Background

- TheKITD816V mutation is the molecular driver in approximately 95% of systemic mastocytosis cases which have been shown to be vulnerable to KITD816V inhibition.1,2
- Avapritinib, a selective and potent KIT D816V inhibitor, is approved for the treatment of systemic mastocytosis.

Methods

- Primary objective of this first-in-human study was to assess the safety and tolerability of BLU-263 following administration of SAD and MAD in healthy adult subjects.
- Secondary objective was to assess the plasma PK of SAD and MAD of BLU-263, as well as to assess the dose-effect and concentration-effect relationships of BLU-263 on electrocardiogram (ECG) intervals in healthy adult subjects. In addition, dose- and concentration-effects of BLU-263 on pharmacodynamic (PD) biomarkers were exploratory objectives.

Results

- All AEs were reported as Grade 1 (mild) in severity and resolved.
- No serious AEs or discontinuations due to AEs were reported.
- None of the TRAEs were associated with dose escalation.
- No abnormal vital sign findings were noted (pulse rates & blood pressure).
- No abnormalities on ECG/EKG intervals were noted.
- No changes in laboratory parameters, including liver function tests, were noted.
- No changes in pharmacodynamic biomarkers were noted.

Conclusions

- In healthy volunteers, BLU-263, a next-generation investigational KIT D816V inhibitor, was safe at all doses tested.
- The pharmacokinetics of BLU-263 were linear across the dose range in SAD and MAD cohorts and the half-life supports once-daily dosing.
- These results support continued development of BLU-263 for patients with systemic mastocytosis.
- The phase 2/3 HARBOR study will evaluate BLU-263 doses ranging from 25 to 100 mg QD in patients with non-advanced systemic mastocytosis, with an anticipated start in mid-2021.

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