Shockwave Initiates U.S. Pivotal Study for Coronary Intravascular Lithotripsy

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Santa Clara, Calif. — January 14, 2019 – Shockwave Medical, Inc., a pioneer in the development and commercialization of Intravascular Lithotripsy (IVL) to treat complex calcified cardiovascular disease, has initiated its U.S. Food and Drug Administration (FDA) Investigational Device Exemption (IDE) study – DISRUPT CAD III – for the use of IVL in heavily calcified coronary arteries. IVL is an innovative lesion preparation tool designed to fracture problematic calcium using sonic pressure waves in order to facilitate stent delivery, deployment and expansion.

The co-principal investigators of the study are Drs. Dean Kereiakes, M.D., FACC, FSCAI, Medical Director of The Christ Hospital Heart and Vascular Center and The Lindner Research Center in Cincinnati, Ohio and Professor of Clinical Medicine, The Ohio State University and Jonathan Hill, M.D., consultant cardiologist at King's College Hospital in London. The first patient was enrolled last week by Richard A. Shlofmitz, M.D., FACC, Chairman, Department of Cardiology, St. Francis Hospital in Roslyn, New York.

Coronary artery calcium physically impairs stent expansion and is perhaps the single most important predictor of early stent thrombosis and restenosis after stent procedures. Current calcium modification treatments, which can be difficult to perform, only address the burden of intimal calcium with varying degrees of success and result in an increased risk for adverse events since these techniques don't differentiate between the calcific lesion and soft, normal intimal tissue.

Coronary IVL is a novel investigational therapy designed to treat calcified artery blockages with sonic pressure waves historically used to treat patients with kidney stones. The technology seeks to minimize trauma within the artery by delivering pulsatile sonic pressure waves locally to fracture both intimal and medial calcium in the artery wall but pass through surrounding soft vascular tissue in a safe manner.

"After previously using the peripheral IVL technology – Shockwave M^5 – to enable transfemoral access for TAVR as well as for mechanical cardiac support and hearing the enthusiasm from Europe about coronary IVL, we are very excited to investigate the clinical potential of the coronary technology in the United States," said Dr. Kereiakes. "This therapy holds tremendous potential from a safety perspective for patients and an ease of use perspective for physicians – if coronary IVL is shown to be safe and effective, it could be a game changer for the way we treat calcified arteries today."

DISRUPT CAD III is a prospective, non-randomized, multicenter global IDE study to demonstrate the safety and effectiveness of the Shockwave Coronary IVL System with the Shockwave C^2 Coronary IVL Catheter in *de novo,* calcified, stenotic, coronary arteries prior to stenting. The study is expected to enroll approximately 392 patients at 50 global centers in the United States and Europe.

The study will assess the freedom from major adverse cardiac events (MACE) within 30 days of the index procedure as the primary safety endpoint. The primary effectiveness endpoint is procedural success which, based on predicate studies, is defined as stent delivery with a residual stenosis of less than 50 percent and without in-hospital MACE. Enrolled study patients will be followed for two years.

The study's chairman is Gregg W. Stone, M.D., FACC, FSCAI, professor of medicine at Columbia University Medical Center in New York, and the angiographic and OCT core labs are the Cardiovascular Research Foundation, also based in New York.

"Having treated nearly 100 patients with IVL since its European launch, the benefits for treating complex patients are evident. I am delighted to be a part of this important global trial to introduce my U.S. interventional colleagues to this novel technology. IVL is easy to use and has been a huge advancement for our management of calcified lesions," said Dr. Hill. "I think U.S. interventionalists will recognize the simplicity and ease of use of the IVL system and will appreciate its ability to be rapidly deployed in any cath lab. I have no doubt that IVL is poised to become the key differentiating technology compared to other calcium modification tools."

Shockwave C^2 Coronary IVL catheters are commercially available for the treatment of *de novo* coronary artery disease in Europe and select other geographies; they are limited to investigational use in the United States. Shockwave M^5 Peripheral IVL catheters are commercially available for treatment of peripheral artery disease, including iliac arteries, in the United States, Europe and select other geographies.

About Intravascular Lithotripsy

We have adapted the use of lithotripsy to the cardiovascular field with the aim of creating what can become the safest, most effective means of addressing the growing challenge of cardiovascular calcification. Lithotripsy has been used to successfully treat kidney stones (deposits of hardened calcium) for over 30 years. By integrating lithotripsy into a device that resembles a standard balloon catheter, physicians can prepare, deliver and treat calcified lesions using a familiar form factor, without disruption to their standard procedural workflow.

Our differentiated IVL System works by delivering shockwaves through the entire depth of the artery wall, modifying calcium in the medial layer of the artery, not just at the superficial most intimal layer.

The IVL System includes a generator, connector cable and a family of IVL catheters designed to treat PAD and CAD. IVL cracks calcium through short

bursts of sonic pressure waves, which are generated within the IVL catheter and travel through the vessel to crack calcium with an effective pressure of up to 50 atmospheres (“atm”) without harming the soft tissue. IVL catheters utilize multiple lithotripsy emitters that are integrated into a standard, semi-compliant balloon-catheter platform, which is advanced to the target lesion and the integrated balloon is inflated with fluid at a low pressure to make contact with the arterial wall. IVL is then activated through the generator with the touch of a button, creating a small bubble within the catheter balloon which rapidly expands and collapses. The rapid expansion and collapse of the bubble creates sonic pressure waves that travel through the vessel and crack the calcium, allowing the blood vessel to expand under low static pressure. To view an animation of the Intravascular Lithotripsy procedure visit https://shockwavemedical.com.

About Shockwave Medical, Inc.

We are a medical device company focused on developing and commercializing products intended to transform the way calcified cardiovascular disease is treated. We aim to establish a new standard of care for medical device treatment of atherosclerotic cardiovascular disease through our differentiated and proprietary local delivery of sonic pressure waves for the treatment of calcified plaque, which we refer to as ‘Intravascular Lithotripsy.’ For more information, visit www.shockwavemedical.com.