Development of Radioimmunoconjugate for Diagnosis and Treatment of Osteosarcoma with a Focus in Pediatric Population

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Introduction

- Cancer remains a leading cause of death globally, with current therapies often limited by off-target effects and poor tumor specificity.
- **Radio Theranostics**; the combination of diagnostic imaging and targeted radiotherapy; offers great promise for improving cancer treatment.
- Among radio theranostic approaches, **radioimmunoconjugates**, antibodies labeled with radionuclides, allow for precise targeting of tumor-associated antigens, reducing harm to healthy tissues. However, there are significant challenges in optimizing radiolabeling techniques, improving tumor uptake, establishing clear Target Product Profiles (TPPs) for clinical application.

Project aims: To explore the development and strategic analysis of a novel radioimmunoconjugate therapy under development by **Frezent Biological Solutions**, a pioneering biotechnology startup. The project aims to address a critical unmet need in the treatment of recurrent cancers, with a focus on **Osteosarcoma**.

Objectives:

1. Research the current landscape in Radiopharmaceuticals and Theranostics
2. Define TPP for new Radiotheranostic for the treatment of Osteosarcoma
3. Propose Beachhead Market and Commercial Opportunity for Frezent

Through a competitive landscape analysis, TPP definition, and market assessment, this report underscores the strong investment potential and opportunities for collaboration, emphasizing the transformative impact of this innovative therapeutic approach.

Strategy

To achieve the project's objectives, the following strategies were employed:

- **Market Landscape:** Analyzed key players, emerging technologies, and growth opportunities in radiopharmaceuticals and theranostics, with a focus on innovation and development in the field.
- **Target Product Profile (TPP):** Defined the optimal characteristics for a radiotheranostic targeting **osteosarcoma**, addressing **pediatric**, **adolescent**, and **adult** dosing and safety profiles. Assessed regulatory hurdles affecting radiopharmaceuticals and theranostics.
- **Commercial Opportunity:** Proposed a beachhead market for osteosarcoma treatment and identified the commercial potential of Frezent's radioimmunoconjugate therapy, focusing on **IGF2R** expression.

By meticulously addressing the objectives, the goal is to provide investors, both current and prospective, with necessary perspectives to effectively evaluate risks & benefits associated with potential collaboration with Frezent.

Findings/Outcomes

Rapidly Evolving Landscape

The field of radiotheranostics is advancing at a remarkable pace, driven by pioneering companies such as Novartis, Telix Pharma, Y-mAbs, RadioPharm, and Defence Therapeutics. The integration of diagnostic and therapeutic capabilities enables more precise cancer treatment by allowing for the targeted delivery of therapeutic agents, significantly enhancing the precision and effectiveness of cancer therapies.

Innovations in Radio Theranostics

- Use of radionuclides such as Lutetium-177, innovation in linker chemistry.
- Emerging technologies like SADA PRIT and Accum®.

Challenges in Development

- Scaling production and ensuring radiation safety.
- Optimizing delivery mechanisms for radioisotopes.

Promising Future

- Potential to improve patient outcomes and minimize side effects.
- Enables personalized therapeutic strategies across diverse cancer types.

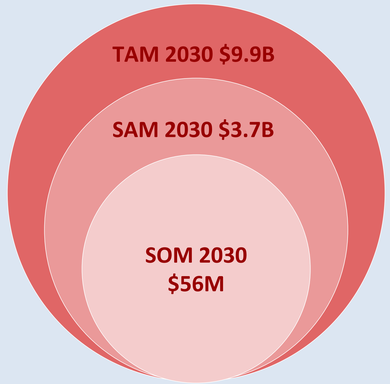
Parameter	Reference Profile	Minimal Essential Profile	Ideal Profile
Product Name	Adreview [MIBG (Metaiodobenzylguanidine)] Iobenguane I 123 Injection)	FZ09 68 Ga- IGF2R	FZ09 99 Te IGF2R
Indication	Metastatic pheochromocytoma or neuroblastoma	Osteosarcoma	Osteosarcoma
Usage	Use in the detection of primary or metastatic pheochromocytoma or neuroblastoma as an adjunct to other diagnostic tests.	Use in the detection of metastatic osteosarcoma in the lungs.	For the detection of metastasis in all organs (brain, bone, lymph nodes, adrenal glands, lungs)
Target Population	Patients with known or suspected pheochromocytoma or neuroblastoma • Adults and children >1 month old	Patients with known osteosarcoma. • children >10 years old	Patients with known osteosarcoma. • children > 5 years old
Dosage Form	• Intravenous injection over 1-2 minutes • A subsequent injection of 0.9% sodium chloride may be used to ensure full dose delivery	• Intravenous injection over 1-2 minutes • A subsequent injection of 0.9% sodium chloride may be used to ensure full dose delivery	• Intravenous injection over 1-2 minutes • A subsequent injection of 0.9% sodium chloride may be used to ensure full dose delivery
Dosage and Administration	Single dose administration. 5 mL of sterile solution for intravenous injection in a single use vial (2 mCi/mL at calibration time) Adult Dosage: For patients ≥16 years of age: Administer 10 mCi (370 MBq) • Pediatric Dosage: For patients <16 years and ≥70 kg: Administer 10 mCi (370 MBq) • For patients <16 years and <70 kg: Dose is scaled based on body weight	Pediatric Dosage: For patients <16 years and ≥70 kg: Administer 10 mCi (370 MBq) For patients <16 years and <70 kg: Dose is scaled based on body weight	Pediatric Dosage: For patients <16 years and ≥70 kg: Administer 10 mCi (370 MBq) For patients <16 years and <70 kg: Dose is scaled based on body weight
Efficacy	Sensitivity: 77-80% Specificity: 69-77%	Sensitivity: 77-80% Specificity: 69-77%	Sensitivity: 85-95% Specificity: 80-90%
Safety Profile	• Mild to moderate adverse reactions (<1.3% of patients) • Common reactions: dizziness, rash, pruritus, flushing, headache, injection site reactions	• Mild to moderate adverse reactions (<1.3% of patients) • Common reactions: dizziness, rash, pruritus, flushing, headache, injection site reactions	No side effects
Tolerability	Patients with severe renal insufficiency may experience increased radiation exposure and impaired imaging results.	Patients with severe renal insufficiency may experience increased radiation exposure and impaired imaging results.	
Contraindications/ Special Considerations	• Requires thyroid blockade prior to administration • Radiation safety precautions necessary Contraindicated in patients with known hypersensitivity to iobenguane or iobenguane sulfate. • Patients with severe renal impairment may have increased radiation exposure and decreased image quality • Contains benzyl alcohol, which may cause serious reactions in premature or low birth-weight infants.	No thyroid blockage necessary. Hydration and frequent urination.	No thyroid blockage necessary. Hydration and frequent urination.

Table 1: TPP Reference for Pediatric Diagnostic: Metaiodobenzylguanidine (MIBG)

Parameter	Essential Profile	Essential Minimal Profile	Ideal Profile
Product Name	131I-omburtamab is an iodine-131 radiolabeled murine monoclonal antibody	FZ08 177- Lu IGF2R	FZ08 225- Ac IGF2R
Indication	Treatment of central nervous system/leptomeningeal (CNS/LM) metastases in pediatric patients with neuroblastoma following standard multimodality treatment for CNS disease.	For the treatment of pediatric patients who have osteosarcoma	Used in the treatment of pediatric patients who have Osteosarcoma
Target Population	Pediatric patients with neuroblastoma and CNS/LM metastases following standard treatment	Pediatric patients with high risk of recurrence following standard treatment for regional and distant metastatic osteosarcoma.	Pediatric patients at high risk of recurrence as a first line therapy for regional and distant metastatic osteosarcoma.
Dosage Form	Solution for intraventricular infusion (via an Ommaya reservoir)	IV	IV
Dosage and Administration	2 age-based doses given 4 weeks apart. Age < 1 year: 25.0 mCi Age 1 to <3: 33.5 mCi Age ≥ 3 years: 50. mCi Administered via an intraventricular access device	Dosing based on age and body weight, administered intravenously Age 5-15 years: 150 mCi every 8 weeks for total of 4 treatments Age ≥ 15 years: 200 mCi every 8 weeks	Dosing based on age and body weight, administered intravenously Age 5-15 years: 75 kBq/kg (Total 0.15 mCi) every 8 weeks for total of 2 treatments Age ≥ 15years: 100 kBq/kg (Total 0.2 mCi) every 8 weeks for total of 2 treatments
Efficacy	Trial 03-132: 3-year overall survival (OS) rate: 57% Median OS: 51 months In the supportive trial 101: 1-year OS rate: 79% from start of treatment 35% objective response rate in patients with evaluable disease at baseline	Demonstrates significant disease-free survival improvement and prolonged progression free survival.	Demonstrates decrease in metastasis. Increase in PFS by 30% 5 Year Survival Rate: For distant: Increase from 24% to 50% For regional: Increase from 64% to 94%
Safety Profile	• Transient myelosuppression (most common) • Decreased lymphocyte count • Fatigue • Headache • Hiccups	Minimal acute toxicity, mostly mild and reversible symptoms	Well-tolerated with minimal adverse effects and no severe radiation-related toxicity.
Tolerability	Generally well tolerated. Acute adverse events were manageable, with transient myelosuppression being the most common	Manageable adverse events that do not significantly impact quality of life	Improved tolerability compared to current standard of care
Contraindications/ Special Considerations	None	None	None

Table 2: TPP Reference for Pediatric Therapeutic: Omburtamab (131I-omburtamab)

Market for Frezent



TAM (Total Addressable Market)
Global Bone Cancer Market: USD 15.2 billion(2024)
CAGR: 4.6%, USD 19.91B (2030)
With IGF2R expression: 9.9B (2030)

SAM (Serviceable Addressable Market):
• Osteosarcoma accounts for 37.5% of the global bone cancer market.

SOM (Serviceable Obtainable Market): 1.5% of SAM
• Initial SOM for U.S. market (2030): USD 111.98 M
• Adjusted SOM considering IGF2R expression (50% of cases): USD 55.99 million.

Conclusions

This study found key opportunities and strategies for advancing Frezent's novel radioimmunoconjugate.

Comprehensive Analysis

- Evaluated FDA-approved therapies, clinical trials, and key industry players.
- Identified risks and opportunities in the radiotheranostic landscape for osteosarcoma.

Strategic Insights

- Positioned Frezent's novel radioimmunoconjugate to meet **unmet clinical needs.**
- Emphasized **IGF2R** as a molecular target and selected optimal **radioisotopes** for diagnostics and therapy.
- Developed a strong **Target Product Profile (TPP)** for improved patient outcomes.

Market Potential

- Significant opportunities identified with an initial **SOM of $56 million.(2030)**

With this analysis, Frezent Biological Solutions is strategically advancing its new radioimmunoconjugate candidate to positively impact survival and redefine osteosarcoma treatment.

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