Cardiology Expert Call

Key Takeaways from the Expert Call on the Evolving Cardiology Landscape

On October 20, we hosted an expert call with Dr. Mark Feinberg, Cardiologist and Professor of Medicine at Harvard Medical School, where we discussed recent data and latest thoughts on the evolving cardiovascular landscape, including lipid/cholesterol management and anticoagulants, with a particular focus on Lp(a), PCSK9 inhibitors, and Factor XI inhibitors. We summarise our key takeaways below:

- **With the presentation of detailed data from Lp(a)HORIZON at AHA 2026, Dr. Feinberg's focus will be on any signals in high-risk subgroups.** Detailed data from the Lp(a) HORIZON trial for pelacarsen in ASCVD with high Lp(a) ≥70mg/dL will be presented at AHA 2026, on November 07 at 8.50am CST. Dr. Feinberg noted that his main focus from the detailed data will be on the level of Lp(a) reduction in patients with baseline Lp(a) above and below 90mg/dL, the absolute level of CV risk across quartiles of baseline Lp(a), and whether there was a signal for benefit in any of these subgroups, potentially in patients with the highest baseline Lp(a). He suggested that the length of time the trial took to accrue events and the limited benefit may have been due to the trial not enrolling enough patients at the highest risk, noting that there is an inflection in CV risk around 90-100mg/dL, whereas c.21% of the trial population had Lp(a) <90mg/dL, and also due to the use of background therapy (see our analysis here) reducing the overall level of CV risk. As a result, he suggested that Lp(a)-lowering therapies may have a better opportunity to show a reduction in CV risk in the primary prevention setting where there is less background therapy use.
- **Oral PCSK9s will help to expand the market, with laroprovstat's lack of a fasting requirement potentially being a compelling point of differentiation, even if it shows efficacy modestly below Lipfendra.** Dr. Feinberg stated that 20-25% of his patients are on PCSK9s (although this is likely higher than in other centres), with the majority using Repatha where uptake has been supported by CV outcomes data in both the primary (VESALIUS-CV) and secondary (FOURIER) prevention settings. He noted that there continue to be barriers to uptake of injectable PCSK9s, including tolerability (mainly injection-site reactions), convenience, and cost, as well as hesitation from patients to inject, and that oral options have the potential to expand the market as a simple add-on therapy with comparable efficacy to injectables, although he mentioned that he would like to see CV outcomes data, and highlighted that this would be a driver of further uptake of the orals. He also noted that while the fasting requirement for Lipfendra is usually manageable for motivated patients, if laroprovstat demonstrates an LDL-C reduction only modestly below Lipfendra, he would see a broad role for the product in the market.
- **Abelacimab would be positioned for AF patients with the highest bleeding risk, while asundexian uptake in secondary stroke prevention is expected to be strong.** Dr. Feinberg sees the ability for milvexian to show non-inferiority to apixaban on stroke/systemic embolism in the LIBREXIA AF trial as a touch and go, with focus likely to be on the net clinical benefit, i.e. the balance of efficacy and bleeding, with potential use depending on the individual risk profile of patients. Assuming slightly worse efficacy for milvexian than apixaban, he would consider milvexian for use in patients with a higher

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bleeding risk, although he noted that abelacimab is being studied directly in patients with the highest risk of bleeding (DOAC-ineligible) and that milvexian would likely have to show data in this setting to support uptake in these highest risk patients. On asundexian, given the strength of the data in OCEANIC-STROKE, Dr. Feinberg expects his neurology colleagues to consider asundexian as an add-on to anti-platelet therapy for secondary stroke prevention and said that he would advocate for its use.

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