Landmark Study Shows Treatment With Abbott's MitraClip® Is Superior To Medical Therapy For Advanced Heart Failure Patients With Significant Secondary Mitral Regurgitation

- The COAPT trial met both the primary safety and efficacy endpoints and all secondary endpoints, including reducing all-cause mortality through two years

- Late-breaking results were presented at TCT and simultaneously published in The New England Journal of Medicine

- COAPT showed MitraClip improved clinical outcomes in select heart failure patients who had clinically significant secondary mitral regurgitation, suggesting the first and only mitral valve intervention to improve prognosis for these difficult-to-treat patients

SAN DIEGO, Sept. 23, 2018 /PRNewswire/ -- Abbott (NYSE: ABT) today announced positive clinical study results from a randomized controlled trial comparing treatment with the MitraClip® device to guideline-directed medical therapy in select patients with secondary (or functional) mitral regurgitation, or a leaky heart valve, as a result of advanced heart failure. The landmark COAPT study met both the primary safety and efficacy endpoints and all secondary endpoints, and showed treatment with MitraClip plus medical therapy was superior to medical therapy alone in reducing rates of heart failure hospitalizations and improving survival at two years. This therapeutic mitral valve intervention is the first and only to demonstrate positive outcomes in a clinical trial for ailing heart failure patients with clinically significant secondary mitral regurgitation.

The data were presented during a late-breaking session at the 30th Transcatheter Cardiovascular Therapeutics (TCT) annual scientific symposium of the Cardiovascular Research Foundation in San Diego, and were simultaneously published in *The New England Journal of Medicine*. The COAPT study data will be submitted to the U.S. Food and Drug Administration (FDA) to support consideration of an expanded indication for Abbott's MitraClip to treat secondary mitral regurgitation.

"These highly anticipated results from the COAPT trial are quite remarkable, and conclusively demonstrate that heart failure patients with clinically significant secondary mitral regurgitation who remain symptomatic despite best medical practices benefit from treatment with MitraClip," said Gregg W. Stone, M.D., co-principal investigator of the COAPT study, director of cardiovascular research and education at NewYork-Presbyterian/Columbia University Irving Medical Center and professor of medicine at Columbia University Vagelos College of Physicians and Surgeons. "These results have the potential to transform clinical practice and help patients who otherwise have an extremely poor prognosis – patients who, to date, have had to rely only on medications to manage their symptoms without treating the underlying cause."

MitraClip repairs the mitral valve without the need for an invasive surgical procedure and is delivered to the heart through the femoral vein, a blood vessel in the leg. The device works by clipping together a portion of the leaflets of the mitral valve to reduce the backflow of blood, which allows the heart to pump blood more efficiently, thereby relieving symptoms and improving patient quality of life. The device was approved by the FDA in 2013 to treat the primary (or degenerative) form of mitral regurgitation (MR), which is caused by an anatomic defect of one or more of the structures of the mitral valve, which prevents the valve from closing properly, and subsequently causes leakage. Approximately one in 10 adults age 75 and older in the U.S., or four million Americans, suffer from MR.[1,2,3,4]

The COAPT trial investigated MitraClip for treating secondary MR, a type of MR in which the damaged left ventricle of the heart – often due to a heart attack or other cause of heart failure – impairs the performance of a normal mitral valve. The COAPT data add to more than 10 years of evidence on the use of MitraClip for treating primary MR, and now provide randomized trial evidence supporting MitraClip as a possible option to treat secondary MR. It's estimated that two to three times as many patients may benefit from MitraClip treatment for secondary MR as a result of underlying heart failure, than those treated now for the primary form of the disease commonly associated with age.[5]

People with heart failure may develop secondary MR when the left chamber of the heart becomes enlarged, preventing the mitral leaflets from closing.[6] Significant secondary MR is difficult to manage, is associated with a poor prognosis[7] and can lead to reduced quality of life, recurrent hospitalizations and decreased survival.[8,9] While there are currently no FDA-approved devices for secondary MR, guideline-directed medical therapy (GDMT) and cardiac resynchronization therapy (CRT, a heart failure treatment that keeps the right and left ventricles pumping in sync) may provide symptomatic relief in some patients.[10]

Most heart failure patients with clinically significant secondary MR are treated with medication only and have few treatment options.[11] The COAPT study aimed to assess the safety and efficacy of MitraClip treatment for heart failure patients with clinically significant secondary MR who remained symptomatic despite receiving optimal medical therapy.

Key results from the trial include:

- Treatment with MitraClip plus medical therapy resulted in a statistically significant reduction in heart failure hospitalization through two years compared to medical therapy alone (annualized rate of 67.9 percent per year vs. 35.8 percent per year; $p<0.001$).
- MitraClip treatment reduced all-cause mortality through two years, from 46.1 percent of patients in the control group to 29.1 percent in the device group at two years of follow-up ($p<0.001$).
- At one year, freedom from device-related complications was 96.6 percent, exceeding the performance goal for the

primary safety endpoint (p<0.001).

- Patients in the device group experienced significant reduction in MR severity (at one year, MR≤ 2+ was present in 94.8 percent of patients in the device group and in 46.9 percent of patients in the control group; p<0.001) and NYHA class (at one year, NYHA class I or II was present in 72.2 percent of patients in the device group and in 49.6 percent of patients in the control group; p<0.001).
- Treatment with MitraClip provided a substantial improvement in patients' perception of their health status, measured by the KCCQ quality-of-life score, and functional capacity at one year.
- MitraClip treatment resulted in a reduction in the composite of death or first heart failure hospitalization by 43.0 percent.

The results were consistent across numerous subgroups, including patients with ischemic and non-ischemic cardiomyopathy – a disease of the heart muscle that weakens the ability of the heart to pump blood to the rest of the body – and those at high and low surgical risk.

"Abbott has led the way in developing minimally invasive solutions for some of the most complex challenges in patients with structural heart disease, and the COAPT study results show that MitraClip has the potential to help many more people with heart failure live better and longer, impacting both quality of life and survival," said Neil Moat, M.D., chief medical officer of Abbott's structural heart business. "While MitraClip is already the gold standard for repairing leaky heart valves in patients with primary mitral valve disease who are not surgical candidates, we now have very robust clinical evidence that MitraClip is a life-changing technology for people whose heart failure has resulted in a leaky mitral valve, providing hope to these very sick heart failure patients and their caregivers."

About the COAPT Study

In the COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation) study, 614 symptomatic heart failure patients with moderate-to-severe or severe secondary MR were randomized to receive treatment with MitraClip plus guideline-directed medical therapy or guideline-directed medical therapy alone at 78 sites in the U.S. and Canada. Eligible patients had diseased heart muscle, known as dilated cardiomyopathy that reduced the amount of blood pumped from the left ventricle; and moderate-to-severe or severe MR assessed by the American Society of Echocardiography guidelines that remained symptomatic despite maximally-tolerated medical therapy and cardiac resynchronization therapy (if appropriate).[9,12] Mean patient age was 72.2 years, and 64.0 percent were male. The primary efficacy endpoint was all heart failure hospitalizations through two years, and the primary safety endpoint was freedom from device-related complications at one year compared to a performance goal of 88.0 percent. Secondary endpoints included all-cause mortality at two years, change in quality-of-life at one year, change in functional capacity (six minute walk distance) at one year, MR severity at one year and left ventricle size at one year.

About MitraClip

MitraClip received CE Mark in Europe in 2008 and was approved by the FDA in 2013 for primary MR prohibitive risk patients (patients not eligible for open-heart surgery). Delivered through a minimally invasive catheter, MitraClip secures a portion of the leaflets of the mitral valve with an implanted clip, allowing the heart to pump blood more efficiently throughout the body, thereby relieving the symptoms of severe MR and improving patient quality of life.

Patients with MR are often not eligible for standard-of-care surgery because of advanced age, frailty, multiple comorbidities or other complicating factors, and the therapy offers a minimally invasive alternative. The transcatheter clip-based therapy, now on a third generation of product innovations, has been used to treat 70,000 people with MR worldwide over the last 10 years.

For more information on MitraClip and the COAPT study, visit:www.coapttrial.com.

For U.S. Important Safety Information about MitraClip, visithttp://mitraclippossibilities.com/#isi-sec.

MitraClip is currently under investigation to treat clinically significant secondary mitral regurgitation in the U.S. and not approved by the FDA for secondary mitral regurgitation. The device has been approved to treat primary mitral regurgitation in the U.S. since 2013.

About Abbott

At Abbott, we're committed to helping people live their best possible life through the power of health. For more than 125 years, we've brought new products and technologies to the world - in nutrition, diagnostics, medical devices and branded generic pharmaceuticals - that create more possibilities for more people at all stages of life. Today, 99,000 of us are working to help people live not just longer, but better, in the more than 150 countries we serve.

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For further information: Abbott Media: Mary Kokkinen, (408) 444-2401; Abbott Financial: Mike Comilla, (224) 668-1872