Lilly's tirzepatide demonstrates benefits in data presented at the American Diabetes Association's® 79th Scientific Sessions®

June 9, 2019

INDIANAPOLIS, June 8, 2019 /PRNewswire/ -- Results from several studies of Eli Lilly and Company's (NYSE: LLY) investigational dual GIP and GLP-1 receptor agonist (RA), tirzepatide, reinforce its potential in lowering A1C and body weight in people with type 2 diabetes. Early research results also support tirzepatide's potential benefit in treating other metabolic conditions. The following findings were presented in oral and poster presentations at the American Diabetes Association's® 79th Scientific Sessions® in San Francisco:

- improvements in markers of beta cell function (how cells in the pancreas produce, store and release insulin) and insulin sensitivity (how cells in the body respond to insulin) that help explain efficacy;[1]
- efficacy and improved tolerability with lower initial doses and smaller subsequent dose escalations;[2]
- significant A1C and body weight reductions in Japanese people with type 2 diabetes after just eight weeks of treatment;[3] and
- improvements in markers of non-alcoholic steatohepatitis (NASH, liver inflammation and cell damage caused by liver fat) in people with type 2 diabetes.[4]

"These new tirzepatide data build upon the positive results seen in people with type 2 diabetes to date," said Juan P. Frias, M.D., Medical Director and Principal Investigator, National Research Institute. "The results offer additional evidence of tirzepatide's potential to meaningfully reduce A1C and body weight in people with type 2 diabetes and treat other metabolic conditions."

Tirzepatide shows improvements in markers that help explain efficacy
A sub-analysis of phase 2b results show tirzepatide improved markers of beta cell function and insulin sensitivity in people with type 2 diabetes. Improvements in insulin sensitivity markers seen with GLP-1 RAs have been primarily explained by weight loss;[5] therefore, researchers further analyzed these markers to better understand if the GIP action in tirzepatide contributes to a unique profile. Unlike GLP-1 RAs, the improvements seen with tirzepatide (10 mg and 15 mg) were only partially attributed to weight loss (28 percent and 22 percent, respectively), suggesting an independent effect of GIP on insulin sensitivity may contribute to the strong and clinically meaningful blood glucose control seen in the 26-week phase 2b study.[1,6]

Tirzepatide shows consistent positive impact on blood glucose control and weight loss while improving tolerability with dose escalations
Data from a 12-week, phase 2 study showed dose escalations with tirzepatide resulted in fewer gastrointestinal (GI) side effects while maintaining the efficacy seen in the phase 2b study. Reduced study discontinuation rates were also observed. To inform optimal dosing for the phase 3 program, researchers evaluated three tirzepatide dose-escalation regimens to determine impact on composite GI side effects (nausea, vomiting and diarrhea) and efficacy. Results showed:[2]

- tirzepatide treatment led to significant A1C reductions (up to 2.0 percent) and weight loss (up to 5.7 kg), consistent with the phase 2b study;
- GI side effects were mild to moderate in intensity and overall lower than in the phase 2b study;
- treatment discontinuation rates due to adverse events with tirzepatide were less than 5 percent, comparable to placebo and overall lower than in the phase 2b study.

Data learned from this and other tirzepatide studies, along with modeling, support that a lower initial dose and smaller incremental dose escalations improve tolerability, which informed the selected dosing approach for the phase 3 clinical trial program – SURPASS – initiated in late 2018.

Results from another study – an eight-week trial in Japanese people with type 2 diabetes – showed significant reductions in A1C (up to 2.05 percent) and body weight (up to 5.1 kg) after treatment with tirzepatide.[3] This study also supports the significant A1C and body weight reductions seen in the phase 2b study, suggesting tirzepatide's potential for effectively treating people with type 2 diabetes is consistent across populations.

Tirzepatide shows potential for therapeutic impact in NASH
Given the relationship between NASH and type 2 diabetes, researchers analyzed tirzepatide's impact on several markers associated with NASH. In an analysis of the phase 2b study of people with type 2 diabetes, researchers found that treatment with tirzepatide led to improvements in NASH-related markers. A phase 2b study exploring tirzepatide in NASH will initiate later this year.

"We are excited about tirzepatide's potential to make an important impact on people with type 2 diabetes and other conditions, including obesity and NASH," said Brad Woodward, M.D., global development leader, Incretins, Lilly. "The tirzepatide results seen in early and mid-stage trials pave the way for our extensive phase 3 programs, reinforce our commitment to researching it further across different populations and support its potential of addressing an unmet treatment need."

Lilly will host an investor call on Monday, June 10, at 10:00 a.m. EDT (7:00 a.m. PDT) to discuss the company's presentations at the American Diabetes Association's 79th Scientific Sessions.

About Diabetes

Approximately 30 million Americans[7] and an estimated 425 million adults worldwide have diabetes.[8] Type 2 diabetes is the most common type internationally, accounting for an estimated 90 to 95 percent of all diabetes cases in the United States alone.[7] Diabetes is a chronic disease that occurs when the body does not properly produce or use the hormone insulin.[8]

About Lilly Diabetes

Lilly has been a global leader in diabetes care since 1923, when we introduced the world's first commercial insulin. Today we are building upon this heritage by working to meet the diverse needs of people with diabetes and those who care for them. Through research, collaboration and quality manufacturing we strive to make life better for people affected by diabetes. We offer a wide range of therapies and a continued determination to provide real solutions—from medicines and technologies to support programs and more. For the latest updates, visithttp://www.lillydiabetes.com/ or follow us on Twitter: @LillyDiabetes and Facebook: LillyDiabetesUS.

About Eli Lilly and Company

Lilly is a global healthcare leader that unites caring with discovery to make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at www.lilly.com and www.lilly.com/newsroom/social-channels. P-LLY

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about tirzepatide as a potential treatment for patients with diabetes and other metabolic conditions and reflects Lilly's current belief. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. Among other things, there can be no guarantee that future study results will be consistent with the results to date or that tirzepatide will achieve its primary study endpoints or receive regulatory approvals. 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.

1. Thomas MK, Nikooienejad A, Bray R, et al. Tirzepatide, a dual GIP and GLP-1 receptor agonist, improves markers of beta cell function and insulin sensitivity in type 2 diabetes patients. Abstract 980-P. Presented at the American Diabetes Association's 79th Scientific Sessions; June 7-11, San Francisco, CA.
2. Frias JP, Nauck MA, Van J, et al. A 12-week, randomized, placebo-controlled study assessing the efficacy and safety of three dose-escalation algorithms of tirzepatide, a novel dual GIP and GLP-1 receptor agonist, in patients with type 2 diabetes. Abstract 993-P. Presented at the American Diabetes Association's 79th Scientific Sessions; June 7-11, San Francisco, CA.
3. Ohwaki K, Furihata K, Mimura H, et al. Effect of tirzepatide, a dual GIP and GLP-1 receptor agonist, on glycemic control and body weight in Japanese patients with T2DM. Abstract 1024-P. Presented at the American Diabetes Association's 79th Scientific Sessions; June 7-11, San Francisco, CA.
4. Hartman ML, Sanyal A, Loomba R, et al. Effects of tirzepatide (TZP), a novel dual GIP and GLP-1 receptor agonist, on biomarkers of nonalcoholic steatohepatitis (NASH) in patients with T2D. Abstract 134-OR. Presented at the American Diabetes Association's 79th Scientific Sessions; June 7-11, San Francisco, CA.
5. Fonseca VA, Capehorn MS, Garg SK, et al. Reductions in insulin resistance are mediated primarily via weight loss in subjects with type 2 diabetes on semaglutide. Journal of Clinical Endocrinology & Metabolism 2019; published online April 2. DOI: 10.1210/jc.2018-02685. Available at: https://academic.oup.com/jcem/advance-article-abstract/doi/10.1210/jc.2018-02685/5423568?redirectedFrom=fulltext.
6. Frias JP, Nauck MA, Van J, et al. Efficacy and safety of LY3298176, a novel dual GIP and GLP-1 receptor agonist, in patients with type 2 diabetes: a randomised, placebo-controlled and active comparator-controlled phase 2 trial. Lancet 2018; published online October 4. DOI: 10.1016/S0140-6736(18)32260-8. Available at: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)32260-8/fulltext.
7. Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2017. Atlanta, GA: Centers for Disease Control and Prevention, U.S. Dept of Health and Human Services; 2017.
8. International Diabetes Federation. *IDF Diabetes Atlas*, 8th edn. Brussels, Belgium: International Diabetes Federation, 2017. http://www.diabetesatlas.org.

Refer to: Dani Barnhizer; dbarnhizer@lilly.com; 317-607-6119 (Lilly Diabetes)

View original content to download multimedia:http://www.prnewswire.com/news-releases/lillys-tirzepatide-demonstrates-benefits-in-data-presented-at-the-american-diabetes-associations-79th-scientific-sessions-300864215.html

SOURCE Eli Lilly and Company