CryoLife Receives FDA Authorization to Commence PROACT Xa Clinical Trial

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Study Designed to Evaluate the Use of Apixaban in On-X Aortic Valve Patients

ATLANTA, Dec. 23, 2019 /PRNewswire/ -- **CryoLife, Inc. (NYSE: CRY)**, a leading cardiac and vascular surgery company focused on aortic disease, announced today that it has received authorization from the U.S. Food and Drug Administration (FDA) pursuant to an Investigational New Drug (IND) application to begin the PROACT Xa clinical trial, a prospective, randomized, trial to determine if patients with an On-X mechanical aortic valve can be maintained safely and effectively on apixaban (Eliquis®) rather than warfarin.

Pat Mackin, Chairman, President, and Chief Executive Officer of CryoLife, said, "We are pleased that the FDA has authorized us to study the use of apixaban in patients with the On-X Aortic Valve. The On-X Aortic Valve was the first mechanical aortic heart valve to receive both FDA and CE Mark approval for labeling to permit use with a reduced warfarin dosage, based on results of the original PROACT trial which demonstrated a greater than a 60% reduction in bleeding events without increasing the risk of stroke." Mr. Mackin added, "If the PROACT Xa trial is successful in proving that On-X Aortic Valve recipients can be maintained safely on apixaban rather than warfarin, we believe that not only will we become the leader in the mechanical valve market, but also that the On-X Aortic Valve will take share from the existing bioprosthetic aortic valve market."

Patients with mechanical heart valves are anticoagulated with warfarin which requires routine blood testing to manage their INR (International Normalized Ratio) within a certain range to minimize the likelihood of bleeding and stroke. INR management within prescribed ranges can be challenging due to dietary restrictions and drug interactions. Despite multiple studies showing that tissue valves are associated with worse outcomes, including higher reoperation rates compared to mechanical valves, younger patients sometimes opt for a tissue valve to avoid the need to take warfarin due to its side effects. Providing an alternative to warfarin, such as apixaban, gives younger patients a strong incentive to choose an On-X Aortic Valve with greater durability, generally better long-term survival and better clinical outcomes.

The PROACT Xa trial is a prospective, multicenter, randomized clinical trial consisting of approximately 1,000 participants (500 participants in each arm) at up to 60 sites in North America, who are 18 years of age or older and have been implanted with the On-X Aortic Valve. Co-chairs for the PROACT Xa Steering Committee are Lars Svensson, MD, PhD, Chairman of the Heart and Vascular Institute at the Cleveland Clinic and John Alexander, Professor of Medicine in Cardiology, Duke University.

Participants will be randomized to either continue warfarin or switch to apixaban. Each participant will be followed for at least 2 years. The co-primary efficacy endpoints are to (1) determine if apixaban is non-inferior to warfarin (INR target range 2.0 - 3.0) for patients with an On-X Aortic Valve for the primary composite outcome of valve thrombosis and valve-related thromboembolism and (2) determine if apixaban provides acceptable anticoagulation for patients with an On-X Aortic Valve for the primary composite outcome of valve thrombosis and valve-related thromboembolism as compared with objective performance criteria. The primary safety endpoint is to determine if apixaban is superior to warfarin (INR target range 2.0 - 3.0) in the safety outcome of major bleeding in participants with an On-X Aortic Valve.

Dr. Alexander said, "Apixaban has been shown to reduce stroke and cause less bleeding than warfarin in patients with atrial fibrillation. If it can be done safely, the possibility of managing patients with an On-X aortic valve with apixaban and eliminating their need for warfarin represents a potential benefit to patients and the physicians who manage them."

Worldwide, there are approximately 340,000 surgical aortic valves replaced annually placing the worldwide aortic surgical valve market at approximately $1.2 billion.

About CryoLife
Headquartered in suburban Atlanta, Georgia, CryoLife is a leader in the manufacturing, processing, and distribution of medical devices and implantable tissues used in cardiac and vascular surgical procedures focused on aortic repair. CryoLife markets and sells products in more than 100 countries worldwide. For additional information about CryoLife, visit our website, www.cryolife.com.

Forward Looking Statements
Statements made in this press release that look forward in time or that express management's beliefs, expectations, or hopes are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements reflect the views of management at the time such statements are made. These statements include our beliefs that, if the PROACT Xa trial is successful in proving that On-X Aortic Valve recipients can be maintained safely on apixaban rather than warfarin, not only will we become the leader in the mechanical valve market, but also that the On-X Aortic Valve will take share from the existing bioprosthetic aortic valve market. These forward-looking statements are subject to a number of risks, uncertainties, estimates, and assumptions that may cause actual results to differ materially from current expectations.

These risks and uncertainties include the risk factors detailed in our Securities and Exchange Commission filings, including our Form 10-K for year ended December 31, 2018. CryoLife does not undertake to update its forward-looking statements, whether as a result of new information, future events, or otherwise.

Contacts:

CryoLife
D. Ashley Lee
Executive Vice President, Chief Financial Officer and Chief Operating Officer
Phone: 770-419-3355

Gilmartin Group LLC
Greg Chodaczek / Lynn Lewis
Phone: 646-924-1769
investors@cryolife.com

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