Goal Achievement after Utilizing an Anti-PCSK9 Antibody in Statin Intolerant Subjects (GAUSS): Interim Results from a Randomized, Double-blind, Placebo-controlled Study

- **Background:** Many patients experience muscle-related side effects to statins and cannot meet goal lipid levels with alternative methods. Plasma proprotein convertase subtilisin/kexin type 9 (PCSK9) binds LDL receptors, therefore increasing levels of LDL-C in the blood. Phase 1 studies of a human monoclonal antibody to PCSK9, AMG145, have shown tolerance and effectiveness in lowering LDL-C.
- **Purpose:** To assess the effectiveness and safety of AMG145 in patients with muscle-related statin intolerance.
- **Methods:** During the 12-week, phase 2, randomized, double-blind, placebo- and ezetimibe-controlled study, 160 patients were randomized to one of 5 treatments: 280 mg, 350 mg, or 420 mg of AMG145, 420 mg AMG145 plus 10 mg ezetimibe, or placebo plus 10 mg ezetimibe administered subcutaneously every 4weeks. Primary endpoint was percent change in LDL-C levels from baseline to 12 weeks.
- **Results:** At week 12, mean percent decrease in LDL-C ranged from -67% in the 280 mg group to -110 in the 420 mg plus ezetimibe group compared with only -14% decrease in the placebo group. Four serious adverse events were reported among the AMG145 patients. Myalgia was the most common side effect reported.

Percent of Patients Treated to LDL-C Goal at Week 12

Treatment	LDL-C < 100 mg/dL	LDL-C < 70 mg/dL
280 mg AMG145	47%	9%
350 mg AMG145	53%	17%
420 mg AMG145	61%	29%
420 mg AMG145 + ezetimibe	90%	62%
Placebo + ezetimibe	7%	0%

- **Conclusions:** Treatment with AMG145 displayed short-term tolerability and significant reduction in LDL-C levels.

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