CryoLife Initiates Enrollment in PROACT Xa Clinical Trial

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

ATLANTA, May 7, 2020 /PRNewswire/ -- **CryoLife, Inc. (NYSE: CRY)**, a leading cardiac and vascular surgery company focused on aortic disease, announced today that it has initiated enrollment in 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 on warfarin.

Pat Mackin, Chairman, President, and Chief Executive Officer of CryoLife, said, "We are pleased to announce that the first patient in our PROACT Xa clinical trial has been enrolled at CHI St. Vincent Heart Institute in Little Rock, Arkansas. Under the PROACT Xa trial, we will study the use of apixaban in patients with the On-X Aortic Valve, the first and only mechanical aortic heart valve to receive both FDA approval and the CE Mark for labeling to permit use with a reduced warfarin dosage, based on results of the original PROACT trial that demonstrated a greater than a 60% reduction in bleeding events without increased risk of stroke." Mr. Mackin added, "Despite the ongoing COVID-19 pandemic, many institutions are continuing to enroll patients in important clinical trials. As a result, if the trial meets its endpoints, we believe we can still achieve FDA approval for the use of apixaban with the On-X Aortic Valve in 2024."

Dr. John Alexander, Chair of the PROACT Xa trial and Professor of Cardiology at Duke, said, "We are excited to have started enrollment in the PROACT Xa study. This pragmatic trial, designed using the principles of Quality-by-Design, will generate high quality evidence on whether apixaban can safely be used as an alternative to warfarin in patients with a mechanical aortic heart valve. If apixaban is proven non-inferior to warfarin, it would offer improved quality of life for these patients who currently require frequent INR testing and would be a paradigm shift for clinicians managing patients with valvular heart disease."

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.

Dr. Thomas Rayburn III, MD, CHI St. Vincent Heart Institute, said, "The CHI St. Vincent Heart Institute is pleased to be the first site in the United States to take the next step in this important research. We look forward to answering this vital clinical question and are especially excited that we can continue to collaborate remotely using telehealth technologies to maintain momentum at this time. Our role in this important research is indicative of CHI St. Vincent's healing ministry and commitment to delivering the most advanced, compassionate care to our communities across Arkansas which suffer from a high prevalence of cardiac disease, stroke, obesity and diabetes."

Dr. Tracy Wang, Principal Investigator of the PROACT Xa coordinating center at the Duke Clinical Research Institute said, "Being able to enroll our first patient under the disruptive cloud of COVID-19 underscores just how much patients and clinicians alike have been looking forward to this study. The pragmatic nature of the study design is appealing to potential participants, enabling enrollment to move forward even during a time when research activities are often curtailed, and enhancing the likelihood of high-quality follow-up by participants even if social distancing remains necessary."

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. 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.

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 trial meets its endpoints, we can still achieve FDA approval for the use of apixaban with the On-X Aortic Valve in 2024; and that the pragmatic nature of the study design will be appealing to potential participants, thereby enabling enrollment in the PROACT Xa clinical trial to move forward during a time when research activities are often curtailed and enhancing the likelihood of high-quality follow-up by participants even if social distancing remains necessary. 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, 2019. 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: 347-620-7010
investors@cryolife.com

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