BACKGROUND

- KRASmut mutations as oncogenic drivers. In China, these mutations occur in approximately 4.3% of lung cancer, 2.5% of colorectal cancer (CRC), and 2.3% of biliary cancer.

- JAB-21822 (Jabco) is a novel, highly selective, orally bioavailable, covalent KRASmut inhibitor.

- Preclinical data have demonstrated that JAB-21822:
  - Has potent in vitro and in vivo antitumor activity
  - Has better oral bioavailability resulted in higher drug exposure compared with two leading KRASmut inhibitors in US
  - Exhibits favorable safety profile with no risk of QT prolongation

- We present the data of the phase I portion of study (NCT05009329).

METHODS

- Key eligibility criteria:
  - Measurable disease according to RECIST v 1.1
  - No more than 3 lines of prior therapy (specifically NSCLC expansion cohort)
  - Malignancy refractory or intolerable to standard of care (SOC), or are not willing to receive SOC therapy
  - Patients with advanced solid tumors who are refractory or intolerable to advanced or metastatic solid tumor with preferable KRAS
  - KRAS G12C mutation.

- Dose Escalation
  - Determined by BID and TID cohort in patients with NSCLC 1
  - Determined by QD cohort comparing grades 1-2

- Expansion dose determined
  - BID: one patient 800 mg QD and one patient 400 mg BID; 
  - TID: 800 mg BID, 400 mg BID, and 400 mg QD

RESULTS

- Study Objectives:
  - Determine maximum tolerated dose (MTD) and recommended phase 2 dose (RP2D)
  - Characterize pharmacokinetic (PK) profile of JAB-21822 after single and multiple doses
  - Evaluate preliminary antitumor activity
  - The trial is being conducted in multiple centers in China
  - The data of study is April 1, 2022

- As of April 1, 2022, a total of 72 patients have received at least one dose of JAB-21822.

- Two NSCLC patients in the 200 mg QD cohort did not have KRAS G12C mutation.

- Most patients are heavily treated with 51% having received ≥ 2 prior lines of therapy.

- By April 1, 2022, a total of 72 patients have received at least one dose of JAB-21822.

- Of 41 evaluable patients, 24 (58.5%) were Asian, and 17 (41.5%) were White.

- Most common AE (frequency ≥ 10%) amongst all cohorts:
  - Blood bilirubin increased
  - Anemia
  - Electrolyte abnormal (sodium, potassium, chloride)
  - Transaminase increased
  - Hypophosphatemia
  - Partial TRAEs in all cohorts

- Notable findings:
  - 88.9% of patients had ≥ 2 prior lines of therapy
  - 79.4% had ≥ 3 prior lines of therapy

- No Grade 3-4 TRAEs in QD cohort comparing with BID or TID cohort

REFERENCES

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Abstract #3089: A Phase I/II study of first-in-human trial of JAB-21822 (KRAS G12C inhibitor) in advanced solid tumors