Lilly's muvalaplin lowered lipoprotein(a) levels in adults with high risk for cardiovascular events by up to 85% at highest tested dose

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Muvalaplin, an oral, once-daily treatment that inhibits lipoprotein(a) formation via a novel mechanism, achieved positive results in a 12-week Phase 2 study

These data were published in the Journal of the American Medical Association (JAMA) and simultaneously presented today at the American Heart Association (AHA) Scientific Sessions 2024

INDIANAPOLIS, Nov. 18, 2024 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced positive Phase 2 results for muvalaplin, an investigational once-daily, orally administered selective inhibitor of lipoprotein(a) [Lp(a)], a genetically inherited risk factor for heart disease. The study demonstrated that muvalaplin significantly reduced elevated Lp(a) levels in adults, meeting its primary endpoint of percent change in Lp(a) from baseline to week 12.

At the 12-week primary endpoint, muvalaplin (10 mg, 60 mg and 240 mg) showed significant reductions in Lp(a) levels compared to placebo. The placebo-adjusted reductions were up to 85.8% using an intact Lp(a) assay and up to 70.0% using an apo(a) assay. Specifically, the reductions were 47.6% (10 mg), 81.7% (60 mg) and 85.8% (240 mg) with the intact Lp(a) assay, and 40.4% (10 mg), 70.0% (60 mg) and 68.9% (240 mg) with the apo(a) assay.

"High levels of Lp(a) have been shown to be a significant risk factor for atherosclerotic cardiovascular disease, affecting over one billion adults globally," said Stephen J. Nicholls, MBBS, Ph.D., director of the Victorian Heart Hospital and Institute, and professor of cardiology at Monash University, Australia. "Current cholesterol-lowering therapies are not approved to lower Lp(a) levels, highlighting an unmet need for people living with cardiovascular disease. These data represent a needed scientific advancement with the potential to reduce the risk of cardiovascular events such as heart attacks or strokes with a once-daily pill."

Lilly is evaluating muvalaplin, a potent, multivalent, small molecule that inhibits the formation of Lp(a) by blocking the initial interaction between apolipoprotein(a) [apo(a)] and apolipoproteinB (apoB). In the U.S., about 20% of people, or approximately 63 million individuals, have high levels of Lp(a).[1,2] Elevated Lp(a) levels can double or even triple the risk of a heart attack and are associated with other cardiovascular issues.[3]

"While injectable approaches for Lp(a) are currently in Phase 3 development, including Lilly's own lepodisiran program, these are the first positive Phase 2 data for an oral approach," said Ruth Gimeno, Ph.D., group vice president, Diabetes and Metabolic Research, Lilly Research Laboratories. "We are very pleased to see these promising results and look forward to further exploring next steps for muvalaplin."

Muvalaplin also met secondary endpoints for all three tested doses (10 mg, 60 mg and 240 mg). The three tested doses achieved statistical significance for Lp(a) thresholds, and the 60 mg and 240 mg doses also achieved statistical significance for apoB reductions. These data also demonstrated:

- Using the intact Lp(a) assay, the percentage of participants achieving an Lp(a) level less than 125 nmol/L at week 12 was 64.2% (10 mg), 95.9% (60 mg) and 96.7% (240 mg), compared to 6.0% in the placebo group.
- Using the apo(a) assay, the percentage of participants achieving an Lp(a) level less than 125 nmol/L was 38.9% (10 mg), 81.9% (60 mg) and 77.4% (240 mg), compared to 3.6% in the placebo group.
- ApoB levels were reduced at all doses, with placebo-adjusted reductions of 8.9% (10 mg), 13.1% (60 mg) and 16.1% (240 mg).

Adverse events were similar in both the muvalaplin and placebo groups. Treatment-emergent adverse events related to the study drug occurred in 14.9% of the placebo group, 5.9% of the 10 mg group, 14.3% of the 60 mg group and 14.7% of the 240 mg group. The incidence of adverse events leading to discontinuation of study drug varied from 0 to 8.8% across treatment groups and were single events spread across system organ classes. No deaths were reported in the study.

About Lilly
Lilly is a medicine company turning science into healing to make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help tens of millions of 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/news, or follow us on Facebook, Instagram, and LinkedIn. P-LLY

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 muvalaplin as a potential treatment for people with high risk for cardiovascular events and reflects Lilly's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug research, development, and commercialization.

Among other things, there is no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with study results to date, that muvalaplin will prove to be a safe and effective treatment for the reduction of cardiovascular events associated with a reduction in Lp(a), that muvalaplin will receive regulatory approval, or that Lilly will execute its strategy as expected. For further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, see Lilly's 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. Family Heart Foundation. Lipoprotein(a) - Family Heart Foundation. Last accessed Nov. 13, 2024.
2. Family Heart Foundation. Diagnosing High Lipoprotein(a) - Family Heart Foundation. Last accessed Nov. 13, 2024.
3. Harvard Medical School. Heart Health: The Latest on Lipoprotein(a), an Inherited Cause of Early Heart Disease. Last accessed Nov. 13, 2024.

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