A Randomized Phase 3 Trial of Sofosbuvir/Velpatasvir/Voxilaprevir for 8 Weeks and Sofosbuvir/Velpatasvir for 12 Weeks for Patients with Genotype 3 HCV Infection and Cirrhosis: The POLARIS-3 Study

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

Abstract Body Introduction: Patients with HCV genotype 3 infection, particularly those with cirrhosis, have emerged in the current era of DAA regimens as a more difficult to cure population. Voxilaprevir (VOX, GS-9857) is a pangenotypic inhibitor of the HCV protease. We hypothesized that the addition of VOX to create a fixed dose combination (FDC) targeting 3 distinct viral proteins would allow treatment to be shortened to 8 weeks while maintaining high rates of SVR12. This Phase 3 study evaluates treatment with SOF/VEL/VOX FDC for 8 weeks and SOF/VEL FDC for 12 weeks in patients with genotype 3 HCV infection and cirrhosis.

Methods: Patients at 84 sites in North America, Europe, Australia, and New Zealand were randomized 1:1 to receive open-label SOF/VEL (400 mg /100 mg daily) FDC for 12 weeks or SOF/VEL/VOX (400 mg /100 mg /100 mg daily) FDC for 8 weeks. Patients were stratified according to their prior treatment with an interferon-based regimen. Patients had cirrhosis defined by liver biopsy, Fibroscan >12.5 kPa, or combined Fibrotest >0.74 and APRI >2.0. HCV RNA was measured with the CAP/CTM HCV 2.0 assay with LLOQ =15 IU/mL. The primary endpoint compares the sustained virologic response 12 weeks after treatment (SVR12) of each treatment, to a pre-specified historic control rate of 83%. Secondary endpoints included safety and tolerability, viral resistance, and additional efficacy outcomes.

Results: Of 219 patients randomized and treated, 72% were male, 89% were white, 42% had the IL28B CC genotype, and 30% had previously failed treatment with an interferon-based regimen. Patients from the US (44%) and other regions (56%) were well represented. Most (90%) patients with treatment experience had received a Peg-IFN+RBV regimen. All patients had cirrhosis; the median platelet count was 139x10^3 cells/µL with 24% of patients having a platelet count of <100 x10^3 cells/µL. Treatment was well tolerated; at the time of abstract submission, one patient has discontinued therapy due to an unrelated adverse event. No serious adverse events attributed to either study medication had been reported. Complete safety and SVR12 data for all patients will be presented.

Conclusions: The single tablet regimen of SOF/VEL/VOX for 8 weeks has the potential to be a safe, well tolerated and effective treatment option for genotype 3 patients with cirrhosis.

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