CARDIAWAVE

Press Release

Deeptech - Aortic Stenosis - Heart Valve Disease

Cardiawave announces the success of its clinical trial to treat aortic stenosis. The trial with VALVOSOFT® its disruptive, non-invasive, ultrasound treatment was proven to:

- ***be safe and feasible***
- ***provide a sustained repair of the aortic valve***
- ***improve quality of life of the 34 patients treated***

Paris, France, March 14, 2022 – Cardiawave SA, a deeptech medical device company that has developed VALVOSOFT® a revolutionary non-invasive medical device to treat aortic stenosis, the most prevalent heart valve disease in adults, today announced the success of its First-In-Human I (FIH I) safety and feasibility clinical trial.

VALVOSOFT® is a breakthrough technology that allows for the remote application of an extremely precise and focused therapeutic ultrasound beam to restore valve function in patients with aortic stenosis. This intense beam decreases the stiffness of the aortic valve and improves its functional opening to allow sufficient oxygenated blood to reach the brain and the rest of the body. This non-invasive therapy is a new treatment option for aortic stenosis, as the only current medical response is to replace the aortic valve with open heart surgery, or with a minimally invasive percutaneous valve (TAVI) for the most severely affected patients. Aortic stenosis has become a public health issue. This pathology affects between 2 and 12% of subjects over 65 years old (1.3 million patients in Europe).

The FIH 1 study

The purpose of the FIH I study was to assess the safety, and operating system of the first generation of VALVOSOFT® as well as the clinical effects of softening calcific aortic valve tissues with a beating heart.

30 patients (average age 84yrs, with 9 patients over 90) have now been successfully treated in France and the Netherlands with the last being in Q4 2021. VALVOSOFT® provided a sustained repair to the aortic valve for up to 12 months post treatment. The study has proven **the safety and efficacy, as well as the ease of the procedure with a 60 minute non-invasive outpatient treatment**. Following the successful VALVOSOFT® treatment, two patients were able to have TAVI valve replacement.

"The positive results of the safety and feasibility clinical studies we observed in our First In Human trial are extremely encouraging. We have shown that VALVOSOFT® can treat patients who are exceedingly fragile and sick for whom no medical solution exists today. This represents a new treatment solution for aortic stenosis, over and above aortic valve replacement from which only a small minority of patients can benefit. Cardiawave's VALVOSOFT® has the potential to become a standard new treatment for this deadly disease", said **Benjamin Bertrand, CEO of Cardiawave.** "*We are currently working on receiving the necessary authorizations in Europe for further clinical trials over the next few months. I am confident that these will once again confirm the therapeutic benefits of VALVOSOFT®." he added.*

VALVOSOFT®'s non-invasive treatment brings great hope for patients with aortic stenosis and for their families. It offers the possibility of an efficient outpatient treatment for fragile patients, for whom valve replacement is too risky. In the longer term, treating patients with less severe stenosis would be a major step forward." declared **Professeur Emmanuel Messas the Georges Pompidou European Hospital (AP-HP), in Paris.**

A second feasibility and safety FIH II study is underway with 10 further patients in Serbia. This includes brain MRI evaluation both before and after treatment to assess the risk of a stroke. Four patients were safely treated by the end of December 2021. None of the MRIs detected an abnormality. Six further patients will be treated during H1 2022.

Next steps

On the back of these promising clinical results, Cardiawave has launched its Series B financing. This is expected to be completed in the second half of 2022. These funds will be used to finance the next phase of clinical trials in Europe and the United States.

Between April and December 2022, Cardiawave plans to enroll around 50 aortic stenosis patients across 10 hospitals in France, the Netherlands and Germany. This new European clinical trial targets the granting of a CE mark. The clinical trial protocol includes patient monitoring after 1, 6 and 12 months.

About VALVOSOFT®

Cardiawave has developed its new breakthrough technology VALVOSOFT® as a result of the work of the prestigious French academic laboratories Institut Langevin (INSERM/CNRS/ESPCI) and Laboratoire Physique pour la Médecine (INSERM/CNRS/ESPCI/PSL). This non-invasive treatment of aortic stenosis combines therapeutic ultrasound, robotics and ultrasound imaging. All software and most hardware components have been developed in-house thanks to the unique know-how of Cardiawave and its academic partners. VALVOSOFT® uses a new and unique ultrasound technology with a remote repair procedure on the aortic valve. Ultrasound softens the tissue, restores leaflet mobility and enables a wider opening of the valve. This non-invasive therapeutic solution is less risky for elderly patients and less costly for the healthcare system. VALVOSOFT® has very favorable environmental credentials, with very low electricity consumption (1kV1kVA max), very little waste (60 g) and no use of chemicals products for the procedure.

About AORTIC STENOSIS

Aortic stenosis is a degenerative and potentially life-threatening condition, caused by calcium buildup which prevents the aortic valve from fully opening. Aortic Stenosis evolves over time leading to heart failure and increases the risk of sudden death during its final stage (severe & symptomatic stenosis). With age, the aortic valve calcifies, becomes more rigid and narrow, and no longer opens properly leading to poor blood circulation.

Aortic Stenosis can be mild, moderate and severe. 2 million people are estimated to suffer from severe AS in Europe and in the USA, of whom 500,000 benefit from Transcatheter Aortic Valve Replacement (TVAI) or open-heart surgery. 1.5 million patients remain untreated and face a low life expectancy of 2 to 5 years. Around 3 million further patients suffer from moderate AS for whom there is no early treatment.

About CARDIAWAVE

Cardiawave has developed a non-invasive medical device VALVOSOFT® for the treatment of valvular heart diseases, and in particular, Aortic Stenosis, the most prevalent heart valve disease in adults and one of the most common causes of cardiovascular mortality worldwide. Based in Paris, Cardiawave is a member of the national research consortium RHU Stop-AS, and has ISO 13485:2016 certification since 2019. Cardiawave employs 28 people and has secured over €22M in funding since its creation in 2014.

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