New Analyses Show Payer Utilization Management Criteria Deny Access To PCSK9 Inhibitors For Patients At The Highest Risk For Subsequent Cardiovascular Events

March 9, 2018

Research Presented at American College of Cardiology's 67th Annual Scientific Session Reveals More Than 110,000 Cardiovascular Events a Year Could Occur in High-Risk Patients With Cardiovascular Disease who are Rejected Access Additional Study Calls for Assessment of Utilization Management Processes to Improve Access for Appropriate Patients and Prioritize Patients at the Highest Risk for Subsequent Cardiovascular Events

THOUSAND OAKS, Calif., March 9, 2018 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced data from two new studies exploring barriers to access for PCSK9 inhibitors and the potential consequences of denying coverage for high-risk patients. The studies will be presented at the American College of Cardiology's 67th Annual Scientific Session (ACC.18).

The first study, "Cardiovascular Risk in Patients Denied Access to PCSK9i Therapy," (Abstract #1129-408) found only 35 percent of 3,472 commercially insured and Medicare patients requesting access to a PSCK9 inhibitor were approved by their health plan in 2016. Among the 65 percent of patients who were denied access, the rate of acute cardiovascular (CV) events was higher than the rate in the overall patient population requesting a PCSK9 inhibitor. Acute CV events were defined as heart attack, ischemic stroke, hospitalization for unstable angina or coronary revascularizations.

"Based on the rejection and event rates observed in the 2016 data, we estimate that among appropriate patients prescribed PCSK9 inhibitors, over 110,000 acute cardiovascular events could have occurred in patients rejected access to a PCSK9 inhibitor," said Seth Baum, M.D., president of the American Society for Preventive Cardiology and lead study investigator. "A particular concern is that, among patients who are at an increased risk of subsequent acute cardiovascular events, two out of three were denied access to a PCSK9 inhibitor in 2016."

Another study presented, "Predicting Cardiovascular Risk Using Common Utilization Management Criteria for Proprotein Convertase Subtilisin/Kexin Type 9 Inhibitors in Commercially Insured Patients With Atherosclerotic Cardiovascular Disease," (Abstract #1129-409) showed commercial payer utilization management criteria fail to prioritize patients at the highest risk for CV events. Researchers evaluated data from 2012 to 2013 among 5,276 commercially insured patients with atherosclerotic CV disease. They found that the stringent utilization management criteria used by commercial payers that may delay or deny appropriate treatment for uncontrolled low-density lipoprotein cholesterol (LDL-C) do not identify patients at the greatest risk for further heart attacks, strokes or with the greatest need for coronary revascularizations.

According to 2017 data from Symphony Health, approximately 70 percent of commercial patients prescribed Repatha® (evolocumab) have their prescriptions denied by their insurance provider.[1]

"These data further highlight what we have seen for the past two years and the need for improved access to medications like Repatha that reduce life-changing events, such as heart attacks and strokes, among high-risk cardiovascular patients," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "Clinical data and experience tell us those at highest risk for further cardiovascular events benefit the most from intensive LDL-cholesterol lowering with a PCSK9 inhibitor, like Repatha. We are in active discussions with payers to align on clinically grounded, utilization management policies with the goal of best serving the needs of appropriate patients and ensuring access to Repatha."

Cardiovascular Risk in Patients Denied Access to PCSK9i Therapy (Abstract #1129-408)

An estimated 65 percent of patients requesting PCSK9 inhibitors were denied access and 35 percent were approved. The baseline rate of acute CV events over a six-month follow-up period in patients rejected for a PCSK9 inhibitor was numerically higher (7.29 per 100 patient years), compared to the overall rate of 6.73 per 100 patient years in the patients requesting PCSK9 inhibitors. At the 2016 rejection and event rates, the data suggest that if all appropriate patients were prescribed PCSK9 inhibitors, over 110,000 acute CV events would occur in patients inappropriately rejected.

This retrospective cohort study analyzed data from the QuintilesIMS Formulary Impact Analyzer (FIA) database across 3,472 patients requesting access to Repatha or Praluent® (alirocumab) from January 2016 to December 2016. The mean patient age was 58 years; 56 percent were male and 44 percent were female. Using the International Classification of Diseases, Volume 9 and 10 (ICD-9 and ICD-10) and Current Procedural Terminology (CPT) billing codes, researchers estimated baseline acute CV event rates (defined as heart attack, stroke, hospitalization for unstable angina, and coronary revascularizations) in the six months following a final decision on PCSK9 inhibitor reimbursement and access requests.

Predicting Cardiovascular Risk Using Common Utilization Management Criteria for Proprotein Convertase Subtilisin/Kexin Type 9 Inhibitors in Commercially Insured Patients With Atherosclerotic Cardiovascular Disease (Abstract #1129-409)

This retrospective study used Truven Health MarketScan Commercial Data from Jan. 1, 2012, through Dec. 31, 2015. The study included 5,276 patients aged 18-64 years identified by an LDL-C value ≥70 mg/dL with evidence of atherosclerotic cardiovascular disease (ASCVD), as defined by the 2013 American College of Cardiology/American Heart Association (ACC/AHA) Guidelines and statin use in the prior year.

Patients with ASCVD and LDL-C levels ≥70 mg/dL on statin therapy were followed for 730 days before and after measurement of LDL values. A multivariate analysis evaluated whether certain components of utilization management criteria could be associated with a CV event. Utilization management criteria included current versus prior statin use; none, one, or multiple high intensity statins; or duration of statin and ezetimibe use.

Long-term (≥180 days) statin use and no ezetimibe use trended towards a lower risk of a CV event, whereas using multiple high-intensity statins trended towards a higher risk of having a CV event. The researchers concluded that utilization management criteria related to CV risk could be used to ensure that patients at highest risk have access to PCSK9 inhibitors – which may maximize value to payers.

Repatha is a groundbreaking medicine for high-risk patients who suffer from a combination of high LDL and CV disease, and who continue to struggle

with lowering LDL-C levels despite statin therapy. In December 2017, the U.S. Food and Drug Administration (FDA) approved Repatha as the first PCSK9 inhibitor to prevent heart attacks, strokes and coronary revascularizations in adults with established CV disease. In the Repatha cardiovascular outcomes study (FOURIER), Repatha reduced the risk of heart attack by 27 percent, the risk of stroke by 21 percent and the risk of coronary revascularization by 22 percent on top of best standard of care.[2]

Statistics on Cardiovascular Disease

In the U.S., about 790,000 people have heart attacks each year. Approximately 610,000 of these are first attacks, and 185,000 are recurrent attacks.[3] Another roughly 795,000 people experience a new or recurrent stroke each year in the U.S. Cardiovascular disease is one of the world's most significant public health challenges, leading to a societal cost that exceeds $600 billion annually.[4] LDL-C is recognized as a major and modifiable risk factor for CV disease, but despite treatment with statin therapy, many patients are still unable to reach the recommended LDL goals and are at high risk for CV events.

Repatha Cardiovascular Outcomes (FOURIER) Study Design

FOURIER (Further Cardiovascular OUtcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk), a multinational Phase 3 randomized, double-blind, placebo-controlled trial, is designed to evaluate whether treatment with Repatha in combination with high- or moderate-intensity statin therapy compared to placebo plus statin therapy reduces cardiovascular events. The hard MACE composite endpoint is the time to cardiovascular death, myocardial infarction or stroke (key secondary endpoint). The extended MACE composite endpoint is the time to cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina or coronary revascularization (primary endpoint).

Eligible patients with high cholesterol (LDL-C ≥70 mg/dL or non-high-density lipoprotein cholesterol [non-HDL-C] ≥100 mg/dL) and established CV disease at more than 1,300 study locations around the world were randomized to receive Repatha subcutaneous 140 mg every two weeks or 420 mg monthly plus high- or moderate-intensity effective statin dose; or placebo subcutaneous every two weeks or monthly plus high- to moderate-intensity statin dose. Statin therapy was defined in the protocol as at least atorvastatin 20 mg or equivalent daily with a recommendation for at least atorvastatin 40 mg or equivalent daily where approved. The study was event driven and continued until at least 1,630 patients experienced a key secondary endpoint.

About Repatha® (evolocumab)

Repatha® (evolocumab) is a human monoclonal antibody that inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9). Repatha binds to PCSK9 and inhibits circulating PCSK9 from binding to the low-density lipoprotein (LDL) receptor (LDLR), preventing PCSK9-mediated LDLR degradation and permitting LDLR to recycle back to the liver cell surface. By inhibiting the binding of PCSK9 to LDLR, Repatha increases the number of LDLRs available to clear LDL from the blood, thereby lowering LDL-C levels.[5]

Repatha is approved in more than 50 countries, including the U.S., Japan, Canada and in all 28 countries that are members of the European Union. Applications in other countries are pending.

U.S. Repatha Indication

Repatha is a PCSK9 (proprotein convertase subtilisin kexin type 9) inhibitor antibody indicated:

- to reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease.
- as an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe), for treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia [HeFH]) to reduce low-density lipoprotein cholesterol (LDL-C).
- as an adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) in patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDLC.

The safety and effectiveness of Repatha have not been established in pediatric patients with HoFH who are younger than 13 years old or in pediatric patients with primary hyperlipidemia or HeFH.

Important U.S. Safety Information

Contraindication: Repatha is contraindicated in patients with a history of a serious hypersensitivity reaction to Repatha.

Allergic reactions: Hypersensitivity reactions (e.g. rash, urticaria) have been reported in patients treated with Repatha, including some that led to discontinuation of therapy. If signs or symptoms of serious allergic reactions occur, discontinue treatment with Repatha, treat according to the standard of care, and monitor until signs and symptoms resolve.

Adverse reactions: The most common adverse reactions (>5 percent of Repatha-treated patients and occurring more frequently than placebo) in controlled trials involving patients with primary hyperlipidemia, including HeFH, were: nasopharyngitis, upper respiratory tract infection, influenza, back pain, and injection site reactions.

In a 52-week trial, adverse reactions led to discontinuation of treatment in 2.2 percent of Repatha-treated patients and 1 percent of placebo-treated patients. The most common adverse reaction that led to Repatha treatment discontinuation and occurred at a rate greater than placebo was myalgia (0.3 percent versus 0 percent for Repatha and placebo, respectively).

Adverse reactions from a pool of the 52-week trial and seven 12-week trials: Local injection site reactions occurred in 3.2 percent and 3.0 percent of Repatha-treated and placebo-treated patients, respectively. The most common injection site reactions were erythema, pain, and bruising. The proportions of patients who discontinued treatment due to local injection site reactions in Repatha-treated patients and placebo-treated patients were 0.1 percent and 0 percent, respectively.

Allergic reactions occurred in 5.1 percent and 4.7 percent of Repatha-treated and placebo-treated patients, respectively. The most common allergic reactions were rash (1.0 percent versus 0.5 percent for Repatha and placebo, respectively), eczema (0.4 percent versus 0.2 percent), erythema (0.4 percent versus 0.2 percent), and urticaria (0.4 percent versus 0.1 percent).

The safety profile of Repatha in the cardiovascular outcomes trial was generally consistent with the safety profile in the 12- and 52-week controlled trials involving patients with primary hyperlipidemia, including HeFH. Serious adverse events occurred in 24.8 percent and 24.7 percent of Repatha-treated and placebo-treated patients, respectively. Adverse events led to discontinuation of study treatment in 4.4 percent of patients assigned to Repatha and 4.2 percent assigned to placebo. Common adverse reactions (>5 percent of patients treated with Repatha and occurring more frequently than placebo) included diabetes mellitus (8.8 percent Repatha, 8.2 percent placebo), nasopharyngitis (7.8 percent Repatha, 7.4 percent placebo) and upper respiratory tract infection (5.1 percent Repatha, 4.8 percent placebo). Among the 16,676 patients without diabetes mellitus at baseline, the incidence of new-onset diabetes mellitus during the trial was 8.1 percent in patients assigned to Repatha compared with 7.7 percent in those assigned to placebo.

Homozygous Familial Hypercholesterolemia (HoFH): In 49 patients with homozygous familial hypercholesterolemia studied in a 12-week, double-blind, randomized, placebo-controlled trial, 33 patients received 420 mg of Repatha subcutaneously once monthly. The adverse reactions that occurred in at least 2 (6.1 percent) Repatha-treated patients and more frequently than in placebo-treated patients, included upper respiratory tract infection (9.1 percent versus 6.3 percent), influenza (9.1 percent versus 0 percent), gastroenteritis (6.1 percent versus 0 percent), and nasopharyngitis (6.1 percent versus 0 percent).

Immunogenicity: Repatha is a human monoclonal antibody. As with all therapeutic proteins, there is a potential for immunogenicity with Repatha.

Please contact Amgen Medinfo at 800-77-AMGEN (800-772-6436) or 844-REPATHA (844-737-2842) regarding Repatha® availability or find more information, including full Prescribing Information, at www.amgen.com and www.Repatha.com.

About Amgen in the Cardiovascular Therapeutic Area

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 portfolio consisting of several approved and 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 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 the current expectations and beliefs of Amgen. 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 reports filed by Amgen, including our most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and current reports on Form 8-K. Unless otherwise noted, Amgen is providing this information as of the date of this news release and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

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. Even when clinical trials are successful, regulatory authorities may question the sufficiency for approval of the trial endpoints we have selected. 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, including our devices, after they are on the market.

Our results may be affected by our ability to successfully market both new and existing products domestically and internationally, clinical and regulatory developments involving current and future products, sales growth of recently launched products, competition from other products including biosimilars, difficulties or delays in manufacturing our products and global economic conditions. In addition, sales of our products are affected by pricing pressure, political and public scrutiny and reimbursement policies imposed by third-party payers, 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. Furthermore, our research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. Our business may be impacted by government investigations,

litigation and product liability claims. In addition, our business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. If we fail to meet the compliance obligations in the corporate integrity agreement between us and the U.S. government, we could become subject to significant sanctions. Further, 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, or we may fail to prevail in present and future intellectual property litigation. We perform a substantial amount of our commercial manufacturing activities at a few key facilities, including in Puerto Rico, and also depend on third parties for a portion of our manufacturing activities, and limits on supply may constrain sales of certain of our current products and product candidate development. In addition, we compete with other companies with respect to many of our marketed products as well as for the discovery and development of new products. Further, some raw materials, medical devices and component parts for our products are supplied by sole third-party suppliers. Certain of our distributors, customers and payers have substantial purchasing leverage in their dealings with us. 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 acquire other companies or products and to integrate the operations of companies we have acquired may not be successful. A breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of our systems and our data. Our stock price is volatile and may be affected by a number of events. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or our ability to pay a dividend or repurchase our common stock. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all.

CONTACT: Amgen, Thousand Oaks
Kristen Davis, 805-447-3008 (Media)
Kristen Neese, 805-313-8267 (Media)
Arvind Sood, 805-447-1060 (Investors)

References

1. Symphony health solutions: New Claims Only. Life Cycle + CLM Cycle Claims. Claims file dated 2/15
2. Sabatine MS, Giugliano RP, Keech AC, et al, for the FOURIER Steering Committee and Investigators. *N Engl J Med*. Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease. 2017;376:1713-22.
3. American Heart Association. Heart Disease and Stroke Statistics 2017 At A Glance. https://www.heart.org/idc/groups/ahamah-public/@wcm/@sop/@smd/documents/downloadable/ucm_491265.pdf. Accessed February 26, 2018.
4. Bhatt, DL et al. Comparative Determinants of 4-Year Cardiovascular Event Rates in Stable Outpatients at Risk of or With Atherosclerosis. *Journal of the American Medical Association.* September 22/29, 2010 – Vol 304, No. 12.
5. Repatha® U.S. Prescribing Information. Amgen.
6. World Health Organization. Cardiovascular diseases (CVDs) fact sheet. http://www.who.int/mediacentre/factsheets/fs317/en/. Accessed October 30, 2017.

View original content with multimedia:http://www.prnewswire.com/news-releases/new-analyses-show-payer-utilization-management-criteria-deny-access-to-pcsk9-inhibitors-for-patients-at-the-highest-risk-for-subsequent-cardiovascular-events-300611399.html

SOURCE Amgen