Title: Pharmacokinetics of Glecaprevir/Pibrentasvir in Children with Chronic HCV Infection: Interim Analysis of Part 2 of the DORA Study

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ABSTRACT (2182 characters/2500 characters)

Background: The pangenotypic regimen of glecaprevir and pibrentasvir (G/P) (GLE; identified by AbbVie and Enanta) is the first approved pangenotypic treatment for adults and adolescents with chronic hepatitis C virus (HCV) infection, and has yielded high cure rates in these populations in Phase 2 and 3 studies. A highly effective pangenotypic regimen with improved tolerability for children 3–11 years of age remains an unmet need.

Methods: DORA (NCT03067129) is an ongoing phase 2/3, non-randomized, open-label, multicenter study evaluating the pharmacokinetics (PK), safety and efficacy of G/P in pediatric patients with chronic HCV infection. For Intensive PK (IPK) analysis after dose adjustment, the

pediatric population was divided into 3 cohorts: cohort 1 (9–11 years, ≥ 30 to < 45 kg, N = 10); cohort 2 (6–8 years, ≥ 20 to < 30 kg, N = 9); and cohort 3 (3–5 years, 12 to < 20 kg, N = 10). Pediatric dosage of G/P was determined as 250 mg GLE + 100 mg PIB for cohort 1, 200 mg + 80 mg for cohort 2, and 150 mg + 60 mg for cohort 3. We present an IPK analysis of treatment-naïve patients aged 3-11 years, who received a novel pediatric pellet formulation.

Results: Part 2 enrolled 48 pediatric patients. 40% (19/48) of patients were male; 77% (37/48) were white. Median (range) age and median (range) weight were 7 (3–11) years and 24 (13–44) kg, respectively. Median (range) HCV RNA level was 6 (3–7) log10 IU/mL. All patients were non-cirrhotic and received G/P for 8 weeks. The primary PK endpoint, steady-state AUC values for GLE and PIB, was evaluated. One patient received double doses the day of the week 2 study visit and was thus excluded from the IPK analysis. The predicted PK exposures (AUC_{24}) of GLE and PIB for the cohorts are shown in **Table.** Compared to the adult target GLE and PIB steady-state exposures in adults (4800 and 1430 hr*ng/mL, respectively), the target AUC/predicted AUC ratio for both GLE and PIB is between 1.00 to 1.31. Efficacy evaluation is ongoing, and to date, 45/46 patients (98%) achieved SVR4 without any on-treatment virologic failures. One GT3 patient experienced relapse by post-treatment week 4; and data is pending for the remaining patients. The safety profile of GLE/PIB demonstrated in these younger cohorts to date is comparable to those in adolescents and adults.

Conclusion: IPK exposures of GLE and PIB in pediatric patients treated with the new pellet formulation were comparable to exposures in adults and adolescents from Part 1 of the study.

Pediatric patients with chronic HCV infection treated with G/P achieved high rates of SVR4, with only one virologic relapse, and comparable safety profile to that in adults and adolescents.

Table: Steady State Pharmacokinetics of GLE and PIB in HCV-Infected Pediatric Patients				
	Glecaprevir		**Pibrentasvir**	
	Pop-PK AUC* (hr*ng/mL)	AUC/Target AUC ratio	Pop-PK AUC* (hr*ng/mL)	AUC/Target AUC ratio
Cohort 1 (9-11 years)	5180	1.08	1440	1.00
Cohort 2 (6-8 years)	5770	1.20	1460	1.02
Cohort 3 (3-5 years)	6310	1.31	1430	1.00
*Pop-PK AUC shows the predicted PK exposures of GLE and PIB based on all the currently available PK information collected in the study (including data from other study weeks)				