

## **CarThera's SonoCloud technology enhances the efficacy of immunotherapies for the treatment of brain tumors**

**Low Intensity Pulsed Ultrasound device can enhance delivery of CAR-T therapies and penetration of checkpoint inhibitors into the brain of preclinical glioma models; increasing probability of long-lasting immunity**

**Article published in AACR's Clinical Cancer Research journal describes results of preclinical work**

**Paris, France, June 9, 2021** – CarThera, a French company that designs and develops innovative ultrasound-based medical devices to treat brain disorders, today announces preclinical results in the testing of the combination of SonoCloud® technology with immunotherapies. This laboratory work was done in collaboration with Dr Amy Heimberger – a renowned expert in immunotherapies for glioblastoma (GBM) at the MD Anderson Cancer Center. The results were recently published online in the prestigious [Clinical Cancer Research journal](#): 'Opening of blood-brain barrier using low-intensity pulsed ultrasound (LIPU) enhances responses to immunotherapy in preclinical glioma models'.

In recent years, the use of immunotherapy has revolutionized the treatment of cancer; but these approaches have failed in multiple trials in GBM. The SonoCloud device uses LIPU to temporarily open the blood-brain barrier (BBB), and can enhance the delivery of various therapeutic approaches including CAR-T cells and checkpoint inhibitors to the tumor and surrounding brain parenchyma, for the treatment of glioblastoma and other brain tumors.

The positive results from this work pave the way for future clinical trials to test this approach. "Our studies clearly demonstrate that using pulsed ultrasound to temporarily disrupt the BBB can enhance the therapeutic effects of a variety of immunotherapeutic strategies for glioblastoma – by enhancing the delivery of antibodies, CAR-T cells and genetically-modified cellular immunotherapies to the tumor microenvironment - ultimately leading to better efficacy," said Michael Canney, Scientific Director at CarThera.

Immunotherapy-based approaches also have the potential to generate long-lasting immunity in the brain - even beyond the treatment zone. "Our preclinical results indicate that the SonoCloud technology can markedly enhance and increase the efficacy of checkpoint inhibitors. This strategy demonstrated protection from subsequent tumor rechallenge in the untreated hemisphere," said Dr Amy Heimberger, Professor of Neurosurgery and Scientific Director of Northwestern Medicine Malnati Brain Tumor Institute of the Lurie Comprehensive Cancer Center at Northwestern University, Chicago.

Immunotherapies are among the most important novel therapeutic advances in cancer treatment of the last decade; however they have not shown efficacy for primary brain tumors. Insufficient brain penetration may contribute to the disappointing results to date. The current preclinical results suggest an enhanced efficacy in combination with ultrasound-based blood-brain barrier opening, and support its use in human clinical trials. CarThera is presently exploring and testing the use of immunotherapies in patients with brain metastases from melanoma, in the SoniMEL study in Paris; similarly researchers from Northwestern University in Chicago are exploring the SonoCloud device in clinical trials for patients with GBM.

**Notes to editors:**

- The goal of the preclinical work was to investigate the following: to see if low-intensity pulsed ultrasound could enhance the therapeutic efficacy of anti-PD-1 in C57BL/6 mice – bearing intracranial GL261 gliomas; epidermal growth factor receptor variant III (EGFRvIII) specific chimeric antigen receptor (CAR) T cells within NSG mice with established EGFRvIII-U87 gliomas (epidermal growth factor receptor variant III); and a genetically-engineered antigen-presenting cells (APC)-based therapy, producing the T-cell attracting chemokine CXCL10 in the GL261-bearing mice
- A preclinical SonoCloud device was used in the study in mice
- The work has been executed at MD Anderson Cancer Center under the leadership of Dr. Amy Heimberger. Dr. Heimberger's current affiliation is Northwestern University, Chicago: [amy.heimberger@northwestern.edu](mailto:amy.heimberger@northwestern.edu)
- This study was funded by the ReMission Alliance Against Brain Tumors, the Traver Walsh Foundation, the Anne C. Brooks and Anthony D. Bullock Foundation, the MD Anderson Cancer Center Provost Fund and NIH/NCI P30CA016672
- Funding was not provided by CarThera
- CarThera has an ongoing collaboration with Northwestern University investigators; for several years it has been exploring, in preclinical studies, a wide range of potential drug therapies in combination with the SonoCloud device

**About SonoCloud**

SonoCloud® is an innovative medical device developed by CarThera. It emits ultrasound to temporarily increase the permeability of the blood vessels in the brain. Invented by Pr. Alexandre Carpentier, SonoCloud is an implant inserted into the skull and activated prior to chemotherapy. Several minutes of low-intensity ultrasound opens the blood-brain barrier for six hours and increases the concentration of therapeutic molecules in the brain. The SonoCloud technology is appropriate for the treatment of brain diseases in general. Oncology indications are the company's primary target, but investigations are ongoing in other conditions, including neurodegenerative diseases and Alzheimer's disease in particular.

**About CarThera**

CarThera designs and develops innovative therapeutic ultrasound-based medical devices for treating brain disorders. The company is a spin-off from AP-HP, Greater Paris University Hospitals, the largest hospital group in Europe, and Sorbonne University. CarThera leverages the inventions of Professor Alexandre Carpentier, a neurosurgeon at AP-HP who has achieved worldwide recognition for his innovative developments in treating brain disorders. CarThera developed SonoCloud, an intracranial ultrasound implant that temporarily opens the blood-brain barrier (BBB).

Founded in 2010, CarThera is based at the Brain Institute (Institut du Cerveau, ICM) in Paris, and has laboratories at the Bioparc Laënnec business incubator in Lyon. The company, led by Frederic Sottolini (CEO), works closely with the Laboratory of Therapeutic Applications in Ultrasound (Laboratoire Thérapie et Applications Ultrasonores, LabTAU, INSERM) in Lyon. Since its inception, the company has received support from the AP-HP, Sorbonne University, the ANR (Nationale Research Agency), France's Ministry of Research, the Ile-de-France region, the Bpifrance public investment bank, the European Union, the Medicen Paris Region and Lyonbiopôle clusters.

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