The Pharmacokinetics (PK) of GBT440 are Similar in Adolescents and Adults with Sickle Cell Disease (SCD)

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INTRODUCTION
- Sickle cell disease (SCD) is a genetic disorder resulting in the production of mutated hemoglobin (HbS) that deoxygenates readily and precipitates in the bloodstream causing vaso-occlusive events.
- SCD is a heterogeneous hemoglobinopathy with disease beginning in childhood; approximately 85% of SCD is HbSS and 15% HbSC disease, respectively. The clinical manifestations of SCD are determined by the severity of acute (vaso-occlusive crises) and chronic disease (organ damage).

METHODS
- A non-compartmental PK analysis usingPhoenix WinNonlin® Version 6.4.0 was performed using data from 2 single dose cohorts (Part A and Part B).
- The adult PPK model was used to simulate the PK in adolescents using the same model structure (3 compartment model with 1st order absorption). The adult PK model was validated using the single dose adolescent cohort data.
- Key model parameters are presented in Table 3.

RESULTS
- All 30 evaluable subjects completed Part A of the study and data are summarized below.
- Based on dose normalization and simulations, the PK of GBT440 in adolescents following a single dose of 900 mg was similar to those observed in adults.

CONCLUSIONS
- Single dose PK results from the study support: GBT440 is well tolerated following a single dose (900 mg) in adolescents.
- The PK exposure and half-life for GBT440 were similar in adults and adolescents and confirm the dosing regimen for GBT440 in adults and adolescents.

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1371.6 (38.2%)

Daily doses of 900 mg and 1500 mg, which are currently being evaluated in the pivotal Phase 3 HOPE study, were selected to be evaluated in adolescents.

Adolescents (12 to 17 years) were selected to be evaluated in the pivotal Phase 3 HOPE study.

Due to dose proportionality in adults, high dose evaluation of GBT440 in a pediatric population was deemed unnecessary.

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