CV Safety Profile of TheracosBio's BRENZAVVY® (bexagliflozin) Confirmed in Research Published in *Diabetes, Obesity and Metabolism*

Meta-Analysis Adds to Evidence that BRENZAVVY Offers a Critical, Cost-Effective Option for Patients with Type 2 Diabetes

Marlborough, MA – January 8, 2024 – TheracosBio today announced the publication of a meta-analysis that confirms the cardiovascular safety profile of BRENZAVVY® (bexagliflozin), 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.

The research, published in *Diabetes, Obesity and Metabolism*, detailed the results of a pre-specified analysis of nine Phase 2 and 3 studies used to gain FDA approval for BRENZAVVY. The study was powered to establish a pre-approval margin of safety specified by the FDA, and the point estimate for major adverse cardiovascular events (MACE) was substantially lower than the value of 1.00 used for planning purposes, so the pre-approval program met the requirements for post-approval safety as well.

Though the meta-analysis did not compare BRENZAVVY to other medicines in the class, the cardiovascular findings were consistent with findings reported for other SGLT inhibitor trials.

"These data clearly demonstrate that long-term use of BRENZAVVY, even in patients at high risk for future cardiovascular disease, does not increase CV risk and should give physicians confidence in the overall safety profile of BRENZAVVY," said Mason W. Freeman, MD, Professor of Medicine at Harvard Medical School and Director of the Translational Medicine Group at Massachusetts General Hospital, who was one of the study's authors. "The point estimate for the hazard ratio of major adverse cardiovascular events in the overall BRENZAVVY program overseen by our group at MGH is similar to

those reported in the cardiovascular outcomes trials of other approved SGLT2 inhibitors".

BRENZAVVY represents a new approach to diabetes care. It is the first affordably priced, once-daily SGLT2 inhibitor. This allows for expanded access for the uninsured and improves care for those with insurance by eliminating the difficulties and expenses of insurance-company utilization management and cost-sharing.

Approximately 1 in 10 adults in the United States have type 2 diabetes, but suboptimal adherence to medication is common. A study of adherence among adults in the Medicare Part D database, published in the journal *Clinical Therapeutics*, estimated that 35.1% of patients were non-adherent to oral hypoglycemic agents. Cost-related nonadherence was reported by 17.6% of diabetic adults in the 18- to 64-year-old age group in a 2022 study published in *Diabetes Care*.

"TheracosBio has provided powerful proof that a smart development program, including well-designed meta-analyses to generate critical safety information, can be done efficiently and effectively, and that the cost-savings from such a program can be passed along directly to patients," said TheracosBio CEO Brian Connelly. "I'm encouraged by the evolution of the supporting data for BRENZAVVY and believe that this study confirms that BRENZAVVY can serve as a critical, cost-effective treatment option for millions of patients with type 2 diabetes mellitus."

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.

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