Pfizer Logo

Merck and Pfizer's SGLT2 Inhibitor STEGLATROTM (ertugliflozin) Meets Primary Endpoint in VERTIS CV Trial for Patients with Type 2 Diabetes and Atherosclerotic Cardiovascular Disease

Tuesday, June 16, 2020 - 01:11pm

Results Presented at the American Diabetes Association's Virtual 80th Scientific Sessions

KENILWORTH, N.J. & NEW YORK – June 16, 2020 – Merck (NYSE: MRK), known as MSD outside the United States and Canada, and Pfizer Inc. (NYSE:PFE), today announced the presentation of results from the Phase 3 VERTIS CV cardiovascular (CV) outcomes trial that evaluated STEGLATRO (ertugliflozin), an oral sodium-glucose cotransporter 2 (SGLT2) inhibitor, versus placebo, added to background standard of care treatment, in more than 8,200 patients with type 2 diabetes and atherosclerotic CV disease across 531 centers in 34 countries. The study met the primary endpoint of non-inferiority on major adverse CV events (MACE), which is composed of a composite of CV death, nonfatal myocardial infarction or nonfatal stroke, compared to placebo.

"The VERTIS CV results add to the growing body of evidence regarding the clinical profile of ertugliflozin, including its safety in patients with a history of cardiovascular disease," said Dr. Christopher P. Cannon, cardiologist at Brigham and Women's Hospital and Professor of Medicine at Harvard Medical School, the study's lead author. "Although not a part of the hierarchical testing sequence, the results indicated the potential of ertugliflozin to reduce the risk of hospitalization for heart failure in patients with type 2 diabetes and established cardiovascular disease."

Overall, the primary MACE outcome was reported in 11.9% (n=653) of patients treated with STEGLATRO (5 mg and 15 mg doses), compared with 11.9% (n=327) of patients treated with placebo (HR=0.97; 95.6% CI [0.85-1.11]; $p<0.001$ for non-inferiority). The key secondary endpoints of superiority for ertugliflozin versus placebo were not met. These key secondary endpoints included: time to the first occurrence of the composite of CV death or hospitalization for heart failure (HHF), time to CV death alone and time to the first occurrence of the composite of renal death, dialysis/transplant or doubling of serum creatinine. The pre-specified endpoint of HHF, while not a part of the hierarchical testing sequence, showed a 30% reduction in the risk of HHF for ertugliflozin versus placebo (2.5% vs. 3.6%; HR=0.70; 95% CI [0.54-0.90]).

"The results of the VERTIS CV trial are a significant and important addition to the overall evidence for the cardiovascular safety profile of ertugliflozin," said Dr. Sam Engel, associate vice president, Merck clinical research, diabetes and endocrinology.

“We sincerely thank the patients and investigators for their participation in the VERTIS CV study and commitment to the clinical evaluation of ertugliflozin,” said Dr. James Rusnak, senior vice president and chief development officer, internal medicine, Pfizer Global Product Development.

The safety profile of STEGLATRO was consistent with that reported in previous studies. STEGLATRO is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

The results of VERTIS CV trial were presented today at the American Diabetes Association’s virtual 80th Scientific Sessions.

About VERTIS CV

The VERTIS CV (NCT01986881) trial is a multicenter, prospective, randomized, eventdriven trial in patients with type 2 diabetes and atherosclerotic CV disease. The primary endpoint of the study was non-inferiority on MACE, a composite of CV death, nonfatal myocardial infarction or nonfatal stroke, compared to placebo. The study was designed to evaluate CV safety (non-inferiority) to satisfy the U.S. Food and Drug Administration (FDA) guidance on demonstration of CV safety for novel anti-hyperglycemic agents in the pre-approval and post-approval time periods. The two doses of ertugliflozin were pre-specified to be pooled for assessment of cardiovascular and renal outcomes.

VERTIS CV enrolled 8,246 adults (40 years of age or older) with type 2 diabetes and atherosclerotic CV disease, including patients 65 years of age or older and those with renal impairment or heart failure. More than 99% of patients had established CV disease. Coronaryartery disease was reported in 75.9% of patients, cerebrovascular disease in 22.9%, peripheral arterial disease in 18.7%, and history of heart failure in 23.7%. Enrolled patients were randomized to receive ertugliflozin 5 mg (n=2,752), ertugliflozin 15 mg (n=2,747) or placebo (n=2,747) once-daily, added to background standard of care treatment at 531 centers in 34 countries. The mean duration of follow-up was 3.5 years and the mean study drug treatment period was 2.9 years for ertugliflozin and 2.8 years for placebo.

Key secondary endpoints included superiority versus placebo on time to the composite of CV death or HHF, CV death alone and the composite of renal death, dialysis/transplant or doubling of serum creatinine. A hierarchical testing sequence was used across the primary and key secondary hypotheses for the pooled ertugliflozin group versus placebo. Other secondary efficacy outcomes that were not part of the hierarchical statistical testing sequence, but were pre-specified in the protocol, included time to first occurrence of: MACE plus (MACE or hospitalization for unstable angina), fatal or nonfatal myocardial infarction, fatal or nonfatal stroke, hospitalization for heart failure, individual components of MACE and all-cause death.

Key Secondary Outcomes

	Ertugliflozin % (#)	**Placebo % (#)**	**Hazard ratio**
Composite of CV death or hospitalization for heart failure	8.1% 444	9.1% 250	0.88; 95.8% CI 0.75-1.03; p=0.11 for superiority
CV death*	6.2% 341	6.7% 184	0.92; 95.8% CI 0.77-1.11
Composite of renal death, dialysis/transplant or doubling of serum creatinine*	3.2% 175	3.9% 108	0.81; 95.8% CI 0.63-1.04

* Statistical testing not performed

The overall incidences of serious adverse events were similar for the ertugliflozin 5 mg (34.9%), ertugliflozin 15 mg (34.1%) and placebo (36.1%) groups. Urinary tract infection occurred in 12.2% and 12.0% of patients in the ertugliflozin 5 mg and 15 mg groups, respectively, and 10.2% in the placebo group ($p<0.05$ for the comparison with placebo). Amputation occurred in 2.1% and 2.0% of patients in the ertugliflozin 5 mg and 15 mg groups, respectively, and 1.6% in the placebo group. Diabetic ketoacidosis occurred in 0.3% and 0.4% of patients in the ertugliflozin 5 mg and 15 mg groups, respectively, and 0.1% in the placebo group. There were no cases of Fournier's gangrene in patients treated with ertugliflozin or placebo and no differences in the incidence of acute kidney injury, hypovolemia, fractures, or symptomatic hypoglycemia.

Indications and Usage for STEGLATRO (ertugliflozin)

STEGLATRO (ertugliflozin) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. STEGLATRO is not recommended in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

Selected Safety Information for STEGLATRO (ertugliflozin)

Contraindications: STEGLATRO is contraindicated in patients with severe renal impairment, end-stage renal disease, or on dialysis, and/or a history of a serious hypersensitivity reaction to ertugliflozin.

Hypotension: STEGLATRO causes intravascular volume contraction. Symptomatic hypotension may occur after initiating STEGLATRO, particularly in patients with impaired renal function (estimated glomerular filtration rate [eGFR] less than 60 mL/min/1.73 m2), elderly patients (?65 years), patients with low systolic blood pressure, or patients on diuretics. Before initiating STEGLATRO, volume status should be assessed and corrected if indicated. Monitor for signs and symptoms after initiating therapy.

Ketoacidosis: Ketoacidosis, a serious life-threatening condition requiring urgent hospitalization, has been reported in patients with type 1 and type 2 diabetes receiving sodium glucose co-transporter 2 inhibitors (SGLT2is), including STEGLATRO. Some cases were fatal. Assess patients with signs and symptoms of metabolic acidosis for ketoacidosis, regardless of blood glucose level. If ketoacidosis is suspected, discontinue STEGLATRO, evaluate, treat promptly, and ensure risks for ketoacidosis are resolved prior to restarting. Before initiating, consider risk factors. Consider temporarily discontinuing STEGLATRO for at least 4 days prior to scheduled surgery. Monitor patients and temporarily discontinue STEGLATRO in clinical situations known to predispose to ketoacidosis (eg, prolonged fasting due to acute illness or post-surgery). Educate patients on the signs and symptoms of ketoacidosis. Instruct patients to discontinue STEGLATRO and seek medical attention immediately if signs and symptoms occur.

Acute Kidney Injury and Impairment in Renal Function: STEGLATRO causes intravascular volume contraction and can cause renal impairment. There have been postmarketing reports of acute kidney injury, some requiring hospitalization and dialysis, in patients receiving SGLT2 inhibitors. Before initiating STEGLATRO, consider factors that may predispose patients to acute kidney injury. Consider temporarily discontinuing STEGLATRO in any setting of reduced oral intake or fluid losses; monitor patients for signs and symptoms of acute kidney injury. If acute kidney injury occurs, discontinue STEGLATRO promptly and institute treatment.

STEGLATRO increases serum creatinine and decreases eGFR. Patients with moderate renal impairment (eGFR 30 to less than 60 mL/min/1.73 m2) may be more susceptible to these changes. Renal function abnormalities can occur after initiating STEGLATRO. Renal function should be evaluated prior to initiating

STEGLATRO and periodically thereafter. Use of STEGLATRO is not recommended when eGFR is persistently between 30 and less than 60 mL/min/1.73 m2 and is contraindicated in patients with an eGFR less than 30 mL/min/1.73 m2 .

Urosepsis and Pyelonephritis: There have been postmarketing reports of serious urinary tract infections, including urosepsis and pyelonephritis, requiring hospitalization in patients receiving SGLT2 inhibitors. Cases of pyelonephritis also have been reported in patients treated with STEGLATRO in clinical trials. Treatment with SGLT2 inhibitors increases the risk for urinary tract infections. Evaluate patients for signs and symptoms of urinary tract infections and treat promptly, if indicated.

Lower Limb Amputations: An increased risk for lower limb amputation has been observed in clinical studies with another SGLT2 inhibitor. Across seven Phase 3 clinical trials with STEGLATRO, nontraumatic lower limb amputations were reported in 1 (0.1%) patient in the comparator group, 3 (0.2%) patients in the STEGLATRO 5-mg group, and 8 (0.5%) patients in the STEGLATRO 15-mg group. A causal association between STEGLATRO and lower limb amputation has not been definitively established. Before initiating STEGLATRO, consider factors that may predispose patients to the need for amputations. Monitor patients and discontinue STEGLATRO if complications occur. Counsel patients about the importance of routine preventative foot care.

Hypoglycemia With Concomitant Use With Insulin and Insulin Secretagogues: Insulin and insulin secretagogues (eg, sulfonylurea) are known to cause hypoglycemia. STEGLATRO may increase the risk of hypoglycemia when used in combination with insulin and/or an insulin secretagogue. Therefore, a lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when used in combination with STEGLATRO.

Necrotizing Fasciitis of the Perineum (Fournier's Gangrene): A rare but serious and lifethreatening necrotizing infection requiring urgent surgical intervention has been reported in postmarketing surveillance in females and males with diabetes mellitus receiving SGLT2 inhibitors. Serious outcomes have included hospitalization, multiple surgeries, and death. Patients treated with STEGLATRO presenting with pain or tenderness, erythema, or swelling in the genital or perineal area, along with fever or malaise, should be assessed for necrotizing fasciitis. If suspected, start treatment immediately with broad-spectrum antibiotics and, if necessary, surgical debridement. Discontinue STEGLATRO, closely monitor blood glucose levels, and provide appropriate alternative therapy for glycemic control.

Genital Mycotic Infections: STEGLATRO increases the risk of genital mycotic infections. Patients who have a history of genital mycotic infections or who are uncircumcised are more likely to develop genital mycotic infections. Monitor and treat appropriately.

Increases in Low-Density Lipoprotein Cholesterol (LDL-C): Dose-related increases in LDL-C can occur with STEGLATRO. Monitor and treat as appropriate.

Macrovascular Outcomes: There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with STEGLATRO.

The most common adverse reactions associated with STEGLATRO (?5%) were female genital mycotic infections.

About Merck

For more than 125 years, Merck, known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases in pursuit of our mission to save and improve lives. We demonstrate our commitment to patients and population health by increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to prevent and treat diseases that threaten people and animals – including cancer, infectious diseases such as HIV and Ebola, and emerging animal diseases – as we aspire to be the premier research-intensive biopharmaceutical company in the world. For more information, visit www.merck.com and connect with us on Twitter, Facebook, Instagram, YouTube and LinkedIn.

Pfizer Inc.: Breakthroughs that change patients' lives

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products, including innovative medicines and vaccines. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us on www.pfizer.com and follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of the recent global outbreak of novel coronavirus disease (COVID-19); the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2019 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

###

Pfizer Disclosure Notice: The information contained in this release is current as of June 16, 2020. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments. This release contains forward-looking information about STEGLATRO (ertugliflozin), including its potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of STEGLATRO; the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when drug applications may be filed in any other jurisdictions for any potential indication for STEGLATRO; whether and when any such other applications for STEGLATRO that may be pending or filed may be approved by regulatory authorities, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of STEGLATRO; competitive developments; and the impact of COVID-19 on our business, operations and financial results. A further description of risks and uncertainties can be found in Pfizer’s Annual Report on Form 10-K for the fiscal year ended December 31, 2019 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned “Risk Factors” and "Forward-Looking Information and Factors That May Affect Future Results”, as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com. Please see Prescribing Information for STEGLATRO at http://www.merck.com/product/usa/pi_circulars/s/steglatro/steglatro_pi.pdf and Patient Information for STEGLATRO at http://www.merck.com/product/usa/pi_circulars/s/steglatro/steglatro_mg.pdf FOR IMMEDIATE RELEASE Merck Media Contacts: Pamela Eisele (267) 305-3558 Sienna Choi (908) 740-1256 Merck Investor Contacts: Peter Dannenbaum (908) 740-1037 Michael DeCarbo (908) 740-1807 Pfizer Media Contact: Steven Danehy (212) 733-1538 Pfizer Investor Contact: Ryan Crowe (212) 733-8160