216 TNF-CSG, Tumor ECM-targeted TNFα

Asset Overview

Product Type	Protein
Indication	Oncology
Current Stage	Lead identification/ optimization
Target(MoA)	Targeting tumor ECM
Brief Description	• A novel immuno modulatory agent developed, exploiting highly selective affinity of a small homing peptide 'CSG' for tumour ECM. • TNF-CSG stimulates local activation of native immune cells, leading to tumour ECM degradation, significantly reduced tumour stiffness and interstitial pressure, and increased tumour perfusion. • Used as an adjunct therapy TNF-CSG has the potential to increase efficacy and reduce toxicity of chemo and immunotherapy drugs (and to enhance tumour detection by imaging agents). • In addition TNF-CSG has direct anti cancer activity as a monotherapy.
Organization	University of Western Australia

Differentiation

□ **Advantages**

- Solid tumours may be 10 times stiffer than normal tissue as a result of aberrant overgrowth of extra cellular matrix (ECM) components.
- High tumour ECM content of solid tumours acts to constrict blood vessels and limit tumour perfusion, presenting a barrier to delivery of activated immune cells and circulatory agents to the tumour microenvironment (TME).
- Reduced tumour stiffness, interstitial pressure and increased tumour perfusion shown by OCT/ micro elastography and DCE MRI, in 4T1 breast, CT26 colon and RIP Tag pancreatic tumour models.
- TNF-CSG has tumour specific activity; comparator PEGPH20 (Halozyme), a hyaluronidase-based drug enzymatically degrades hyaluronan; a ubiquitous ECM component.
- Enhanced tumour uptake of doxorubicin and iron oxide micelles (for MRI/ PET imaging).
- Monotherapeutic activity: reduced tumour growth, and tumour clearance associated with immune cell activation and infiltration, and increased cytotoxic T cell abundance.
- Reduced secondary metastasis in a 4T1 mouse model no loss of containment effect.
- No signs of systemic toxicity; native TNF (2μg, IV) resulted in death of 6/6 mice after 2 doses; TNF CSG had no cytotoxic effects after 20 doses (2μg, IV) over 10 wks.

□ **Differentiated profiles**

- There is no other known agent which acts to stimulate native immune cells in the TME to degrade aberrant ECM and increase delivery of circulatory agents.
- TNF CSG has activity as a monotherapy owing to immune cell activation and infiltration.
- An 'immuno mechanical' approach suited to combination with checkpoint blockade and chemotherapy agents.

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Intellectual Property

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Application Date	
Status	Application Pending
Country	US, EP

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