A phase 1, single and multiple ascending dose study of safety, tolerability, pharmacokinetics and pharmacodynamics of AG-519, an allosteric activator of pyruvate kinase-R in healthy subjects

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BACKGROUND

- Pyruvate kinase (PK) deficiency as an oral etiologic variant in Mediterranean anemia is associated with several complications.
- PK deficiency is caused by a functional deficiency of the PK-R isozymes due to mutations in the PKLR gene, more than 20% of which have been identified.
- This results in defective glycolysis in tissue and therefore decreased oxygen-dependent glycolytic ATP production.

METHODS

- An ongoing phase 1 study in healthy volunteers aims to identify a safe and pharmacodynamically active dose and pharmacokinetic profile of AG-519.

OBJECTIVES

- To assess the safety and pharmacokinetics/pharmacodynamics (PK/PD) results from the first phase 1 study of AG-519.

RESULTS

- Dose administered.
  - Placebo
  - 125 mg AG-519 q12h
  - 375 mg AG-519 q12h

CONCLUSIONS

- AG-519 has a tolerable safety profile to date and was well tolerated in healthy subjects receiving a single dose up to 1250 mg or 375 mg q12h for 14 days.
- The dose-related changes in PK-R activation in AG-519 in healthy individuals are consistent with increased activity of PK-R.

REFERENCES