FDA Approves Corlanor® (ivabradine) To Reduce The Risk Of Hospitalization For Worsening Heart Failure In Patients With Chronic Heart Failure

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Corlanor is the First New Chronic Heart Failure Medicine Approved by the FDA in Nearly a Decade

THOUSAND OAKS, Calif., April 15, 2015 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced that the U.S. Food and Drug Administration (FDA) has granted approval of Corlanor® (ivabradine), an oral medication indicated to reduce the risk of hospitalization for worsening heart failure in patients with stable, symptomatic chronic heart failure with left ventricular ejection fraction (LVEF) ≤35 percent, who are in sinus rhythm with resting heart rate ≥70 beats per minute (bpm) and either are on maximally tolerated doses of beta blockers or have a contraindication to beta blocker use.

To view the multimedia assets associated with this release, please click: http://www.multivu.com/players/English/7414051-amgen-corlanor-fda-approval/.

Heart failure is a common condition that affects approximately 5.7 million people in the U.S., about half of which have reduced left ventricular function.[1,2] Despite broad use of standard treatments, the prognosis for patients with heart failure is poor.[3] Projections show that by 2030, the prevalence of heart failure will increase 46 percent from 2012 estimates.[1]

"We are excited to introduce Corlanor, the first new chronic heart failure medicine approved by the FDA in nearly a decade, for patients who are at a significantly greater risk of hospitalization due to worsening heart failure in the U.S.," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "Many heart failure patients are repeatedly admitted to the hospital, which can cause a great burden on the patient and on healthcare resources. We hope that today's approval of Corlanor as an innovative therapeutic option will address a major unmet need for patients, their families and the healthcare system."

Heart failure costs an estimated $31 billion in the U.S. each year, with the majority of the cost related to hospitalizations.[4] By 2030, the cost of heart failure in the U.S. is expected to increase almost 127 percent totaling $70 billion.[4]

"The approval of Corlanor is an important step forward for the treatment of patients with chronic heart failure in the U.S. Because its mechanism of action is unique, it will complement the use of standard heart failure therapies, including beta blockers," said Jeffrey S. Borer, M.D., professor of Medicine, Cell Biology, Radiology and Surgery, and chief of Cardiovascular Medicine at State University of New York, Downstate Medical Center. "Despite beta blockade and other therapies, many people with chronic heart failure continue to suffer hospitalizations due to worsening heart failure. For these patients, when heart rate is greater than or equal to 70 bpm, Corlanor may be an appropriate treatment option and can be expected to add benefit."

Corlanor blocks the hyperpolarization-activated cyclic nucleotide-gated (HCN) channel responsible for the cardiac pacemaker, which regulates heart rate. Corlanor reduces the spontaneous pacemaker activity of the cardiac sinus node by selectively inhibiting the I_f current ("funny" current) to slow the heart rate with no effect on ventricular repolarization and no effects on myocardial contractility.[5]

The Corlanor approval is based on global clinical trial data including a large, multicenter, randomized, double-blind, placebo-controlled, outcomes trial. The Phase 3 SHIFT (Systolic Heart failure treatment with the I_f inhibitor ivabradine Trial) study compared Corlanor to placebo on top of standard of care (SOC) therapies, including beta blockers, in more than 6,500 clinically stable (≥4 weeks) patients in sinus rhythm with reduced left ventricular function (LVEF ≤35 percent) and heart rate ≥70 bpm, with a hospitalization for heart failure within the past 12 months. Patients received SOC, including beta blockers (89 percent), angiotensin converting enzyme (ACE) inhibitors and/or angiotensin II receptor blockers (ARB) (91 percent), diuretics (83 percent) and anti-aldosterone agents (60 percent).

Results from the Phase 3 SHIFT study showed Corlanor significantly reduced the risk of the primary composite endpoint of hospitalization or cardiovascular death for worsening heart failure, with 18 percent relative risk reduction (RRR) (p<0.0001, 4.2 percent absolute risk reduction [ARR]) versus placebo. The treatment effect reflected only a reduction in the risk of hospitalization for worsening heart failure; there was no favorable effect on the mortality component of the primary endpoint. There was a 26 percent RRR (4.7 percent ARR) in the risk of hospitalizations for worsening heart failure.

The most common adverse drug reactions in the SHIFT study occurring in ≥1 percent of patients on Corlanor compared to placebo were bradycardia (10 percent vs. 2.2 percent), hypertension or increased blood pressure (8.9 percent vs. 7.8 percent), atrial fibrillation (8.3 percent vs. 6.6 percent), and luminous phenomena (phosphenes) or visual brightness (2.8 percent vs. 0.5 percent).

The recommended starting dose of Corlanor is a 5 mg tablet twice daily with meals. After two weeks of treatment, the dose should be assessed and adjusted depending on heart rate. In patients with a history of conduction defects, or other patients in whom bradycardia could lead to hemodynamic compromise, initiate therapy at 2.5 mg twice daily before increasing the dose based on heart rate.

Corlanor is expected to be available to patients in approximately one week.

About Corlanor® (ivabradine)

Corlanor blocks the hyperpolarization-activated cyclic nucleotide-gated (HCN) channel responsible for the cardiac pacemaker, which regulates heart rate. Corlanor reduces the spontaneous pacemaker activity of the cardiac sinus node by selectively inhibiting the I_f current ("funny" current) to slow the heart rate with no effect on ventricular repolarization and no effects on myocardial contractility.[5] Corlanor was developed by Les Laboratoires Servier. Through a collaboration with Servier, Amgen has rights to commercialize Corlanor in the U.S.

Important U.S. Product Information

Corlanor® is indicated to reduce the risk of hospitalization for worsening heart failure in patients with stable, symptomatic chronic heart failure with left ventricular ejection fraction ≤ 35%, who are in sinus rhythm with resting heart rate ≥ 70 beats per minute (bpm) and either are on maximally tolerated doses of beta blockers or have a contraindication to beta blocker use.

Important Safety Information

- **Contraindications:** Corlanor® is contraindicated in patients with acute decompensated heart failure, blood pressure < 90/50 mmHg, sick sinus syndrome, sinoatrial block, 3rd degree AV block (unless a functioning demand pacemaker is present), a resting heart rate < 60 bpm prior to treatment, severe hepatic impairment, pacemaker dependence (heart rate imposed exclusively by the pacemaker) and concomitant use of strong cytochrome P450 3A4 (CYP3A4) inhibitors.
- **Fetal Toxicity:** Corlanor® may cause fetal toxicity when administered to a pregnant woman.
- **Atrial Fibrillation:** Corlanor® increases the risk of atrial fibrillation. The rate of atrial fibrillation in patients treated with Corlanor® compared to placebo was 5% vs. 3.9% per patient-year, respectively.
- **Bradycardia and Conduction Disturbances:** Bradycardia, sinus arrest and heart block have occurred with Corlanor®. Concurrent use of verapamil or diltiazem also increases Corlanor® exposure and should be avoided. Avoid use of Corlanor® in patients with 2nd degree atrioventricular block unless a functioning demand pacemaker is present.
- **Adverse Reactions:** The most common adverse drug reactions in the SHIFT study occurring in ≥ 1% higher on Corlanor® than placebo were bradycardia (10% vs. 2.2%), hypertension or increased blood pressure (8.9% vs. 7.8%), atrial fibrillation (8.3% vs. 6.6%), and luminous phenomena (phosphenes) or visual brightness (2.8% vs. 0.5%).

Please contact Amgen Medinfo at 800-77-AMGEN (800-772-6436) regarding Corlanor availability or find out more information, including full Prescribing Information and Medication Guide, at www.amgen.com.

About Amgen Cardiovascular
Building on more than three decades of experience in developing biotechnology medicines for patients with serious illnesses, Amgen is dedicated to addressing important scientific questions to advance care and improve the lives of patients with cardiovascular disease, the leading cause of morbidity and mortality worldwide.[6] Amgen's research into cardiovascular disease, and potential treatment options, is part of a growing competency at Amgen that utilizes human genetics to identify and validate certain drug targets. Through its own research and development efforts, as well as partnerships, Amgen is building a robust cardiovascular pipeline consisting of several investigational molecules in an effort to address a number of today's important unmet patient needs, such as high cholesterol and heart failure.

About Amgen
Amgen is committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools like advanced human genetics to unravel the complexities of disease and understand the fundamentals of human biology.

Amgen focuses on areas of high unmet medical need and leverages its biologics manufacturing expertise to strive for solutions that improve health outcomes and dramatically improve people's lives. A biotechnology pioneer since 1980, Amgen has grown to be one of the world's leading independent biotechnology companies, has reached millions of patients around the world and is developing a pipeline of medicines with breakaway potential.

For more information, visit www.amgen.com and follow us on www.twitter.com/amgen.

Forward-Looking Statements
This news release contains forward-looking statements that are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission (SEC) reports filed by Amgen, including Amgen's most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and Form 8-K. Please refer to Amgen's most recent Forms 10-K, 10-Q and 8-K for additional information on the uncertainties and risk factors related to our business. Unless otherwise noted, Amgen is providing this information as of April 15, 2015 and expressly disclaims any duty to update information contained in this news release.

No forward-looking statement can be guaranteed and actual results may differ materially from those we project. Discovery or identification of new product candidates or development of new indications for existing products cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate or development of a new indication for an existing product will be successful and become a commercial product. Further, preclinical results do not guarantee safe and effective performance of product candidates in humans. The complexity of the human body cannot be perfectly, or sometimes, even adequately modeled by computer or cell culture systems or animal models. The length of time that it takes for us to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and we expect similar variability in the future. We develop product candidates internally and through licensing collaborations, partnerships and joint ventures. Product candidates that are derived from relationships may be subject to disputes between the parties or may prove to be not as effective or as safe as we may have believed at the time of entering into such relationship. Also, we or others could identify safety, side effects or manufacturing problems with our products after they are on the market. Our business may be impacted by government investigations, litigation and products liability claims. We depend on third parties for a significant portion of our manufacturing capacity for the supply of certain of our current and future products and limits on supply may constrain sales of certain of our current products and product candidate development.

In addition, sales of our products are affected by the reimbursement policies imposed by third-party payors, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and guideline developments and domestic and international trends

toward managed care and healthcare cost containment as well as U.S. legislation affecting pharmaceutical pricing and reimbursement. Government and others' regulations and reimbursement policies may affect the development, usage and pricing of our products. In addition, we compete with other companies with respect to some of our marketed products as well as for the discovery and development of new products. We believe that some of our newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Our products may compete against products that have lower prices, established reimbursement, superior performance, are easier to administer, or that are otherwise competitive with our products. In addition, while we routinely obtain patents for our products and technology, the protection offered by our patents and patent applications may be challenged, invalidated or circumvented by our competitors and there can be no guarantee of our ability to obtain or maintain patent protection for our products or product candidates. We cannot guarantee that we will be able to produce commercially successful products or maintain the commercial success of our existing products. Our stock price may be affected by actual or perceived market opportunity, competitive position, and success or failure of our products or product candidates. Further, the discovery of significant problems with a product similar to one of our products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on our business and results of operations. Our efforts to integrate the operations of companies we have acquired may not be successful. We may experience difficulties, delays or unexpected costs and not achieve anticipated benefits and savings from our recently announced restructuring plan. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or their ability to pay a dividend or repurchase our common stock.

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