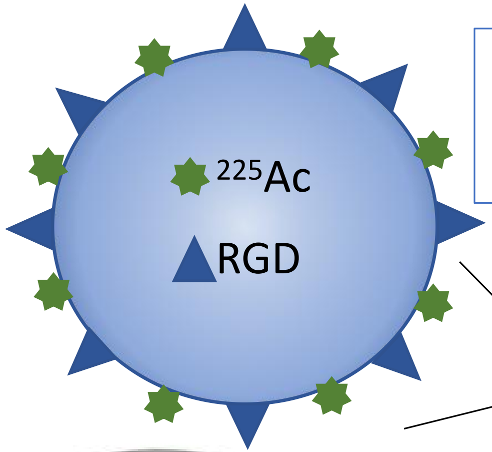
ARAspheres is Poised to Overcome Limitations of Current GBM Treatments

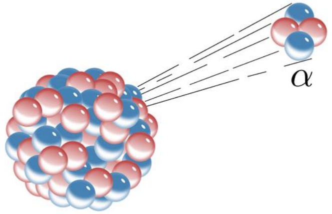
Clinically validated target, targeting αVβ3 integrin



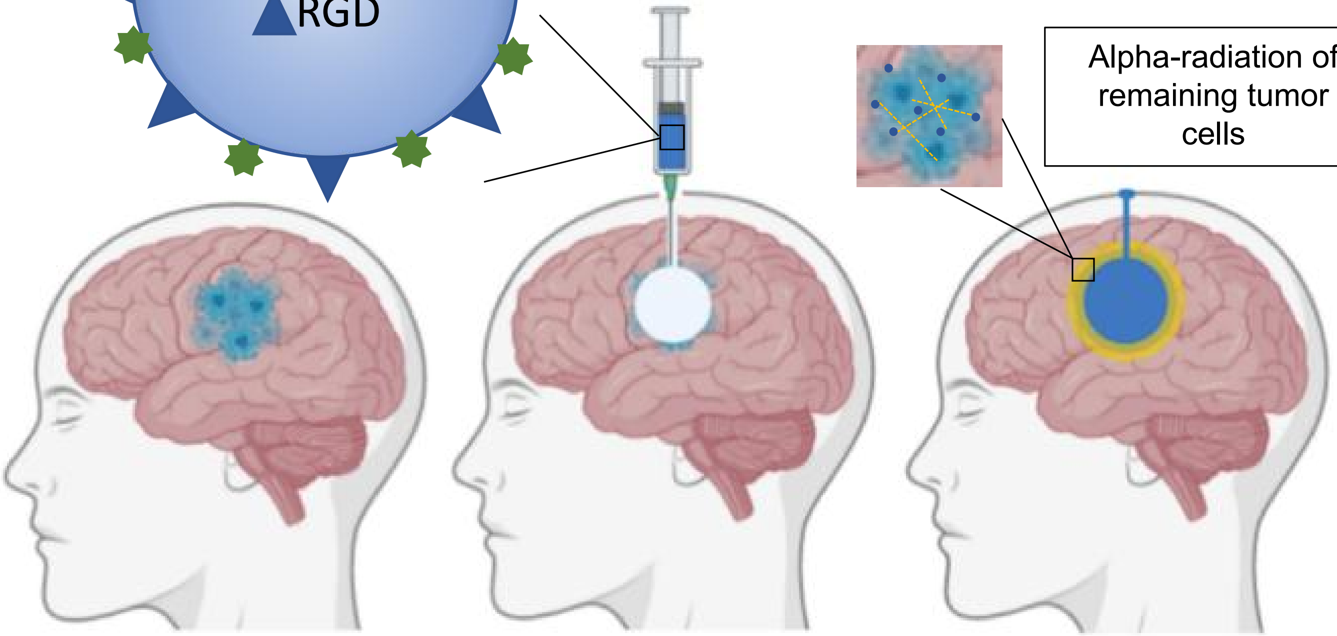


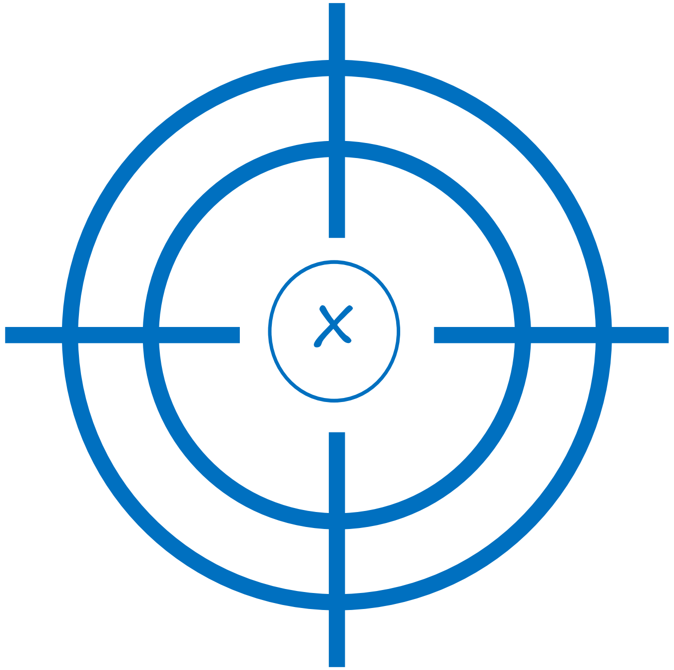
Direct injection of radioactive nanoparticles after surgery

Actinium-225 ($T_{1/2}$ = 10 days)



Alpha-radiation of remaining tumor cells





↑ Life Expectancy

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Market Opportunity

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Market Opportunity (1/3)

- The **GBM market** across eight major pharmaceutical markets (U.S., Switzerland, Japan, Germany, France, Italy, Spain, U.K.) is projected to reach **$3.1 billion** in annual sales by 2031*.
- **Expanding** applications in other **solid tumors**
- Fast-growing **$30B radiopharmaceutical** space.

* Global Data, GBM Forecast

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Market Opportunity (2/3)

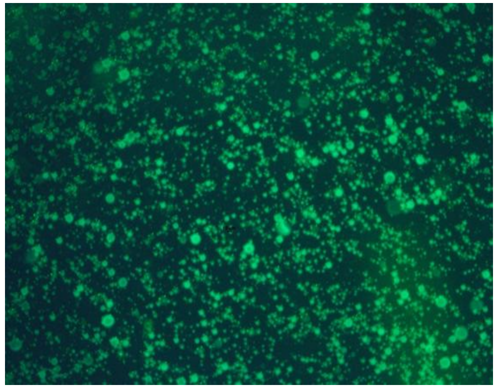
The **Total Addressable Market** (TAM) is estimated at approximately **CHF 3.9 billion**, based on the following assumptions:

- approx. 45,000 new GBM cases across the 8 major markets, 75% of whom (34,000) receive treatment.
- recurrence in 69% of cases, with 63% of recurring patients getting additional treatment (47,000 in total).
- 90% of newly diagnosed and 50% of recurring patients undergo surgery (**36,500 eligible patients in total**).
- **improved mOS** supporting premium pricing: average selling price per patient of **CHF 200K in the US** and **CHF 100k in the other markets**

Market Opportunity (3/3)

- The **Serviceable Addressable Market** (SAM) is estimated at approximately CHF 1.3 billion, based on the following assumption:
  - anticipated market penetration **at peak** of approx. **30%**, consistent with other radioligand therapy launches in niches with high unmet medical need.
- The **Serviceable Obtainable Market** (SOM) is estimated at approximately CHF 1 billion, based on the following assumption:
  - anticipated YoY price increase in the US.
  - anticipated YoY price erosion in other markets.
  - **performance-based agreements**, mostly in EU.

Differentiation Drivers Enhance Value and Set ARAspheres Apart



Fluorescence-labelled alginate particles

- **Pre-formulated & Ready-to-Use:**
  - A radioactive suspension designed for seamless clinical application.
- **Targeted Administration:**
  - Easily delivered into the tumor resection cavity right after surgery, biodegradable.
- **Precision Tumor Targeting:**
  - Short-range alpha radiation spares healthy tissues while effectively killing tumor cells.
- **Nanometer-Sized for Optimal Diffusion:**
  - Penetrates the brain to bind residual tumor cells, delivering continuous alpha radiation.
- **Enhanced Efficacy, Reduced Side Effects:**
  - Designed to improve treatment outcomes with minimized toxicity.
- **Compatible with Standard Care:**
  - Can be combined with existing therapies to amplify anti-tumor effects.

There is Potential Beyond the First Product Candidate

- Once ARAspheres is validated, our **platform** has the **potential** to develop additional product candidates to treat underserved tumors
- Our patent provides **flexibility** to include other radionuclides and targeting peptides
  - enabling the inclusion of a series of **radioisotope payloads,** such as alpha emitters, including actinium-225, as well as beta emitters
  - it also accommodates alternative **targeting peptides**, including those that bind to RGD, LDL, MMP-2, IL13R2a, VDAC1, NBD, c-MYC, CXCR4, and MDGI, along with combinations of these peptide sequences.

Competitive Landscape: Current and Future Players

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Potentially Outperforming Current and Future Competitors

Competitor	Limitations	ARAspheres' advantages
Temozolomide	Low efficacy, resistance	Targeted precision therapy
Standard radiotherapy	Off-target toxicity	Higher tumor selectivity
Small molecules	Ineffective (BBB), non-selective, resistant	Direct administration to the brain, highly localized radiation, low off-target toxicity
Cell therapies	Impractical, slow-acting, immunosuppressible	Scalable, not dependent on immune activation, one shot and done
Radio-pharmaceuticals	Lack GBM focus	Proprietary delivery tech

ARAspheres vs. GBM-Targeted Radio Pharmaceuticals: Differentiated Positioning

- **Precision targeting**: αvβ3 integrin via RGD, overexpressed in GBM vasculature and tumor cells
- **High-energy alpha radiation**: potent, short-range cytotoxic effect
- **Sustained-release**: forms a local depot in the surgical cavity without the need for pumps or implants
- **No systemic exposure**: minimizes off-target effects and toxicity

ARAspheres vs. Other GBM-Targeted Product Candidates: Differentiated Positioning

- **Modality**: Most competitors rely on immunotherapy, gene therapy, small molecules, or oncolytic viruses: none use targeted alpha radiation.
- **Delivery**: Like some CAR-Ts and viruses, ARAspheres is **locoregionally administered**, but **does not require catheters or pumps**, a key advantage in surgical resection follow-up.
- **Depot effect**: Unlike T-cell therapies or viral vectors, ARAspheres **releases a potent alpha-emitter locally over time**, creating sustained radiation at the resection margin, with **no need** for **repeated dosing** or **systemic exposure**.

Intellectual Property (IP) Position

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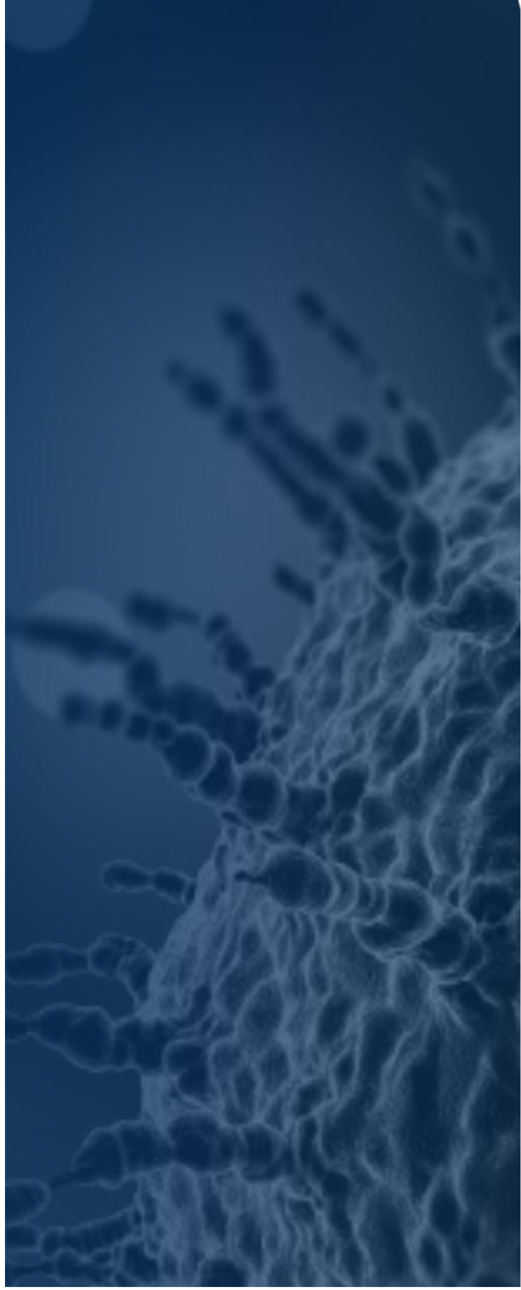
IP Strategy: First Patent Granted, Expanding Protection Worldwide

- **Norwegian Patent:** achieved patent NO 347755 on March 18, 2024, securing Blue Wave's innovation in peptide-coupled alginate nanoparticles comprising radionuclides.
- **PCT Application:** Progressed into the national application phase of WO2023066994A1 in April 2024, strategically protecting Blue Wave's intellectual property globally.
- Existing IP estate grants Blue Wave's platform **unique flexibility**
  - enabling the inclusion of a series of **radioisotope payloads**, such as **alpha emitters**, including actinium-225, as well as **beta emitters**
  - it also accommodates alternative targeting peptides, including those that bind to **RGD, LDL, MMP-2, IL13R2a, VDAC1, NBD, c-MYC, CXCR4, and MDGI,** along with combinations of these peptide sequences.



Development Plan

Capital-Efficient Development Plan to Deliver Clear Exit Opportunity

- Blue Wave plans to develop ARAspheres **to clinical PoC** (Phase IIa) **inflection point,** to then seek biopharma partnership
  - **Valuation** of **analogue** Ph. IIa stage radiopharma companies ranges **CHF 0.5-1B**
- Virtual **biotech** model: **low-burn**, high expertise
- Roadmap and future funding rounds are **milestone-based**

2025
In vivo Proof of Concept

2027
CTA/IND

2029
Clinical PoC

2030
Exit opportunity

Delivery of Upcoming Milestones Poised to Increase Value of Enterprise

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Outlook on Funding Rounds and Inflection Points

Ongoing Seed Funding (**2025**)

- Targeting **CHF 1.5M**, to advance in vivo animal studies and scale production of alginate nanoparticles

2nd Seed Funding (**2026**):

- Targeting **CHF 1.5M**, to complete IND-enabling studies and file for IND/CTA

Series A (2027):

- Targeting **CHF 20-25M** from international VCs' syndicate to fund Phase I/IIa clinical development.

Ongoing **Non-Dilutive** Grants:

- Active pursuit of **Swiss**, **European**, and U.S. research grants to maximize capital efficiency.

2025
In vivo Proof of Concept

2027
CTA/IND

2029
Clinical PoC

2030
Exit opportunity

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Current Status

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Significant Progress To-Date, Thanks to Relevant Strategic Collaborations

- Secured **patent approval** in the first jurisdiction, now in the PCT national phase*
- Established **R&D lab** and signed **strategic partnerships** (Minerva Imaging, Sintef, Oslo University)
- **Validated prototype**: <100nm alginate nanoparticles loaded with ^{225}Ac
- **Preclinical experiments** ongoing in first animal species
- Raised nearly **CHF 2 million**, including **equity financing** and Norwegian Research Council **non-dilutive funding**

*Norwegian Patent: achieved patent NO 347755 on March 18, 2024, securing Blue Wave's innovation in peptide-coupled alginate nanoparticles comprising radionuclides.
PCT Application: Progressed into the national application phase of WO2023066994A1 in April 2024, strategically protecting Blue Wave's intellectual property globally.

Validated by Key Scientific and Industry Stakeholders

The idea is backed by rigorous science from esteemed institutions

- **Proven Mechanism**: Radionuclide therapy shows strong activity across various cancers
- **Trusted** Partnerships: Collaborations with top research institutions
- Endorsement: Significant grant awarded by the **Norwegian Research Council**; Top 10 finalist in **2025 Venture Innovation** competition
- **Expert** Collaboration: Working with leading experts in cancer and nuclear medicine research

Highlights from Preclinical Plan (1/3)

In Vitro Evidence of Target Engagament

- **Target expression confirmed**: High expression of αvβ3 integrin was confirmed in U-87 MG human glioblastoma cells, validating the tumor-relevance of the RGD targeting mechanism.
- **Binding validation**: Fluorescent-labeled RGD-alginate nanoparticles demonstrated specific binding to the surface of glioblastoma cells, visualized via fluorescence microscopy.

In Vivo Tumor Model Establishment and Tumor Growth Data

- **Orthotopic glioblastoma models** were established using **U-87 MG cells** implanted intracranially in **BALB/c nude mice** and **RNU/nu rats**.
- Tumor growth kinetics showed **faster** and **more robust growth in rats**, which were selected as the preferred species for efficacy and toxicity studies.

Highlights from Preclinical Plan (2/3)

Biodistribution and Retention Studies (Ongoing)

- Studies are underway to assess **biodistribution** and **retention of Ac-225 and its decay daughters** (Fr-221, Bi-213) following intracranial implantation of ARAspheres.
- Time points range from 1 hour to 24 days post-injection, with SPECT/CT and MR imaging, as well as gamma-counting across relevant organs.

Safety and Tolerability Studies

- A formal **dose-escalation toxicity** study is ongoing in rats, using **four escalating doses** (100–400 kBq/kg).
- Safety readouts include:
  - Body weight monitoring
  - White blood cell counts
  - Histology of brain tissue

Highlights from Preclinical Plan (3/3)

Efficacy Study – In Vivo Proof-of-Concept (Ongoing)

- A definitive **efficacy study** is ongoing using the **rat orthotopic GBM model**.
- A **single intracranial administration of ARAspheres** is being evaluated at three dose levels versus control.
- Primary **endpoints**:
  - Tumor volume reduction (via MR imaging)
  - Histological confirmation of tumor cell death (H&E staining)
  - Systemic toxicity (hematology panels up to 120 days)
- Final **readout** is expected by **December 2025**, with full reporting in early 2026.

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Team Overview: Current Structure & Future Needs

Leadership Rooted in Expertise, Passion and Innovation

Marco G Renoldi, MD

Chief Executive Officer

Michael Dornish, PhD

Chief Scientific Officer
Co-Founder

Jostein Dahle, PhD

Chief Technology Officer
Co-Founder

Luca Sereni, EE, MBA

Chief Operating Officer
Co-Founder

Stefania Poli, MPsych

Chief Human Resources Officer

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Manufacturing Scale-Up

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Manufacturing Scale-Up

Component / Step	Early Preclinical Grade	Late Preclinical – Early Clinical Grade	Late Clinical – Commercial Grade
Alginate – sourcing	*Ultrapure alginate from Norwegian supplier (research-grade).*	*Ultrapure GMP-grade alginate from same Norwegian supplier.*	*Same GMP-grade supplier or validated alternate within Europe.*
Alginate nanoparticles – manufacturing	*In-house production at Blue Wave lab (non-GMP); 0.5 – 1 gram scale.*	*Scale-up internally under controlled conditions or via qualified CMO; 1 – 100 gram scale; shelf-life 1 yr.*	*Full GMP-compliant CMO or internal GMP production; >100 gram scale.*
Peptide targeting moiety – sourcing	*Custom synthesis by UK supplier (research-grade).*	*GMP-grade synthesis by same UK partner (ISO 9001 / ISO 17025 / UKAS).*	*Long-term contract with GMP peptide manufacturer.*
Peptide conjugation – manufacturing	*In-house conjugation at Blue Wave lab (non-GMP).*	*Validated semi-automated process, internal or with GMP-ready partner.*	*GMP-compliant conjugation at qualified CMO.*
Actinium-225 – sourcing	*Research-grade Ac-225 from two leading EU suppliers.*	*GMP-grade Ac-225 from same suppliers or qualified EU-based GMP source.*	*Long-term supply agreement with EU/US GMP-certified suppliers.*
Ac-225 radiolabelling – manufacturing	*Conducted at Blue Wave lab (non-GMP) and Minerva Imaging (GMP).*	*Performed at Minerva Imaging or equivalent GMP radiopharmaceutical site.*	*Performed at Agilera/PharmaLogics or equivalent commercial grade GMP radiopharmaceutical site.*

Blue Wave Positioning / Investment Proposition

Blue Wave Differentiation: ARAspheres De-Risked Innovation

- **High Unmet Need** – recurrent glioblastoma has no effective therapy.
- **Clinically Validated Components** – Actinium-225, RGD targeting moiety, alginate nanoparticles.
- **Alginate Advantage** – natural chelator eliminates need for synthetic linker.
- **Safety by Design** – alginate matrix retains daughter radionuclides, reducing off-target toxicity vs other alpha-emitters.
- **Local Administration** – direct delivery into the brain cavity, bypassing systemic exposure.
- **Scalable Platform** – IP-protected, expandable to multiple radionuclides and tumor targets.
- **Seasoned Team** – proven pharma/biotech leadership to drive translation.

Thank You

For further information, visit our website

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