FDA approves Lilly's Mounjaro™ (tirzepatide) injection, the first and only GIP and GLP-1 receptor agonist for the treatment of adults with type 2 diabetes

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Mounjaro delivered superior A1C reductions versus all comparators in phase 3 SURPASS clinical trials

While not indicated for weight loss, Mounjaro led to significantly greater weight reductions versus comparators in a key secondary endpoint

Mounjaro represents the first new class of diabetes medicines introduced in nearly a decade and is expected to be available in the U.S. in the coming weeks

INDIANAPOLIS, May 13, 2022 /PRNewswire/ -- The U.S. Food and Drug Administration (FDA) approved Mounjaro™ (tirzepatide) injection, Eli Lilly and Company's (NYSE: LLY) new once-weekly GIP (glucose-dependent insulinotropic polypeptide) and GLP-1 (glucagon-like peptide-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. Mounjaro has not been studied in patients with a history of pancreatitis and is not indicated for use in patients with type 1 diabetes mellitus.

As the first and only FDA-approved GIP and GLP-1 receptor agonist, Mounjaro is a single molecule that activates the body's receptors for GIP and GLP-1, which are natural incretin hormones.[1]

"Mounjaro delivered superior and consistent A1C reductions against all of the comparators throughout the SURPASS program, which was designed to assess Mounjaro's efficacy and safety in a broad range of adults with type 2 diabetes who could be treated in clinical practice. The approval of Mounjaro is an exciting step forward for people living with type 2 diabetes given the results seen in these clinical trials," said Juan Pablo Frías, M.D., Medical Director, National Research Institute and Investigator in the SURPASS program.

Mounjaro will be available in six doses (2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg) and will come in Lilly's well-established auto-injector pen with a pre-attached, hidden needle that patients do not need to handle or see.

The approval was based on results from the phase 3 SURPASS program, which included active comparators of injectable semaglutide 1 mg, insulin glargine and insulin degludec. Efficacy was evaluated for Mounjaro 5 mg, 10 mg and 15 mg used alone or in combination with commonly prescribed diabetes medications, including metformin, SGLT2 inhibitors, sulfonylureas and insulin glargine. Participants in the SURPASS program achieved average A1C reductions between 1.8% and 2.1% for Mounjaro 5 mg and between 1.7% and 2.4% for both Mounjaro 10 mg and Mounjaro 15 mg. While not indicated for weight loss, mean change in body weight was a key secondary endpoint in all SURPASS studies. Participants treated with Mounjaro lost between 12 lb. (5 mg) and 25 lb. (15 mg) on average.[1]

Side effects reported in at least 5% of patients treated with Mounjaro include nausea, diarrhea, decreased appetite, vomiting, constipation, indigestion (dyspepsia), and stomach (abdominal) pain. The labeling for Mounjaro contains a Boxed Warning regarding thyroid C-cell tumors. Mounjaro is contraindicated in patients with a personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2.[1]

"Lilly has a nearly 100-year heritage of advancing care for people living with diabetes – never settling for current outcomes. We're not satisfied knowing that half of the more than 30 million Americans living with type 2 diabetes are not reaching their target blood glucose levels," said Mike Mason, president, Lilly Diabetes. "We are thrilled to introduce Mounjaro, which represents the first new class of type 2 diabetes medication introduced in almost a decade and embodies our mission to bring innovative new therapies to the diabetes community."

Mounjaro is expected to be available in the United States in the coming weeks. Lilly is committed to helping people access the medicines they are prescribed and will work with insurers, health systems and providers to help enable patient access to Mounjaro. Lilly plans to offer a Mounjaro savings card for people who qualify. Patients or healthcare professionals with questions about Mounjaro can visit www.Mounjaro.com or call The Lilly Answers Center at 1-800-LillyRx (1-800-545-5979).

Tirzepatide is also under regulatory review for the treatment of type 2 diabetes in Europe, Japan and several additional markets. A multimedia gallery is available on Lilly.com.

About the SURPASS clinical trial program
The SURPASS phase 3 global clinical development program for tirzepatide began in late 2018 and included five global registration trials and two regional trials in Japan. These studies ranged from 40 to 52 weeks and evaluated the efficacy and safety of Mounjaro 5 mg, 10 mg and 15 mg as a monotherapy and as an add-on to various standard-of-care medications for type 2 diabetes. The active comparators in the studies were injectable semaglutide 1 mg, insulin glargine and insulin degludec. Collectively, the five global registration trials consistently demonstrated A1C reductions for participants taking Mounjaro across multiple stages of their type 2 diabetes journeys, from an average around five to 13 years of having diabetes.[2-8]

- SURPASS-1 (NCT03954834) was a 40-week study comparing the efficacy and safety of Mounjaro 5 mg (N=121), 10 mg (N=121) and 15 mg (N=120) as monotherapy to placebo (N=113) in adults with type 2 diabetes inadequately controlled with diet and exercise alone. From a baseline A1C of 7.9%, Mounjaro reduced participants' A1C by a mean of 1.8%* (5 mg) and 1.7%* (10 mg and 15 mg) compared to 0.1% for placebo. In a key secondary endpoint, from a baseline weight of 189 lb., Mounjaro reduced participants' weight by a mean of 14 lb.* (5 mg), 15 lb.* (10 mg) and 17 lb.* (15 mg) compared

to 2 lb. for placebo.[2,3]

- SURPASS-2 (NCT03987919) was a 40-week study comparing the efficacy and safety of Mounjaro 5 mg (N=470), 10 mg (N=469) and 15 mg (N=469) to injectable semaglutide 1 mg (N=468) in adults with type 2 diabetes inadequately controlled with ≥1500 mg/day metformin alone. From a baseline A1C of 8.3%, Mounjaro reduced participants' A1C by a mean of 2.0%□ (5 mg), 2.2%* (10 mg) and 2.3%* (15 mg) compared to 1.9% for semaglutide. In a key secondary endpoint, from a baseline weight of 207 lb., Mounjaro reduced participants' weight by a mean of 17 lb.□ (5 mg), 21 lb.* (10 mg) and 25 lb.* (15 mg) compared to 13 lb. for semaglutide.[4,5]
- SURPASS-3 (NCT03882970) was a 52-week study comparing the efficacy of Mounjaro 5 mg (N=358), 10 mg (N=360) and 15 mg (N=358) to titrated insulin degludec (N=359) in adults with type 2 diabetes treated with metformin with or without an SGLT-2 inhibitor. From a baseline A1C of 8.2%, Mounjaro reduced participants' A1C by a mean of 1.9%* (5 mg), 2.0%* (10 mg) and 2.1%* (15 mg) compared to 1.3% for insulin degludec. From a baseline weight of 208 lb., Mounjaro reduced participants' weight by a mean of 15 lb.* (5 mg), 21 lb.* (10 mg) and 25 lb.* (15 mg) compared to an increase of 4 lb. for insulin degludec.[6]
- SURPASS-4 (NCT03730662) was a 104-week study comparing the efficacy and safety of Mounjaro 5 mg (N=328), 10 mg (N=326) and 15 mg (N=337) to insulin glargine (N=998) in adults with type 2 diabetes inadequately controlled with at least one and up to three oral antihyperglycemic medications (metformin, sulfonylureas or SGLT-2 inhibitors), who have increased cardiovascular (CV) risk. The primary endpoint was measured at 52 weeks. From a baseline A1C of 8.5%, Mounjaro reduced participants' A1C by a mean of 2.1%* (5 mg), 2.3%* (10 mg) and 2.4%* (15 mg) compared to 1.4% for insulin glargine. From a baseline weight of 199 lb., Mounjaro reduced weight by a mean of 14 lb.* (5 mg), 20 lb.* (10 mg) and 23 lb.* (15 mg) compared to an increase of 4 lb. for insulin glargine.[7]
- SURPASS-5 (NCT04039503) was a 40-week study comparing the efficacy and safety of Mounjaro 5 mg (N=116), 10 mg (N=118) and 15 mg (N=118) to placebo (N=119) in adults with inadequately controlled type 2 diabetes already being treated with insulin glargine, with or without metformin. From a baseline A1C of 8.3%, Mounjaro reduced A1C by a mean of 2.1%* (5 mg), 2.4%* (10 mg) and 2.3%* (15 mg) compared to 0.9% for placebo. From a baseline weight of 210 lb., Mounjaro reduced participants' weight by a mean of 12 lb.* (5 mg), 17 lb.* (10 mg) and 19 lb.* (15 mg) compared to an increase of 4 lb. for placebo.[8]

**p<0.001 for superiority vs. placebo or active comparator, adjusted for multiplicity*
□p<0.05 for superiority vs. semaglutide 1 mg, adjusted for multiplicity

About Mounjaro™ (tirzepatide) injection[1]
Mounjaro™ (tirzepatide) injection is FDA-approved as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. As the first and only FDA-approved GIP and GLP-1 receptor agonist, Mounjaro is a single molecule that activates the body's receptors for GIP (glucose-dependent insulinotropic polypeptide) and GLP-1 (glucagon-like peptide-1). Mounjaro will be available in six doses (2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg) and will come in Lilly's well-established auto-injector pen with a pre-attached, hidden needle that patients do not need to handle or see.

PURPOSE AND SAFETY SUMMARY WITH WARNINGS
Important Facts About Mounjaro™ (mown-JAHR-OH). It is also known as tirzepatide.

- Mounjaro is an injectable prescription medicine for adults with type 2 diabetes used along with diet and exercise to improve blood sugar (glucose).
- It is not known if Mounjaro can be used in people who have had inflammation of the pancreas (pancreatitis). Mounjaro is not for use in people with type 1 diabetes. It is not known if Mounjaro is safe and effective for use in children under 18 years of age.

Warnings
Mounjaro may cause tumors in the thyroid, including thyroid cancer. Watch for possible symptoms, such as a lump or swelling in the neck, hoarseness, trouble swallowing, or shortness of breath. If you have a symptom, tell your healthcare provider.

- Do not use Mounjaro if you or any of your family have ever had a type of thyroid cancer called medullary thyroid carcinoma (MTC).
- Do not use Mounjaro if you have Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).
- Do not use Mounjaro if you are allergic to tirzepatide or any of the ingredients in Mounjaro.

Mounjaro may cause serious side effects, including:

Inflammation of the pancreas (pancreatitis). Stop using Mounjaro and call your healthcare provider right away if you have severe pain in your stomach area (abdomen) that will not go away, with or without vomiting. You may feel the pain from your abdomen to your back.

Low blood sugar (hypoglycemia). Your risk for getting low blood sugar may be higher if you use Mounjaro with another medicine that can cause low blood sugar, such as a sulfonylurea or insulin. **Signs and symptoms of low blood sugar** may include dizziness or light-headedness, sweating, confusion or drowsiness, headache, blurred vision, slurred speech, shakiness, fast heartbeat, anxiety, irritability, or mood changes, hunger, weakness and feeling jittery.

Serious allergic reactions. Stop using Mounjaro and get medical help right away if you have any symptoms of a serious allergic reaction, including swelling of your face, lips, tongue or throat, problems breathing or swallowing, severe rash or itching, fainting or feeling dizzy, and very rapid heartbeat.

Kidney problems (kidney failure). In people who have kidney problems, diarrhea, nausea, and vomiting may cause a loss of fluids (dehydration), which may cause kidney problems to get worse. It is important for you to drink fluids to help reduce your chance of dehydration.

Severe stomach problems. Stomach problems, sometimes severe, have been reported in people who use Mounjaro. Tell your healthcare provider if you have stomach problems that are severe or will not go away.

Changes in vision. Tell your healthcare provider if you have changes in vision during treatment with Mounjaro.

Gallbladder problems. Gallbladder problems have happened in some people who use Mounjaro. Tell your healthcare provider right away if you get symptoms of gallbladder problems, which may include pain in your upper stomach (abdomen), fever, yellowing of skin or eyes (jaundice), and clay-colored stools.

Common side effects
The most common side effects of Mounjaro include nausea, diarrhea, decreased appetite, vomiting, constipation, indigestion, and stomach (abdominal) pain. These are not all the possible side effects of Mounjaro. Talk to your healthcare provider about any side effect that bothers you or doesn't go away.

Tell your healthcare provider if you have any side effects. **You can report side effects at 1-800-FDA-1088 or www.fda.gov/medwatch.**

Before using

- **Your healthcare provider should show you how to use Mounjaro before you use it for the first time.**
- **Before you use Mounjaro, talk to your healthcare provider about low blood sugar and how to manage it.**

Review these questions with your healthcare provider:

- Do you have other medical conditions, including problems with your pancreas or kidneys, or severe problems with your stomach, such as slowed emptying of your stomach (gastroparesis) or problems digesting food?
- Do you take other diabetes medicines, such as insulin or sulfonylureas?
- Do you have a history of diabetic retinopathy?
- Are you pregnant or plan to become pregnant or breastfeeding or plan to breastfeed? It is not known if Mounjaro will harm your unborn baby.
- Do you take birth control pills by mouth? These may not work as well while using Mounjaro. Your healthcare provider may recommend another type of birth control when you start Mounjaro or when you increase your dose.
- Do you take any other prescription medicines or over-the-counter drugs, vitamins, or herbal supplements?

How to take

- Read the **Instructions for Use** that come with Mounjaro.
- Use Mounjaro exactly as your healthcare provider says.
- Mounjaro is injected under the skin (subcutaneously) of your stomach (abdomen), thigh, or upper arm.
- **Use Mounjaro 1 time each week, at any time of the day.**
- **Do not** mix insulin and Mounjaro together in the same injection.
- If you take too much Mounjaro, call your healthcare provider or seek medical advice promptly.

Learn more
For more information, call 1-800-LillyRx (1-800-545-5979) or go to **www.mounjaro.com.**

This information does not take the place of talking with your healthcare provider. Be sure to talk to your healthcare provider about Mounjaro and how to take it. Your healthcare provider is the best person to help you decide if Mounjaro is right for you.

Please click to access full Prescribing Information and Medication Guide.

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About Lilly
Lilly unites caring with discovery to create medicines that make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help more than 47 million people across the globe. Harnessing the power of biotechnology, chemistry and genetic medicine, our scientists are urgently advancing new discoveries to solve some of the world's most significant health challenges, redefining diabetes care, treating obesity and curtailing its most devastating long-term effects, advancing the fight against Alzheimer's disease, providing solutions to some of the most debilitating immune system disorders, and transforming the most difficult-to-treat cancers into manageable diseases. With each step toward a healthier world, we're motivated by one thing: making life better for millions more people. That includes delivering innovative clinical trials that reflect the diversity of our world and working to ensure our medicines are accessible and affordable. To learn more, visit Lilly.com and Lilly.com/newsroom or follow us on Facebook, Instagram, Twitter and LinkedIn. P-LLY

Lilly Cautionary Statement Regarding Forward-Looking Statements

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Mounjaro™ (tirzepatide 2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg and 15 mg) injection as a treatment to improve glycemic control in adults with type 2 diabetes, the timeline for supply of Mounjaro to become available, and certain other milestones and ongoing clinical trials of Mounjaro and reflects Lilly's current beliefs and expectations. However, as with any pharmaceutical product or medical device, there are substantial risks and uncertainties in the process of research, development and commercialization. Among other things, there can be no guarantee that Mounjaro will be commercially successful, that future study results will be consistent with results to date, or that we will meet our anticipated timelines for the commercialization of Mounjaro. For further discussion of these and other risks and uncertainties, see Lilly's most recent Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

References

1. Mounjaro. Prescribing Information. Lilly USA, LLC.
2. Rosenstock, J, et. al. Efficacy and Safety of Once Weekly Tirzepatide, a Dual GIP/GLP-1 Receptor Agonist Versus Placebo as Monotherapy in People with Type 2 Diabetes (SURPASS-1). Abstract 100-OR. Presented virtually at the American Diabetes Association's 81st Scientific Sessions; June 25-29.
3. Rosenstock, J, et. al. (2021). Efficacy and safety of a novel dual GIP and GLP-1 receptor agonist tirzepatide in patients with type 2 diabetes (SURPASS-1): a double-blind, randomised, phase 3 trial. *Lancet*. 2021;398(10295):143-155. doi: 10.1016/S0140-6736(21)01324-6.
4. Frías JP, Davies MJ, Rosenstock J, et al; for the SURPASS-2 Investigators. Tirzepatide versus semaglutide once weekly in patients with type 2 diabetes. N Engl J Med. 2021;385(6)(suppl):503-515. doi: 10.1056/NEJMoa2107519
5. Frias, J.P. Efficacy and Safety of Tirzepatide vs. Semaglutide Once Weekly as Add-On Therapy to Metformin in Patients with Type 2 Diabetes. Abstract 84-LB. Presented virtually at the American Diabetes Association's 81st Scientific Sessions; June 25-29.
6. Ludvik B, Giorgino F, Jódar E, et al. Once-weekly tirzepatide versus once-daily insulin degludec as add-on to metformin with or without SGLT2 inhibitors in patients with type 2 diabetes (SURPASS-3): a randomised, open-label, parallel-group, phase 3 trial. Lancet. 2021;398(10300):583-598. doi: 10.1016/S0140-6736(21)01443-4
7. Del Prato S, Kahn SE, Pavo I, et al; for the SURPASS-4 Investigators. Tirzepatide versus insulin glargine in type 2 diabetes and increased cardiovascular risk (SURPASS-4): a randomised, open-label, parallel-group, multicentre, phase 3 trial. Lancet. 2021;398(10313):1811-1824. doi: 10.1016/S0140-6736(21)02188-7
8. Dahl D, Onishi Y, Norwood P, et al. Effect of subcutaneous tirzepatide vs placebo added to titrated insulin glargine on glycemic control in patients with type 2 diabetes: the SURPASS-5 randomized clinical trial. JAMA. 2022;327(6):534-545. doi:10.1001/jama.2022.0078

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