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Bococizumab (RN316) Significantly Reduced LDL Cholesterol In Statin-Treated Adults With High Cholesterol In A Phase 2b Study

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Results Presented at the American College of Cardiology's (ACC) 63rd Annual Scientific Session in Washington D.C. Phase 3 Program Focused on CV Outcomes in Patient Populations at High Risk for Cardiovascular Events

Pfizer Inc. (NYSE: PFE) today announced the Phase 2b results of a 24 week, randomized, placebo-controlled, dose-ranging study of investigational bococizumab, the proposed generic name for RN316. Statin treated patients with high cholesterol were randomized to various doses of either bococizumab twice or once monthly subcutaneous administration or placebo. The study met its primary endpoint across all doses, showing that bococizumab significantly reduced low density lipoprotein cholesterol (LDL-C) from baseline compared to placebo in adults with high cholesterol also taking statin therapy.[1] The percentage of patients reporting adverse events or serious adverse events was similar across placebo- and bococizumab-treatment groups. The Phase 3 program for bococizumab was initiated in October 2013.

Elevated LDL-C is recognized as a major risk factor for cardiovascular disease,[2] the number one cause of death worldwide despite the widespread availability of statin therapy.[3]

"I am hopeful that bococizumab, as a member of the PCSK9 class, will play an important role in understanding and addressing the unmet need for patients at high risk for cardiovascular events. The Phase 3 CV outcome studies for this class of medicine will be the most critical in defining future clinical practice," said Christie M Ballantyne, Chief of the Section of Cardiology and Cardiolvascular Research from Baylor College of Medicine.

This dose-ranging, double-blind, placebo-controlled study in 354 patients examined two dosing regimens: twice monthly (bococizumab 50 mg, 100 mg or 150 mg) and once monthly (bococizumab 200 mg or 300 mg). For both regimens, the bococizumab dose was lowered if LDL-C was reduced to ?25 mg/dL. The first opportunity for dose reduction was at Week 6 for the twice monthly and Week 8 for the once monthly regimen. The primary efficacy analysis was the placebo-adjusted change from baseline in LDL-C at Week 12.[1] The mean baseline LDL across doses was 109 mg/dL.

Bococizumab twice and once monthly dosing regimens were associated with significant placebo-adjusted reductions in LDL-C at Week 12, with the greatest reductions seen with 150 mg for the twice monthly regimen

and 300 mg for the once monthly regimen.[1]

Prior to the majority of dose reductions due to an LDL-C ?25mg/dL, the LDL-C changes seen with these regimens were greater than those observed at Week 12 (primary endpoint).[1]

Dosing regimens1	Primary Analysis: Mean change from baseline in LDL-C at Week 12 (placebo-adjusted)	Maximum mean change from baseline in LDL-C (placebo-adjusted)
150mg twice monthly	-53.4 mg/dL	-66.9 mg/dL (week 8)
300mg once monthly	-44.9 mg/dL	-54.9 mg/dL (week 4)

“We are pleased with the outcome of this Phase 2b study and continue to maintain focus on delivering our Phase 3 program, which includes two CV outcome studies in populations at high risk from cardiovascular events,” said Dr. Steven Romano, Global Medicines Development Lead for the Pfizer Global Innovative Pharmaceutical business. “Recent guidelines emphasize the reduction of CV risk as the primary goal of lipid therapy for patients at risk for CV events.”

The bococizumab Phase 3 program consists of two cardiovascular outcome studies as well as multiple lipid-lowering studies in more than 22,000 patients. One of the two CV outcome studies, SPIRE-1, will assess whether lowering LDL-C to levels well below current guideline-recommended targets will lead to further reduction in cardiovascular events.[4] This study includes a high-risk patient population with baseline levels of LDL-C ranging from 70 to 100 mg/dL. The second CV outcome study, SPIRE-2, will evaluate the efficacy and safety of bococizumab in a range of high-risk patients who have not achieved LDL levels lower than 100 mg/dL despite the use of high-dose statins or who are partially or completely statin intolerant.[5] The Phase 3 program will evaluate the efficacy and safety of 150 mg twice monthly as a starting dose.

About bococizumab

Bococizumab, the proposed generic name for RN316 (PF-04950615), is an injectable monoclonal antibody in development that works by blocking the function of a protein called Proprotein Convertase Subtilisin Kexin type 9, better known as “PCSK9”, which interferes with the clearance of LDL-C, a leading known risk factor for heart disease. Bococizumab is an investigational compound and has not received regulatory approval in any country.

More information about the bococizumab Phase 3 program studies that have been initiated can be found at www.clinicaltrials.gov.

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This release contains forward-looking information about a product candidate, bococizumab, including its potential benefits, that involves substantial risks and uncertainties. Such risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the ability to meet anticipated clinical trial completion dates, as well as the possibility of unfavorable clinical trial results; whether and when any drug applications may be filed in any jurisdictions for bococizumab; whether and when any such applications may be approved by regulatory authorities as well as their decisions regarding labeling and other matters that could affect its availability or commercial potential; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2013 and in its subsequent reports on Form 10-Q and Form 8-K.

[1] Ballantyne C, Neutel J, et al. Efficacy and Safety of Bococizumab (RN316/PF-04950615), a Monoclonal Antibody Against Proprotein Convertase Subtilisin/Kexin Type 9 in Statin-Treated Hypercholesterolemic Subjects: Results from a Randomized, Placebo-Controlled, Dose-Ranging Study (NCT: 01592240). Poster presented at: American College of Cardiology 63rd Annual Scientific Session and Expo, March 30, 2014, Washington, D.C.

[2] Grundy Scott M. Promise of Low-Density Lipoprotein–Lowering Therapy for Primary and Secondary Prevention, *Circulation.* 2008; 117: 569-573. http://circ.ahajournals.org/content/117/4/569.full.Published January 29, 2008. Accessed March 6, 2014.

[3] Cardiovascular diseases. World Health Organization. http://www.who.int/mediacentre/factsheets/fs317/en/.Published March 2013. Accessed March 6, 2014.

[4] ClinicalTrials.gov. The Evaluation Of PF-04950615 (RN316), In Reducing The Occurrence Of Major Cardiovascular Events In High Risk Subjects (SPIRE-1). http://clinicaltrials.gov/ct2/show/study/NCT01975376?term=SPIRE-1&rank=1. Published March 6, 2014. Accessed March 19, 2014

[5] ClinicalTrials.gov. The Evaluation Of PF-04950615 (RN316) In Reducing The Occurrence Of Major Cardiovascular Events In High Risk Subjects (SPIRE-2). http://clinicaltrials.gov/ct2/show/NCT01975389?term=SPIRE-2&rank=1. Published March 4, 2014. Accessed March 19, 2014.

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