Lp(a) International Task Force Statement on the Lp(a)HORIZON Phase III Topline Announcement

Amsterdam, 7 September 2026 - The Lp(a) International Task Force (ITF) has taken note of the announcement on 4 September 2026 that the Phase III Lp(a)HORIZON cardiovascular outcomes trial of pelacarsen did not meet its primary composite cardiovascular endpoint[1].

Lp(a)HORIZON is an important and pioneering cardiovascular outcomes study involving 8,323 people with elevated lipoprotein(a) [Lp(a)] and established cardiovascular disease. It was designed to investigate whether lowering Lp(a) with pelacarsen could reduce cardiovascular events in people already receiving guideline-directed treatment for cardiovascular disease and other major risk factors. According to the topline announcement, pelacarsen lowered Lp(a), but the study did not meet its primary endpoint of reducing a composite of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke and urgent coronary revascularisation requiring hospitalisation, compared with placebo[2].

At this stage only topline information has been released. The full trial results are not yet available and are expected to be presented and published soon.

Important information needed to interpret the study, including the magnitude of the observed treatment effect, hazard ratios, confidence intervals, individual components of the composite endpoint and detailed subgroup analyses, has not yet been publicly presented. This includes results from the pre-specified population with Lp(a) ≥90 mg/dL. For this reason, the ITF considers it premature to draw definitive conclusions from this announcement about the causal role of Lp(a) in atherosclerotic cardiovascular disease or about Lp(a) lowering as a therapeutic approach.

Lp(a) remains an important cardiovascular risk factor

Elevated Lp(a) remains a well-established, inherited and genetically validated cardiovascular risk factor[3]. A substantial body of genetic, epidemiological and clinical evidence links elevated Lp(a) with atherosclerotic cardiovascular disease, while Lp(a) is also strongly implicated in calcific aortic valve disease[3]. This evidence cannot be interpreted solely through the topline result of a single therapeutic trial, the readouts from other ongoing trials are also important to establish a full picture.

It is particularly important to distinguish between testing for Lp(a) as part of cardiovascular risk assessment [3,4] and treating elevated Lp(a) with a specific investigational therapy. The Lp(a)HORIZON announcement concerns the latter. It does not invalidate the clinical value of knowing a person's Lp(a) concentration. Lp(a) testing can help refine cardiovascular risk assessment and identify people whose inherited risk may be higher than suggested by traditional risk factors alone. This information can support more personalised assessment and

management of overall cardiovascular risk. Current European and US guidelines[5,6] recommend Lp(a) measurement at least once in lifetime to help identify people at increased cardiovascular risk. Recommendations concerning Lp(a) testing and cardiovascular risk assessment therefore remain relevant.

Cardiovascular prevention must continue

The timing of this announcement makes careful interpretation particularly important. Across the globe health systems are increasingly moving towards earlier identification of cardiovascular risk and a shift from treating cardiovascular disease after it occurs towards promoting cardiovascular health and preventing disease wherever possible. In Europe, the Safe Hearts Plan[7] places health promotion, prevention, early detection and screening at the centre of the EU cardiovascular health agenda and foresees an EU protocol on cardiovascular health checks. ***The result of one therapeutic trial should not slow progress towards earlier cardiovascular risk identification, Lp(a) testing and evidence-based cardiovascular disease prevention.***

The complete evidence is still to come

The complete Lp(a)HORIZON dataset will provide valuable new scientific information, including findings that may differ from prior expectations. The study was conducted in people with established cardiovascular disease who were receiving contemporary guideline-directed treatment and who, on average, had very well-controlled traditional risk factors such as LDL-cholesterol and blood pressure. Understanding the findings within this specific population and clinical context will therefore be essential.

A message to people diagnosed with elevated Lp(a)

The ITF recognises that this announcement may be disappointing or concerning for people living with elevated Lp(a), their families and especially those who participated in the trial. We sincerely thank the 8,323 participants, investigators, and clinical teams whose contributions make this important scientific evidence possible. Science advances through every result, including those that challenge expectations. Other cardiovascular outcomes studies of Lp(a)-lowering approaches are ongoing, and the ITF will review the complete Lp(a)HORIZON findings alongside the wider evidence as they become available.

Until then, our message is clear: wait for the complete data, avoid premature conclusions, continue to understand and manage CV risk, and maintain the momentum towards early testing, detection and prevention.

On behalf of the Lp(a) International Task Force (ITF)
Professor Florian Kronenberg, Chair

Independence and transparency:

The Lp(a) International Task Force (ITF) is an independent, international, multi-stakeholder initiative whose Secretariat is hosted by FH Europe Foundation (FHEF), an independent non-profit patient organisation. FHEF receives financial support for the Lp(a) ITF -related activities from multiple industry partners, currently including Amgen, Eli Lilly and Company, Novartis and Roche Diagnostics. Industry partners participate in the ITF as non-voting observers. This statement was developed independently by the ITF based on the scientific information currently available, with input from scientific experts and people with lived experience. No industry partner was involved in determining its conclusions or approving its content. https://lpa-taskforce.org/

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