Head-to-Head Study Finds BRENZAVVY® (bexagliflozin) Non-Inferior to Dapagliflozin in Chinese Patients With Type 2 Diabetes

-- Research Adds to Evidence Showing BRENZAVVY's Similarity to Other SGLT2 Inhibitors --

Marlborough, MA – April 12, 2024 – TheracosBio today announced the publication of a study titled "Efficacy and safety of bexagliflozin compared with dapagliflozin as an adjunct to metformin in Chinese patients with type 2 diabetes mellitus: a 24-week, randomized, double-blind, active-controlled, phase 3 trial" in *Journal of Diabetes*. The study results demonstrated the noninferiority of BRENZAVVY® (bexagliflozin) to dapagliflozin, marketed as Farxiga in the United States, in patients with type 2 diabetes mellitus.

BRENZAVVY is an FDA-approved oral sodium-glucose cotransporter 2 (SGLT2) inhibitor indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. BRENZAVVY is not recommended for use to improve glycemic control in patients with type 1 diabetes mellitus.

The randomized, double-blind, active-controlled trial enrolled 406 patients with type 2 diabetes mellitus at sites in China. It successfully met its primary endpoint of noninferiority in HbA_{1c} levels.

Treatment with BRENZAVVY as an adjunct to metformin showed the following results compared to dapagliflozin:

- BRENZAVVY treatment was noninferior to dapagliflozin. The change in HbA_{1c} from baseline to week 24 was -1.08% in the BRENZAVVY arm and -1.10% in the dapagliflozin arm.
- Significant changes from baseline to week 24 in fasting plasma glucose were observed in the BRENZAVVY arm (-1.95 mmol L^{-1} (-35.1 mg dL^{-1})) and in the dapagliflozin arm (-1.87 mmol L^{-1} (-33.17 mg dL^{-1})).

- BRENZAVVY or dapagliflozin treatment decreased body mass in patients from baseline to week 24. The change from baseline body mass in the BRENZAVVY arm was -2.52 kg (5.56 lb) compared to -2.2 kg (4.89 lb) in the dapagliflozin arm.
- Systolic blood pressure also decreased from baseline to week 24 in patients treated with BRENZAVVY or dapagliflozin. The change in systolic blood pressure in the BRENZAVVY arm was -6.4 mm Hg whereas patients in the dapagliflozin arm observed a change of -6.3 mm Hg.

In addition to other measures of metabolic health, the study also assessed safety showing the number of patients that experienced adverse events was comparable between the BRENZAVVY and dapagliflozin arms.

“The results of the study comparing the clinical activity of two different medications within the same class of diabetes medications should be good news to all physicians, nurses, and pharmacists who manage type 2 diabetes in clinical practice. The data demonstrates that Brenzavvy’s clinical activity is indistinguishable from the metabolic effects and safety of dapagliflozin, the most commonly prescribed diabetes medication in the same broad category of medications known as sodium-glucose cotransporter 2 inhibitors,” said J. Paul Lock, MD, co-author of the publication, medical monitor at TheracosBio, and endocrinologist at MetroWest Medical Center, Framingham, MA.

“In addition, healthcare professionals selecting effective medical resources for the treatment of individual patients will be buoyed by the availability of Brenzavvy as an effective and truly affordable alternative for diabetes management because of the favorable price structuring of Brenzavvy. This is a welcome event for real-world physicians.”

The study was performed by clinicians from several Chinese hospitals with guidance from researchers affiliated with TheracosBio and Newsoara Biopharma Co., Ltd., which has licensed bexagliflozin in China.

“It is important for patients with diabetes to have affordable treatment options such as BRENZAVVY to control their disease. We do not think that

patients should have to compromise on efficacy or safety when they receive a more affordable option," said TheracosBio CEO Brian Connelly. "This head-to-head study offers additional evidence that BRENZAVVY-treated patients with type 2 diabetes see metabolic outcomes similar to those with other SGLT2 inhibitors."

In the United States, BRENZAVVY is sold at a simple, low cash-pay price through a network of pharmacies. Patients prescribed BRENZAVVY often do not have insurance, making the medicine affordable for those without insurance and, for those who are insured, BRENZAVVY avoids insurance-plan hurdles that impact the ability of patients to start and stay on therapy.

BRENZAVVY is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. BRENZAVVY is not recommended for use to improve glycemic control in patients with type 1 diabetes mellitus. Phase 3 clinical studies have shown BRENZAVVY significantly reduces hemoglobin A1c and fasting blood sugar after 24 weeks, either as a monotherapy, in combination with metformin, or as an add-on to standard-of-care treatment consisting of a variety of regimens, including metformin, sulfonylureas, insulin, DPP4 inhibitors or combinations of these agents. Although BRENZAVVY is not approved for weight or blood pressure reduction, modest decreases in both weight and blood pressure have been observed in the clinical program.

BRENZAVVY is available as 20 mg oral tablets recommended to be taken once daily, in the morning with or without food. BRENZAVVY is contraindicated in patients who are hypersensitive to bexagliflozin or any other ingredient in the BRENZAVVY tablet. The most common side effects of taking BRENZAVVY include female genital mycotic infections, urinary tract infections, and changes in urination, but more serious side effects are possible (see below, Important Safety Information about BRENZAVVY).

BRENZAVVY treatment can be initiated in adults with type 2 diabetes with an estimated glomerular filtration rate (eGFR) greater than or equal to 30 mL/min/1.73 m^2. Patients with eGFR between 30 and 59 mL/min/1.73 m^2 are said to be in stage 3 chronic kidney disease. BRENZAVVY was the first SGLT2

inhibitor shown in a randomized, controlled clinical trial to be effective for glycemic control in adults with type 2 diabetes and stage 3 (3a + 3b) chronic kidney disease.

To learn more about BRENZAVVY and for full prescribing information visit https://www.brenzavvy.com. To report suspected adverse reactions, contact TheracosBio at 1-855-BRENZAVVY (1-855-273-6928) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Important Safety Information about BRENZAVVY

Limitation of Use: BRENZAVVY (bexagliflozin) is not recommended for use to improve glycemic control in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.

Contraindications
BRENZAVVY is contraindicated in patients with hypersensitivity to bexagliflozin or any excipient in BRENZAVVY. Anaphylaxis and angioedema have been reported with sodium-glucose co-transporter 2 (SGLT2) inhibitors.

Warnings and Precautions

Diabetic Ketoacidosis in Patients with Type 1 Diabetes Mellitus and Other Ketoacidosis
BRENZAVVY increases the risk of life-threatening ketoacidosis in patients with type 1 diabetes. Type 2 diabetes and pancreatic disorders are also risk factors for ketoacidosis and fatal events of ketoacidosis have been reported in patients with type 2 diabetes using SGLT2 inhibitors. Precipitating conditions for diabetic ketoacidosis or other ketoacidosis include under-insulinization due to insulin dose reduction or missed insulin doses, acute febrile illness, reduced caloric intake, ketogenic diet, surgery, volume depletion, and alcohol abuse. Signs and symptoms of diabetic ketoacidosis are consistent with dehydration and severe metabolic acidosis and include nausea, vomiting, abdominal pain, generalized malaise, and shortness of breath. Assess patients who present with signs and symptoms of metabolic

ketoacidosis, regardless of blood glucose levels. If suspected, discontinue BRENZAVVY, treat promptly and monitor for resolution before restarting. Consider ketone monitoring in patients with type 1 diabetes mellitus as well as in others at risk for ketoacidosis. Withhold BRENZAVVY in clinical situations known to predispose to ketoacidosis and resume when clinically stable. Educate all patients on the signs and symptoms of ketoacidosis and instruct patients to discontinue BRENZAVVY and seek medical attention immediately if signs and symptoms occur.

Lower Limb Amputation

Lower limb amputations have been observed in patients treated with BRENZAVVY in a study of patients with type 2 diabetes who had either established cardiovascular disease (CVD) or were at risk for CVD. Of the 23 BRENZAVVY-treated patients who had amputations, 15 were amputations of the toe and midfoot and 8 were amputations above and below the knee. Some patients had multiple amputations. Lower limb infections, gangrene, ischemia, and osteomyelitis were the most common precipitating medical events leading to the need for an amputation. The risk of amputation was highest in patients with a baseline history of prior amputation, peripheral vascular disease, and neuropathy.

Before initiating BRENZAVVY, consider factors in the patient's history that may predispose to the need for amputations, such as a history of prior amputation, peripheral vascular disease, neuropathy, and diabetic foot ulcers. Counsel patients receiving BRENZAVVY about the importance of routine preventative foot care and monitor for signs and symptoms of diabetic foot infection (including osteomyelitis), new pain or tenderness, sores or ulcers involving the lower limbs, and institute appropriate treatment.

Volume Depletion

BRENZAVVY can cause intravascular volume contraction which may sometimes manifest as symptomatic hypotension or acute transient changes in creatinine. Acute kidney injury requiring hospitalization and dialysis has been reported in patients with type 2 diabetes receiving SGLT2 inhibitors. Before initiating, assess volume status and renal function in patients with impaired renal function (eGFR less than 60 mL/min/1.73 m^2), elderly

patients, patients with low systolic blood pressure, or patients on loop diuretics. In patients with volume depletion, correct this condition. After initiating, monitor for signs and symptoms of volume depletion and renal function.

Urosepsis and Pyelonephritis
Serious urinary tract infections including urosepsis and pyelonephritis requiring hospitalization have been identified in patients receiving SGLT2 inhibitors, including BRENZAVVY. Treatment with BRENZAVVY increases the risk for urinary tract infections. Evaluate patients for signs and symptoms of urinary tract infections and treat them promptly.

Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues
Insulin and insulin secretagogues (e.g., sulfonylureas) are known to cause hypoglycemia. BRENZAVVY may increase the risk of hypoglycemia when used in combination with insulin and/or an insulin secretagogue. A lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when used in combination with BRENZAVVY.

Necrotizing Fasciitis of the Perineum (Fournier's Gangrene)
Serious, life-threatening cases requiring urgent surgical intervention have been identified in postmarketing surveillance in both males and females with diabetes mellitus receiving SGLT2 inhibitors. Serious outcomes have included hospitalization, multiple surgeries, and death. Assess patients presenting with pain or tenderness, erythema, or swelling in the genital or perineal areas, along with fever or malaise. If suspected, start treatment, and discontinue BRENZAVVY.
Genital Mycotic Infections
BRENZAVVY 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.

MOST COMMON ADVERSE REACTIONS (>5%): Female genital mycotic infections, urinary tract infection and increased urination.

USE IN SPECIFIC POPULATIONS

- Pregnancy: BRENZAVVY is not recommended during the second and third trimesters.
- Lactation: BRENZAVVY is not recommended when breastfeeding.
- Geriatric patients: There is a higher incidence of adverse reactions related to volume depletion.
- Renal Impairment: There is a higher incidence of adverse reactions related to reduced renal function.
- Hepatic Impairment: BRENZAVVY is not recommended for patients with severe hepatic impairment.

DRUG INTERACTIONS:

Inducers of UGT1A9 could result in more rapid clearance of BRENZAVVY by metabolism. Doses of insulin and sulfonylureas may need to be reduced to offset the action of BRENZAVVY. The safety of BRENZAVVY is compromised when it is coupled with insulin or an insulin secretagogue (sulfonylureas and meglitinides – the latter rarely used in the US). Lithium carbonate is used as a mood stabilizer in bipolar disorder. Lithium ions might be preferentially (compared to sodium ions) taken up with glucose in the kidney. Empirical evidence has shown that lithium levels can be lower when SGLT2 inhibitors are administered. SGLT2 inhibitors produce pronounced glucosuria, which makes urine testing for glucose diagnostically useless. Measurements of 1,5 anhydroglucitol are also compromised.

For additional important safety information about BRENZAVVY, please see the full Prescribing Information.

About TheracosBio

TheracosBio develops novel therapeutics for diseases with significant societal impact. The mission of TheracosBio is to expand access to new medications for patients with common diseases.

Media Contact

Brian Reid for TheracosBio
brian@reidstrategic.com