FDA grants Fast Track designation for FARXIGA in chronic kidney disease

(WILMINGTON, Del., August 27, 2019) – AstraZeneca today announced that the US Food and Drug Administration (FDA) has granted Fast Track designation for the development of FARXIGA (dapagliflozin) to delay the progression of renal failure and prevent cardiovascular (CV) and renal death in patients with chronic kidney disease (CKD).

The FDA's Fast Track program is designed to accelerate the development and review of new medicines for the treatment of serious conditions where there is an unmet treatment need. The designation was assigned to CKD patients with and without type 2 diabetes (T2D).

Mene Pangalos, Executive Vice President, BioPharmaceuticals R&D, said: "Chronic kidney disease affects an estimated 37 million people in the US, and is often associated with an increased risk of heart disease and stroke. This Fast Track designation is an important step towards more quickly addressing unmet treatment needs in chronic kidney disease, and we will work closely with the FDA to explore the potential for FARXIGA to improve outcomes for these patients."

The Phase III DAPA-CKD clinical trial is currently underway to evaluate the effect of FARXIGA on renal outcomes and CV mortality in patients with CKD with and without T2D versus placebo, on top of standard of care.

Indication and Limitations of Use for FARXIGA® (dapagliflozin) tablets

FARXIGA is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

FARXIGA is not recommended for patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

Important Safety Information for FARXIGA® (dapagliflozin) tablets

Contraindications

- Prior serious hypersensitivity reaction to FARXIGA
- Severe renal impairment (eGFR <30 mL/min/1.73 m^2), end-stage renal disease, or patients on dialysis

Warnings and Precautions

- **Hypotension:** FARXIGA causes intravascular volume contraction, and symptomatic hypotension can occur. Assess and correct volume status before initiating FARXIGA in patients with impaired renal function, elderly patients, or patients on loop diuretics. Monitor for hypotension

- **Ketoacidosis** has been reported in patients with type 1 and type 2 diabetes receiving FARXIGA. Some cases were fatal. Assess patients who present with signs and symptoms of metabolic acidosis for ketoacidosis, regardless of blood glucose level. If suspected, discontinue FARXIGA, evaluate and treat promptly. Before initiating FARXIGA, consider risk factors for ketoacidosis. Patients on FARXIGA may require monitoring and temporary discontinuation in situations known to predispose to ketoacidosis

- **Acute Kidney Injury and Impairment in Renal Function:** FARXIGA causes intravascular volume contraction and renal impairment, with reports of acute kidney injury requiring hospitalization and dialysis. Consider temporarily discontinuing in settings of reduced oral intake or fluid losses. If acute kidney injury occurs, discontinue and promptly treat.

  FARXIGA increases serum creatinine and decreases eGFR. Elderly patients and patients with impaired renal function may be more susceptible to these changes. Before initiating FARXIGA, evaluate renal function and monitor periodically. FARXIGA is not recommended when the eGFR is <45 mL/min/1.73 m^2

- **Urosepsis and Pyelonephritis:** SGLT2 inhibitors increase the risk for urinary tract infections [UTIs] and serious UTIs have been reported with FARXIGA. Evaluate for signs and symptoms of UTIs and treat promptly

- **Hypoglycemia:** FARXIGA can increase the risk of hypoglycemia when coadministered with insulin and insulin secretagogues. Consider lowering the dose of these agents when coadministered with FARXIGA

- **Necrotizing Fasciitis of the Perineum (Fournier's Gangrene):** Rare but serious, life-threatening cases have been reported in patients receiving SGLT2 inhibitors including FARXIGA. Cases have been reported in females and males. Serious outcomes have included hospitalization, surgeries, and death. Assess patients presenting with pain or tenderness, erythema, swelling in the genital or perineal area, along with fever or malaise. If suspected, institute prompt treatment and discontinue FARXIGA.

- **Genital Mycotic Infections:** FARXIGA increases the risk of genital mycotic infections, particularly in patients with prior genital mycotic infections. Monitor and treat appropriately

- **Increases in Low-Density Lipoprotein Cholesterol (LDL-C)** occur with FARXIGA. Monitor LDL-C and treat per standard of care

- **Bladder cancer**: An imbalance in bladder cancers was observed in clinical trials. There were too few cases to determine whether the emergence of these events is related to FARXIGA, and insufficient data to determine whether FARXIGA has an effect on pre-existing bladder tumors. FARXIGA should not be used in patients with active bladder cancer. Use with caution in patients with a history of bladder cancer

- **Macrovascular Outcomes:** There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with FARXIGA

Adverse Reactions
In a pool of 12 placebo-controlled studies, the most common adverse reactions (≥5%) associated with FARXIGA 5 mg, 10 mg, and placebo respectively were female genital mycotic infections (8.4% vs 6.9% vs 1.5%), nasopharyngitis (6.6% vs 6.3% vs 6.2%), and urinary tract infections (5.7% vs 4.3% vs 3.7%).

Use in Specific Populations

- **Pregnancy:** Advise females of potential risk to a fetus especially during the second and third trimesters.
- **Lactation:** FARXIGA is not recommended when breastfeeding.

Please see accompanying US Full Prescribing Information and Medication Guide for FARXIGA.

– ENDS –

NOTES TO EDITORS

About chronic kidney disease
CKD is a serious, progressive condition defined by decreased kidney function (shown by reduced estimated glomerular filtration rate (eGFR), markers of kidney damage, or both, for at least three months.[1] The most common causes of CKD are diabetes and hypertension.[1] CKD affects an estimated 37 million adults in the US.[2]

CKD is associated with increased risk of therapy-resistant hypertension,[3] chronic fluid overload,[2] heart failure,[4] and CV and all-cause death.[5,6] In its most severe form, known as end-stage renal disease (ESRD), kidney damage and deterioration of kidney function have progressed to the stage where dialysis or kidney transplantation are required.[2] More than half of all deaths among patients with ESRD are from CV causes.[7]

About the DapaCare Clinical Program
AstraZeneca is taking a holistic, patient-centric approach to disease management by addressing the underlying morbidity, mortality and organ damage associated with cardiovascular (CV), metabolic and renal diseases. Due to the interconnectivity of these diseases, AstraZeneca has developed the DapaCare clinical program to explore the CV and renal profile of FARXIGA in people with and without type 2 diabetes. The clinical program will enroll nearly 30,000 patients in randomized clinical trials and is supported by a multinational real-world evidence study. DapaCare will generate data across a spectrum of people with established CV disease, CV risk factors and varying stages of renal disease, both with and without type 2 diabetes, providing healthcare providers with evidence needed to improve patient outcomes.

FARXIGA is also being developed for patients with heart failure in the DELIVER (HFpEF) and DETERMINE (HFrEF and HFpEF) trials, in addition to chronic kidney disease in the DAPA-CKD trial. DapaCare underscores our commitment to following the science by pursuing a holistic patient approach to address the multiple risk factors associated with CV,

renal and metabolic diseases. FARXIGA is not indicated to reduce the risk of heart failure, CV death or kidney disease.

About AstraZeneca in CV, Renal & Metabolism (CVMD)
CV, renal and metabolism together form one of AstraZeneca's main therapy areas and a key growth driver for the Company. By following the science to understand more clearly the underlying links between the heart, kidneys and pancreas, AstraZeneca is investing in a portfolio of medicines to protect organs and improve outcomes by slowing disease progression, reducing risks and tackling co-morbidities. Our ambition is to modify or halt the natural course of CVMD diseases and potentially regenerate organs and restore function, by continuing to deliver transformative science that improves treatment practices and CV health for millions of patients worldwide.

About AstraZeneca
AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialization of prescription medicines, primarily for the treatment of diseases in three therapy areas - Oncology, Cardiovascular, Renal & Metabolism and Respiratory. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information, please visit www.astrazeneca-us.com and follow us on Twitter @AstraZenecaUS.

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