Updated safety and efficacy results from phase I/II study of HM6173 in patients (pts) with EGFR mutation positive non-small cell lung cancer (NSCLC) who failed previous EGFR-tyrosine kinase inhibitor (TKI)

INTRODUCTION
- NSCLC patients having an activating EGFR mutation initially benefit from epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs), however, the majority of them develop resistance to treatment 1,2.
- The T790M mutation in EGFR, found in approximately 50-60% cases, is known to be associated with the acquired resistance to EGFR TKIs 1,2.
- HM6173 is an orally active, novel EGFR mutant selective inhibitor showing an anti-cancer activity in several EGFR mutant lung cancer cell lines including T790M mutation harboring cell line.
- HM6173 300 mg showed clinical activity in NSCLC patients, most prominent in T790M positive tumors (ORR 29.2%, DCR 79.0%) and in T790M negative (ORR 11.4%, DCR 56.5%). Therefore, separate expansion cohorts opened at 800 mg QD dose, to investigate efficacy of HM6173 in patients with confirmed T790M positive NSCLC.

METHODS
- This was a Phase III, open-label, multicenter study of HM6173 administered orally in NSCLC patients with EGFR mutation (NCT01588148).
- Figure 1. HM6170-101 study design

RESULTS
- Table 2. Baseline characteristics (FAS)
- Table 3. Summary of safety
- Table 4. Summary of overall safety
- Table 5. Adverse events, regardless of causality in any subject
- Table 6. Summary of Best ORR in T790M positive patients at 800 and 300 mg QD
- Figure 2. Dose escalation and dose limiting toxicity
- Figure 3. Dose limiting toxicities (DLTs) occurred in 5 subjects during the first cycle of treatment (Table 3). 500 mg QD is defined as maximum tolerated dose (MTD).
- Figure 4. Change in target lesions over time in T790M positive patients at 800 mg QD
- Figure 5. Duration of treatment and best ORR in T790M positive patients at 800 mg QD
- Figure 6. Best change from baseline and best ORR in T790M positive patients at 800 mg QD

CONCLUSIONS
- The MTD of HM6173 was determined as 800 mg QD.
- HM6173 was well tolerated with the majority of AEs being mild to moderate. Most AEs were well manageable and reversible.
- HM6173 shows significant and clinically meaningful anti-tumor activity in patients with T790M positive NSCLC. Data support further evaluation of HM6173 in this population. PR was observed in 34 of 62 evaluable patients (ORR: 54.8% and DCR: 92.2%).
- Global Phase II trial to assess the clinical efficacy of HM6173 in NSCLC patients with T790M mutation is planned to launch.

REFERENCES

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