A Randomized, Controlled, Phase 3 Trial of Sofosbuvir/Velpatasvir/Voxilaprevir or Sofosbuvir/Velpatasvir for 12 Weeks in Direct Acting Antiviral-Experienced Patients with Genotype 1-6 HCV Infection: The POLARIS-4 Study

Stefan Zeuzem,1 Steven L. Flamm,2 Myron J. Tong3, John M. Vierling4, Stephen Pianko5, Peter Buggisch6, Victor de Ledinghen7, Robert H. Hyland8, Xiaoru Wu8, Eugenia S. Suvoskiausk8, Luisa M. Stamm8, Diana M. Brainard10, John G. McHutchison8, Elizabeth C. Verna9, Meena B. Bansal10, Charles S. Lands11, Simone I. Strasser12, Curtis Cooper13, Kris V. Kowdley14,

1Johann Wolfgang Goethe University Medical Center, 2Northwestern University, 3Huntington Medical Research Institutes, 4Baylor College of Medicine, 5Monash University, 6ifi-Institute for Interdisciplinary Medicine, 7University Hospital of Bordeaux, 8Gilead Sciences, Inc, 9Columbia University Medical Center, 10Ichan School of Medicine at Mount Sinai, 11University of Washington, 12Royal Prince Alfred Hospital, 13Ottawa Hospital, 14Swedish Medical Center

Sponsorship - This study was sponsored by: (If this abstract was not sponsored please indicate) Gilead Sciences, Inc

Abstract Body

Introduction: Direct acting antivirals (DAAs) provide safe and highly efficacious therapies for HCV infection. However, the small proportion of patients who do not achieve a sustained virologic response with DAA-based regimens represent a population with an unmet medical need. Sofosbuvir (SOF) and velpatasvir (VEL) are pangenotypic inhibitors of the HCV NS5B and NS5A proteins, respectively, and voxilaprevir (VOX, GS-9857) is a pangenotypic HCV NS3/4A protease inhibitor. This Phase 3 study evaluates treatment with a SOF/VEL/VOX fixed dose combination (FDC) for 12 weeks and a SOF/VEL FDC for 12 weeks as salvage regimens in DAA-experienced patients who had not previously received an NS5A inhibitor.

Methods: Patients at 101 sites in North America, Europe, Australia and New Zealand were enrolled and those with genotypes 1, 2 or 3 were randomized 1:1 to receive open-label SOF/VEL/VOX or SOF/VEL for 12 weeks, stratified according to genotype and cirrhosis status. Patients of all other genotypes were assigned to receive SOF/VEL/VOX for 12 weeks. DAA-experienced patients who previously were treated with an NS5A inhibitor or with an NS3/4A protease inhibitor in combination with ribavirin and Peg-IFN were excluded. The primary endpoint evaluates the superiority of the sustained virologic response 12 weeks after treatment (SVR12) of each treatment to a pre-specified performance goal of 85%.

Results: Of the 333 patients who were randomized and treated, 77% were male, 86% were white, 18% had the IL28B CC genotype, 46% had compensated cirrhosis, 57% were from the United States and 40% had genotype 1 HCV infection. Most patients had prior DAA experience with either an NS5B inhibitor alone (73%) or an N5SB inhibitor and an NS3/4A protease inhibitor in combination with ribavirin and Peg-IFN were excluded. The primary endpoint evaluates the superiority of the sustained virologic response 12 weeks after treatment (SVR12) of each treatment to a pre-specified performance goal of 85%.

Conclusions: The single tablet regimens of SOF/VEL/VOX and SOF/VEL for 12 weeks have the potential to provide safe, well tolerated and effective retreatment options for patients who did not previously achieve SVR following treatment with non-NS5A inhibitor-containing DAA regimens.