TheracosBio Announces Publication of Data on the Safety and Effectiveness of Brenzavvy™ (bexagliflozin) as an Adjunct to Metformin

Phase 3 study shows improved glycemic control and decreased systolic blood pressure and fasting plasma glucose

Marlborough, MA – August 4, 2023 – TheracosBio today announced the publication of a study titled "Bexagliflozin as an Adjunct to Metformin for the Treatment of Type 2 Diabetes in Adults: a 24-Week, Randomized, Double-Blind, Placebo-Controlled Trial" in *Diabetes, Obesity and Metabolism*. The Phase 3 study assessed the safety and effectiveness of Brenzavvy™ (bexagliflozin), 20 mg, in adults with type 2 diabetes mellitus as an adjunct to metformin, as compared to placebo. The study results showed that BRENZAVVY treatment improved glycemic control and decreased systolic blood pressure levels and fasting plasma glucose levels in patients with type 2 diabetes.

BRENZAVVY is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes, including those with chronic kidney disease that has progressed to stage 3. BRENZAVVY was the first SGLT2 inhibitor shown in a randomized, controlled clinical trial to be effective in adults with type 2 diabetes and stage 3 (3a + 3b) chronic kidney disease. BRENZAVVY is not recommended for use to improve glycemic control in patients with type 1 diabetes mellitus.

"These data illustrate the potential benefits of BRENZAVVY for adults with type 2 diabetes," said Brian Connelly, President and CEO of TheracosBio. "These data strengthen the evidence that BRENZAVVY supports improvements in systolic blood pressure, which is beneficial for patients with kidney disease. BRENZAVVY represents an important addition to the treatment options for type 2 diabetes."

The randomized, double-blind, placebo-controlled trial enrolled 317 adults with type 2 diabetes mellitus. In addition, an open label group consisting of 34 patients with severe diabetes (HbA_{1c} > 10.5 and ≤ 12.0%) was analyzed separately. The primary endpoint was the change in HbA_{1c} from baseline to week 24.

Treatment with BRENZAVVY as an adjunct to metformin was associated with the following results:

- A clinically meaningful and statistically significant 1.09% reduction of HbA_{1c} from baseline with a placebo-adjusted treatment effect of −0.53%, as well as a mean change of −2.82% in the open label group. Rescue medication was provided to 6 patients in the BRENZAVVY arm and 32 in the placebo arm. Exclusion of values observed after treatment with rescue medication gave a reduction of 1.07% from baseline HbA_{1c} and a placebo-corrected treatment effect of −0.67%.
- A decrease in systolic blood pressure levels by 5.03 mm Hg with a placebo-adjusted reduction of 7.07 mm Hg, as well as a mean change reduction of 8.19 mm Hg in the high glycemic group.
- A decrease in fasting plasma glucose levels by 45.2 mg dL^{-1} with a placebo-adjusted reduction of 24.3 mg dL^{-1}.

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 and is not indicated for the treatment of type 2 diabetes in patients who are receiving dialysis. 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.

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

Diabetic Ketoacidosis in Patients with Type 1 Diabetes Mellitus and Other Ketoacidosis

In patients with type 1 diabetes mellitus, BRENZAVVY significantly increases the risk of diabetic ketoacidosis, a life-threatening event, beyond background rate. In placebo-controlled trials of patients with type 1 diabetes mellitus, the risk of ketoacidosis was markedly increased in patients who received sodium glucose transporter 2 (SGLT2) inhibitors compared to patients who received placebo. BRENZAVVY is not indicated for glycemic control in patients with type 1 diabetes mellitus.

Type 2 diabetes mellitus and pancreatic disorders (e.g., history of pancreatitis or pancreatic surgery) are also risk factors for ketoacidosis. There have been postmarketing reports of fatal events of ketoacidosis in patients with type 2 diabetes mellitus using SGLT2 inhibitors, including BRENZAVVY.

Precipitating conditions for diabetic ketoacidosis or other ketoacidosis include acute febrile illness, reduced caloric intake, ketogenic diet, surgery, insulin dose reduction, volume depletion, and alcohol abuse.

Signs and symptoms are consistent with dehydration and severe metabolic acidosis and include nausea, vomiting, abdominal pain, generalized malaise, and shortness of breath. Blood glucose levels at presentation may be below those typically expected for diabetic ketoacidosis (e.g., less than 250 mg/dL). Ketoacidosis and glucosuria may persist longer than typically expected. Urinary glucose excretion persists for 3 days after discontinuing BRENZAVVY; however, there have been postmarketing reports of ketoacidosis and glucosuria lasting greater than 6 days and some up to 2 weeks after discontinuation of SGLT2 inhibitors.

Consider ketone monitoring in patients at risk for ketoacidosis if indicated by the clinical situation. Assess for ketoacidosis regardless of presenting blood glucose levels in patients who present with signs and symptoms consistent with severe metabolic acidosis. If ketoacidosis is suspected, discontinue BRENZAVVY, promptly evaluate, and treat ketoacidosis, if confirmed. Monitor patients for resolution of ketoacidosis before restarting BRENZAVVY.

Withhold BRENZAVVY, if possible, in temporary clinical situations that could predispose patients to ketoacidosis. Resume BRENZAVVY when the patient is clinically stable and has resumed oral intake.

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

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 genital 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.

Media Contact
Lauren Arnold
MacDougall Advisors
1 (617) 694-5387
larnold@macdougall.bio