



Theraclion and Co-Lead Investigator Discuss Rationale and Design of First Clinical Trial Combining Echotherapy and Immunotherapy to Treat Metastatic Breast Cancer

Malakoff - FRANCE, September 11th, 2017 - THERACLION (Alternext, FR0010120402 - ALTHE), a company specialized in leading-edge medical equipment for echotherapy, and co-lead investigator, David Brenin, M.D., Chief of Breast Surgery at the University of Virginia School (UVA) of Medicine, discussed the rationale and design of the first clinical trial combining Theraclion's Echotherapy (also known as High Intensity Focused Ultrasound, HIFU) with the checkpoint inhibitor, pembrolizumab, in women with metastatic breast cancer. Dr. Brenin, presented that:

Breast cancer is one of the most common malignancies with approximately 250,000 new cases expected in the U.S. in 2017. One in eight women will be diagnosed with breast cancer in their lifetimes. It is the second leading cause of death from cancer with approximately 40,000 annual deaths. Although diagnosis, treatment and survival has improved, advanced stage IV metastatic disease remains a significant challenge with no curative therapies and a 22 percent five-year survival rate. Although immune-oncology approaches have revolutionized treatment for several cancers, such as lung cancer and melanoma, breast cancer has been resistant to immune-oncology approaches. The immune system does not mount an immune response against most breast cancers as tumor cells are not recognized as foreign.

A summary of Dr. Brenin's key points are:

- HIFU induce localized tissue heating and disruption at the treatment focal point, with minimum impact on surrounding structures; studies demonstrate that it is very well tolerated and efficacious in non-invasively removing lesions.
- Studies have demonstrated that HIFU treatment induces an immune system response with significant increases in immune cells.
- Pembrolizumab is able to induce an immune response to some breast cancers and HIFU are able to induce an immune response in most tumors, but not enough on its own to be curative. The rationale for the clinical study is that the combination might be more effective. HIFU facilitate infiltration of T-cells and Pembrolizumab blocks PD-1 receptors on cytotoxic T-cells greatly up-regulating the T-cell response to the breast cancer cells.
- The clinical trial is expected to begin patient accrual at UVA in October 2017, and will be a two-arm study of 12 patients. Patients in Arm A will be treated with pembrolizumab first followed by HIFU treatment; Arm B will be the reverse. Primary objectives are to assess the adverse event profile of pembrolizumab and focused ultrasound therapy in patients with metastatic breast cancer, and to determine whether the addition of pembrolizumab to focused ultrasound increases the proportion of CD8+ tumor infiltrating lymphocytes (ratio CD8+/CD4+) in the primary ablation zone.
- Secondary objectives are to compare CD8+ T-cell responses at peri-ablation zones when pembrolizumab is given before or after HIFU, to evaluate clinical responses at local and distant metastatic sites by CT scan and to evaluate progression free and overall survival.

“Our Echopulse® echotherapy system has already been shown to be a non-invasive option to treat benign breast fibroadenomas and thyroid nodules and it is approved for these indications in several countries worldwide,” said David Caumartin, Chief Executive Officer of Theraclion. *“Another focus area for us is the application of our echotherapy system to oncology. This clinical trial both demonstrates our commitment to this area and targets an unmet need in Stage IV metastatic breast cancer patients. We look forward to this collaboration with Dr. Brenin and the results of this initial study.”*

A replay of the webcast is available on the Theraclion website at www.theraclion.com.

David Brenin, M.D., FACS, is chief of breast surgery, co-director of both the University of Virginia (UVA) Breast Care Program and the High-Risk Breast and Ovarian Cancer Clinic and is an associate professor of surgery at UVA’s School of Medicine. His clinical practice specializes in the treatment of breast cancer, and benign diseases of the breast. Dr. Brenin is a fellowship trained breast surgeon and is an expert on surgical procedures involving the breast including lumpectomy, sentinel node biopsy, axillary dissection, nipple sparing mastectomy and IORT. His primary research interests include focused ultrasound ablation of breast tumors and immunotherapy.

About Theraclion

Theraclion is a French company specializing in high-tech medical equipment using therapeutic ultrasound. Drawing on leading-edge technologies, Theraclion has designed and manufactured an innovative solution for echotherapy, the Echopulse®, allowing non-invasive tumor treatment through ultrasound-guided high-intensity focused ultrasound. Theraclion is ISO 13485 certified and has received the CE mark for non-invasive ablation of breast fibroadenomas and thyroid nodules. Based in Malakoff, near Paris, France Theraclion has brought together a team of 34 people, 50% of whom are dedicated to R&D and clinical trials. For more information, please visit Theraclion’s website: www.theraclion.com.

**Theraclion is listed on Alternext Paris
PEA-PME eligible
Mnemonic: ALTHE - ISIN Code: FR0010120402**



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