TheracosBio Announces FDA Approval of Brenzavvy™ (bexagliflozin) for the Treatment of Adults with Type 2 Diabetes

Once-daily, oral SGLT2 inhibitor shown to reduce blood sugar and improve glycemic control as an adjunct to diet and exercise

Marlborough, MA – January 23, 2023 – TheracosBio today announced that the U.S. Food and Drug Administration (FDA) has approved Brenzavvy™ (bexagliflozin), an oral sodium-glucose cotransporter 2 (SGLT2) inhibitor. 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 patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. BRENZAVVY is contraindicated in patients who are hypersensitive to bexagliflozin or any tablet ingredient and is not indicated for the treatment of type 2 diabetes in patients with end stage renal disease or who are receiving dialysis.

The FDA approval is based on results from a clinical program that evaluated the safety and efficacy of BRENZAVVY in 23 clinical trials enrolling more than 5,000 adults with type 2 diabetes mellitus. Phase 3 studies showed BRENZAVVY significantly reduced 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 systolic blood pressure have been observed in the clinical program.

“As a class of drugs, SGLT2 inhibitors have shown tremendous benefit in treating adults with type 2 diabetes,” said Dr. Mason Freeman, M.D., Director of the Translational Research Center at Massachusetts General

Hospital. “Being involved in all of the clinical trials for BRENZAVVY, I am greatly impressed with the efficacy of the drug in reducing blood glucose levels and I believe it is an important addition to the SGLT2 inhibitor class of drugs.”

BRENZAVVY treatment can be initiated in adults with type 2 diabetes with an estimated glomerular filtration rate (eGFR) greater than 30 mL/min/1.73 m^2. Patients with eGFR less than 60 and greater than 30 mL/min/1.73 m^2 are said to be in stage 3 chronic kidney disease, and for these patients metformin is often avoided due to the risk of lactic acidosis.

“Today's FDA approval represents a significant milestone for TheracosBio and provides an important treatment option to patients who suffer from type 2 diabetes. We look forward to bringing BRENZAVVY to market,” said Albert R. Collinson, Ph.D., President and CEO of TheracosBio. “The approval of the BRENZAVVY NDA is a result of the tireless work of the TheracosBio team and investigators. I want to thank all of the patients who took part in our clinical trials.”

According to the U.S. Centers for Disease Control and Prevention, more than 33 million Americans have type 2 diabetes, which means their bodies don’t use insulin correctly and as a result their blood sugar levels are too high. While some people can control their blood sugar levels with exercise and a healthy diet, others may need additional help to achieve good blood sugar (glycemic) control.

SGLT2 inhibitors are a class of prescription medicines that lower blood sugar by causing the kidneys to remove sugar from the body through urine.

BRENZAVVY is available as 20 mg oral tablets recommended to be taken once daily, in the morning with or without food.

Important Safety Information about BRENZAVVY

<u>Ketoacidosis</u>

Reports of ketoacidosis, a serious life-threatening condition requiring urgent hospitalization, have been identified in clinical trials and postmarketing surveillance in patients with type 1 and type 2 diabetes mellitus who received SGLT2 inhibitors, including BRENZAVVY. Fatal cases of ketoacidosis have been reported for patients taking SGLT2 inhibitors. In placebo-controlled trials of patients with type 1 diabetes, the risk of ketoacidosis was increased in patients who received SGLT2 inhibitors compared to patients who received placebo. BRENZAVVY is not indicated for the treatment of patients with type 1 diabetes mellitus.

Patients treated with BRENZAVVY who present with signs and symptoms consistent with severe metabolic acidosis should be assessed for ketoacidosis regardless of blood glucose levels, as ketoacidosis associated with BRENZAVVY may be present even if the blood glucose levels are less than 250 mg/dL. If ketoacidosis is suspected, BRENZAVVY should be discontinued, the patient should be evaluated, and prompt treatment should be instituted. Treatment of ketoacidosis may require insulin, fluid, and carbohydrate replacement.

In many of the reported cases, and particularly in patients with type 1 diabetes, the presence of ketoacidosis was not immediately recognized, and the institution of treatment was delayed because the presenting blood glucose levels were below those typically expected for diabetic ketoacidosis (often less than 250 mg/dL). Signs and symptoms at presentation were consistent with dehydration and severe metabolic acidosis and included nausea, vomiting, abdominal pain, generalized malaise, and shortness of breath. In some but not all cases, factors predisposing to ketoacidosis, such as insulin dose reduction, acute febrile illness, reduced caloric intake, surgery, pancreatic disorders suggesting insulin deficiency (e.g., type 1 diabetes, history of pancreatitis or pancreatic surgery), and alcohol abuse were identified.

Before initiating BRENZAVVY, consider factors in the patient history that may predispose to ketoacidosis, including pancreatic insulin deficiency from any cause, caloric restriction, and alcohol abuse.

For patients who undergo scheduled surgery, consider temporarily discontinuing BRENZAVVY for at least 3 days prior to surgery. Consider monitoring for ketoacidosis and temporarily discontinuing BRENZAVVY in clinical situations known to predispose to ketoacidosis (e.g., prolonged fasting due to acute illness or post-surgery). Ensure risk factors for ketoacidosis are resolved prior to restarting BRENZAVVY. Educate 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

An increased incidence of lower limb amputations occurred in BRENZAVVY-treated patients compared to placebo-treated patients (8.3 versus 5.1 events per 1,000 patient-years) in a randomized, placebo-controlled trial evaluating 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 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 about the importance of routine preventative foot care. Monitor patients receiving BRENZAVVY for signs and symptoms of infection (including osteomyelitis), new pain or tenderness, sores or ulcers involving the lower limbs, and discontinue BRENZAVVY if these complications occur.

Volume Depletion

BRENZAVVY can cause intravascular volume contraction which may sometimes manifest as symptomatic hypotension or acute transient changes

in creatinine. There have been postmarketing reports of acute kidney injury, some requiring hospitalization and dialysis, in patients with type 2 diabetes mellitus receiving SGLT2 inhibitors. 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 may be at increased risk for volume depletion or hypotension. Before initiating BRENZAVVY in patients with one or more of these characteristics, assess volume status and renal function. In patients with volume depletion, correct this condition before initiating BRENZAVVY. Monitor for signs and symptoms of volume depletion, and renal function after initiating therapy.

Urosepsis and Pyelonephritis

There have been reports of serious urinary tract infections, including urosepsis and pyelonephritis, requiring hospitalization in patients receiving SGLT2 inhibitors, including BRENZAVVY. Treatment with SGLT2 inhibitors, including BRENZAVVY, increases the risk for urinary tract infections. Evaluate patients for signs and symptoms of urinary tract infections and treat promptly, if indicated.

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)

Reports of necrotizing fasciitis of the perineum (Fournier's Gangrene), a rare but serious and life-threatening necrotizing infection requiring urgent surgical intervention, have been identified in postmarketing surveillance in patients with diabetes mellitus receiving SGLT2 inhibitors. Cases have been reported in both females and males. Serious outcomes have included hospitalization, multiple surgeries, and death.

Patients treated with BRENZAVVY presenting with pain or tenderness, erythema, or swelling in the genital or perineal areas, 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 BRENZAVVY, closely monitor blood glucose levels, and provide appropriate alternative therapy for glycemic control.

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.

The most common adverse reactions (incidence > 5%) were female mycotic infections, urinary tract infection and increased urination.

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.

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