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 IB CLINICAL TRIAL OF PORUSTOBART (HBM4003) IN COMBINATION WITH TORIPALIMAB IN ADVANCED HIGH-GRADE NEUROENDOCRINE NEOPLASMS

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 the latest business update of the Group.

The board of directors of the Company (the "**Board**") is pleased to announce the results of its Phase Ib clinical trial of porustobart (HBM4003), independently developed by the Company, in combination of toripalimab in patients with advanced high-grade neuroendocrine neoplasms ("**NENs**") (trial code: NCT05167071, the "**Phase Ib Study**") had been scheduled for presentation in a poster session at the American Association for Cancer Research (AACR) Annual Meeting 2023 and published in the online proceedings of the AACR.

This is an open label Phase Ib clinical study to evaluate the safety, tolerability, PK/PD and preliminary efficacy of HBM4003 combined with toripalimab in patients with advanced NEN and other solid tumors.

Title: A Phase Ib dose-expansion study of porustobart, an anti-CTLA-4 heavy chain only monoclonal antibody, in combination with toripalimab in patients with advanced high-grade NENs

Location: Poster Section 47

Poster Board Number: 3

Abstract Presentation Number: CT263

Methods

Patients (pts) with pretreated advanced high-grade NENs received porustobart at one of the two dose levels (0.3 mg/kg and 0.45 mg/kg) plus toripalimab 240 mg every three weeks (Q3W). The primary endpoint is objective response rate (ORR) per RECIST 1.1 by investigator.

Results

As of 9 November 2022, 21 pts had been dosed. The median follow up time was 5.9 months for 0.3mg/kg dose group and 2.8 months for 0.45mg/kg dose group, respectively.

- Porustobart in combination of toripalimab showed promising anti-tumor activity in advanced high-grade NENs. No significant difference in efficacy was observed between the two dose groups.
    - The overall objective response rate (ORR) and disease control rate (DCR) were 38.9% and 61.1%, respectively, and 3-month duration of response (DOR) rate was 80%, while the median DOR was not reached
    - For patients with neuroendocrine carcinoma (NEC) the ORR and DCR were 38.5% and 69.2%, respectively
- Porustobart in combination of toripalimab showed acceptable safety profile

Treatment-related adverse events (TRAEs) were reported in 100.0% (21/21) patients, and ≥Grade 3 TRAEs were reported in 33.3% (7/21) patients. The most common (≥20%) TRAEs were hepatic function abnormal, hyperthyroidism, rash, leukopenia, anaemia, pyrexia, neutrophil count decreased, hypothyroidism and thrombocytopenia

- Porustobart in combination of toripalimab showed unique PK/PD signature.
    - PK data indicated no potential interaction between porustobart and toripalimab
    - Porustobart promoted T_{reg} reduction and $CD4^+$ and $CD8^+$ T cell proliferation in periphery attested to its mechanism of action.

Conclusions

Porustobart 0.3 mg/kg or 0.45 mg/kg plus toripalimab 240mg Q3W showed promising anti-tumor activity and an acceptable safety profile in pts with advanced high-grade NENs.

The above results demonstrated robust clinical response rate in difficult-to-treat high-grade NENs that were generally not sensitive to current therapies. The results showed great potential to develop porustobart 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 melanoma.

About Porustobart

Porustobart 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, Porustobart 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 successfully develop or ultimately market any of our products referenced in this announcement. 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, 14 April 2023

As at the date of this announcement, the Board 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.