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AMGEN SINKS AS CVOT RESULTS DRAW MIXED PAYER REACTIONS

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New cardiovascular outcomes trial data from **Amgen Inc.** (NASDAQ:AMGN) on **PCSK9** inhibitor **Repatha** evolocumab disappointed investors, but payers are still evaluating the data and Amgen's proposed outcome-based pricing model, which could alleviate their risk.

Amgen lost $11.50 to $168.61 Friday after detailed **results** from FOURIER, its Phase III CVOT, showed the hypercholesterolemia drug significantly reduced risk of myocardial infarction (MI) and stroke, but failed to cut the risk of cardiovascular death.

On a key secondary endpoint evaluating Repatha across all three of those CV outcomes, the drug led to a 20% risk reduction (HR:0.80; CI:0.73, 0.88; p<0.001). Amgen said the outcome was driven by benefit in MI and stroke, with a reduced risk of 27% (HR:0.73; CI:0.65, 0.82; p<0.001) and 21% (HR:0.79; CI:0.66, 0.95; p=0.01), respectively, through the study's median follow-up of 26 months.

Repatha failed to reduce the risk of cardiovascular death (HR:1.05; CI:0.88, 1.25; p=0.62) or all-cause death (HR:1.04; CI:0.91, 1.19; p=0.54).

Risk reduction was less pronounced in the primary endpoint, which measured the same three components as the key secondary endpoint along with hospitalization for unstable angina or coronary revascularization. Overall risk reduction was 15% (p<0.001). Repatha did not significantly affect unstable angina (HR:0.99; CI:0.82, 1.18; p=0.89), but reduced risk of coronary revascularization by 22% (HR:0.78; CI:0.71, 0.86; p<0.001).

Payers and pharmacy benefit managers have told BioCentury that unless Repatha led to a risk reduction of at least 20%, they would limit access to the treatment **(see BioCentury, Feb. 3)**.

On Friday, Amgen proposed a risk-sharing plan to stimulate payer coverage, the limitations of which have blunted Repatha's sales thus far. Amgen spokesperson Kristen Neese told BioCentury that "for any compliant Repatha patient who had a heart attack or stroke after taking Repatha for at least six months, payers would receive a refund in the form of an additional rebate." She said Amgen would negotiate details with individual insurers.

Amgen did not respond to inquiries regarding whether it is considering a change in Repatha's price, whether it will provide services or incentives to increase compliance, or its compliance requirements. In a study of 4,853 patients, adherence was 57% among patients receiving Repatha or **Praluent** alirocumab, according to an to be presented Saturday at the **American College of Cardiology** meeting in Washington, D.C.

CVS Health Corp. (NYSE:CVS) spokesperson Christine Cramer told BioCentury that the company "expects an increase" in patients using PCSK9 inhibitors and anticipates "a broader group of patients being eligible for treatment," but it will wait for updated expert guidelines before making changes.

Roger Longman, CEO of health consultancy Real Endpoints LLC, said he was "surprised" by Amgen's results, adding that a 25% risk reduction might be necessary for physicians to be motivated to cut the red tape around prior authorization. **Express Scripts Holding Co.** (NASDAQ:ESRX) said that "while having this data does not expand the current indication," it "may make physicians more likely to prescribe the medications." Via a partnership with The **Familial Hypercholesterolemia Foundation** (Pasadena, Calif.), Express Scripts recently expanded its coverage of PCSK9s to treat familial hypercholesterolemia **(see BioCentury Extra, March 15)**.

On a conference call Friday, Amgen SVP of Global Value, Access and Policy Joshua Ofman said the company has "numerous" innovative contracts in place for Repatha, and the company expects "interest" from payers, but is "not sure how extensive it will be."

The FOURIER data drove down shares of other companies with cholesterolemia candidates. **Esperion Therapeutics Inc.** (NASDAQ:ESPR) sank $5.98 (20%) to $23.67, while **The Medicines Co.** (NASDAQ:MDCO) lost $4.20 to $48.38. Esperion is studying the effects of bempedoic acid (**ETC-1002**), an **ATP citrate lyase (ACLY)** inhibitor, on LDL-C lowering in three Phase III trials. Medicines Co. said last year it plans to "aggressively" move its PCSK9-inhibiting RNA therapy, **inclisiran**, into Phase III studies.

Regeneron Pharmaceuticals Inc. (NASDAQ:REGN) lost $12.30 to $380.29 on Friday. **Sanofi** (Euronext:SAN; NYSE:SNY) and Regeneron expect data this year from a CVOT of competing PCSK9 inhibitor Praluent. The partners are appealing a federal court decision that would bar U.S. sales of Praluent **(see BioCentury Extra, Feb. 8)**.