和鉑醫藥控股有限公司

HBM Holdings Limited

(incorporated in the Cayman Islands with limited liability)

(Stock Code: 02142)

VOLUNTARY ANNOUNCEMENT
RESULTS FROM PHASE I CLINICAL TRIAL OF PORUSTOBART (HBM4003) IN COMBINATION WITH TORIPALIMAB IN ADVANCED MELANOMA

This announcement is made by HBM Holdings Limited (the "**Company**", together with its subsidiaries, the "**Group**") on a voluntary basis to inform the shareholders and potential investors of the Company about its latest business updates.

The board of directors of the Company (the "**Board**") is pleased to announce results from its Phase I clinical trial of porustobart (HBM4003), independently developed by the Company, in combination of toripalimab in advanced melanoma and other solid tumors (trial code: NCT04727164, the "**Phase I Study**"). The clinical data abstract has been published at the European Society for Medical Immuno-Oncology (ESMO I-O) 2022 Annual Congress.

The Phase I Study Design

The Phase I Study is an open-label study to evaluate the safety, tolerability, pharmacokinetics (PK)/ pharmacodynamic (PD) and preliminary efficacy of HBM4003 in combination with toripalimab in patients with advanced melanoma and other solid tumors.

The Phase I Study includes two parts: (i) in the dose-escalation part (Part 1), patients with solid tumors received HBM4003 at 3 dose levels (0.03 mg/kg n=1, 0.1 mg/kg n=3, and 0.3 mg/kg n=10) plus toripalimab 240 mg every three weeks (Q3W); (ii) in the dose-expansion part (Part 2), patients with advanced melanoma (n=26) received the recommended Phase II dose (RP2D) of HBM4003 0.3 mg/kg plus toripalimab 240 mg Q3W.

Key Results of the Phase I Study

Key results of the Phase I Study include:

(i) As of 31 August 2022, a total of 40 patients had been dosed and the median follow-up time was 106.5 days.

(ii) HBM4003 in combination of toripalimab in advanced melanoma showed a favourable safety profile.

Treatment-related adverse events (TRAEs) were reported in 87.5% (35/40) patients, and ≥Grade 3 TRAEs were reported in 20.0% (8/40) patients. The most commonly reported TRAE was rash (30.0%).

(iii) HBM4003 in combination of toripalimab showed great anti-tumor activity regardless of prior-line treatment:

- In anti-PD-(L)1 naïve group, the ORR and DCR were 53.3% and 73.3%
- In anti-PD-(L)1 pretreated group, the ORR and DCR were 11.8% and 35.3%

Patients with advanced melanoma treated with RP2D (including 8 patients in Part 1 and 26 patients in Part 2) were categorized as anti-PD-(L)1 naïve group (Cohort A, 17 patients) and anti-PD-(L)1 pretreated group (Cohort B, 17 patients).

For cohort A, the ORR and DCR were 53.3% (95%CI: 26.6-78.7) and 73.3% (95%CI: 44.9-92.2) respectively in the 15 patients with post-treatment tumor assessment. The ORR of cutaneous, acral, mucosal and unknown subtype were 66.7% (2/3), 50% (2/4), 60.0% (3/5) and 33.3% (1/3), respectively.

For Cohort B, the ORR and DCR were 11.8% (95%CI: 1.5-36.4) and 35.3% (95%CI: 14.2-61.7) respectively, including one patient achieving PR after pseudo-progression. Both of the PR cases were mucosal subtype.

Conclusions

HBM4003 0.3 mg/kg plus toripalimab 240mg Q3W showed promising anti-tumor activity in patients with advanced melanoma including acral and mucosal subtypes, as well as an acceptable safety profile.

The above results demonstrated robust clinical response rate in difficult-to-treat melanoma subtypes in Asians, such as mucosal and acral melanoma that were generally not sensitive to immunotherapy including anti-PD-(L)1 antibodies. The results showed great potential to develop HBM4003 as a cornerstone therapy in immuno-oncology. The Company is also conducting other clinical studies of combination therapy for other advanced solid tumors, such as hepatocellular carcinoma and neuroendocrine tumors/neuroendocrine carcinoma.

About HBM4003

HBM4003 is a fully human anti-CTLA-4 monoclonal heavy chain only antibody (HCAb) generated from Harbour Mice®. By enhancing antibody-dependent cell cytotoxicity (ADCC) killing activity, HBM4003 has demonstrated significantly improved depletion specific to high CTLA-4 Treg cells in tumor tissues. The potent anti-tumor efficacy and differentiated pharmacokinetics with durable pharmacodynamic effect presents a favorable product profile. This novel and differentiated mechanism of action has the potential to improve efficacy while significantly reducing the toxicity of the drug in monotherapy and combo-therapy.

Cautionary Statement: We cannot guarantee that we will be able to develop, or ultimately market, HBM4003 successfully. Shareholders and potential investors of the Company are advised to exercise due care when dealing in the shares of the Company.

By order of the Board
HBM Holdings Limited
Dr. Jingsong Wang
Chairman and Executive Director

Hong Kong, 8 December 2022

As at the date of this announcement, the board of directors of the Company comprises Dr. Jingsong Wang and Dr. Yiping Rong as executive Directors; Mr. Yu Min Qiu, Mr. Junfeng Wang and Ms. Weiwei Chen as non-executive Directors; Dr. Robert Irwin Kamen, Dr. Xiaoping Ye and Mr. Ka Chi Yau as independent non-executive Directors.