HBM4003 Phase I Dose-Escalation Study
Summary of Phase I Data Readout

September 2021

HBM HOLDINGS-B
02142.HK
www.harbourbiomed.com
Executive Summary

- **Unmet medical needs**: current anti-CTLA-4 monotherapy and combination therapies are still limited by safety profile

- **HBM4003**: a next generation anti-CTLA-4 fully human heavy-chain-only antibody with enhanced ADCC for Treg depletion
  - Endorsed by global leading experts in IO therapy aiming to transform the global IO landscape with breakthrough innovation

- **Phase 1 trial**: the preliminary data demonstrated favorable safety and efficacy
  - Well tolerated
  - Preliminary efficacy data are encouraging

- **It represents significant clinical needs with potential to be backbone of next gen IO therapy**

- **Next step**: global development kicked off aiming to unlock potential of broad tumor setting
Agenda

01 Company Overview

02 HBM4003 Phase I Data Readout

03 HBM4003 Outlook
**Differentiated Innovative Portfolio**

<table>
<thead>
<tr>
<th>Count</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>near-term commercialization assets</td>
</tr>
<tr>
<td>7</td>
<td>ongoing clinical trials</td>
</tr>
<tr>
<td>8</td>
<td>significant preclinical assets</td>
</tr>
</tbody>
</table>

**Unique Market Position**

- first-in-class, T cell engager, bispecific antibodies

---

**Rapid Progress on Product Development**

- **3** BLA in 2022
- **7** IND in 2021/2022
Harbour Biomed
Leading the Next Wave of Antibody Therapeutics in Immunology and Oncology

**Highly Effective and Disruptive Engine**

<table>
<thead>
<tr>
<th>Leading Discovery Platforms</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 fully human antibody platforms</td>
</tr>
<tr>
<td>1 single B cell technology</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>World Class Research Team</th>
</tr>
</thead>
<tbody>
<tr>
<td>105+ discovery scientists, 60+ PhD</td>
</tr>
<tr>
<td>3 global research centers</td>
</tr>
<tr>
<td>10+ in-house late-stage preclinical/clinical products within 4 years</td>
</tr>
</tbody>
</table>

**Global Collaboration**

45+ global partners
license-out

- abbvie
- Dana-Farber Cancer Institute
- Lilly
- Mount Sinai
- BioMap

**Manufacturing Commercialization**

- 8500 m² pilot factory in Suzhou
- Fast building core commercial team
Integrated Platforms Enable Sustainable Invention of Novel Molecules

*Harbour Antibody Platforms Combined with Single B Cell Cloning Offers A Complete and Advanced Technology Solution for Consistently Discovering Next-Gen Fully Human Antibody Therapeutics*

**Antibody generation with Single B Cell cloning method in 3-5 months***

- Animal Immunization: 1-2 months
- SBC: 1-2 weeks
- SC Sequence: (1-2 weeks)
- Recombinant Antibody: (4-5 weeks)
- Lead Characterization: 1-2 weeks

* Traditional hybridoma method need 7-9 months with an additional 3-6 months of humanization

---

**H2L2 —Full IgG Antibody Discovery Platform**

- HBM1007: A allosteric fully human antibody against CD73 for the treatment of solid tumors
- HBM7015: A bifunctional fusion protein for the treatment of solid tumors

Robust and highly efficient, global IP and clinically validated

**HCAb —Next-Generation Heavy-Chain-Only Antibody Discovery Platform**

- HCAb: ~80 KDa

Unique fully human HCAb, versatile for broad applications

**HBICE™ — HCAb-Based Platform for Immune Cell Engagers**

- HBICE: A Unique, HCAb-Based Platform For Immune Cell Engagers
- HBM4003: A next generation anti-CTLA4 antibody

Self-developed, unique geometric flexibility, promising bispecific biology

---

Confidential & Not for Further Distribution
Agenda

01. Company Overview

02. HBM4003 Phase I Data Readout
   Section 1: Target Selection & Molecule Overview

03. HBM4003 Outlook
Current Anti-CTLA-4 Monotherapy and Combination Therapies are Still Limited by Safety Profile

Toxicity limits the potential of PD-1/CTLA-4 combo

Increasing the therapeutic ceiling is the next step

James Larkin, Long-term data from the CheckMate 067 study, ESMO 2019
HBM4003: Target Selection & Molecule Design Was Recommended & Endorsed by Global SAB Members & Thought Leaders to Achieve Breakthrough of IO Therapy

PD-1(L1) and CTLA-4 are the only 3 proven IO targets

HBM4003 is endorsed by global leading experts in IO therapy aiming to transform the global IO landscape with breakthrough innovation

CTLA-4 is the most preferred combo choice

Dr. Frank Grosveld
Fellow of Royal Society and Member of Royal Netherlands Academy of Arts and Sciences
Professor and former Head of Department of Cell Biology & Department of Clinical Genetics at Erasmus University Medical Center

Dr. Jon Wigginton
Chief Medical Officer, Cullinan Oncology; Advisos of MPM Capital
Former Therapeutic Area Head of Immuno-Oncology, Early Clinical Research at BMS
Former President of the Society for Immunotherapy of Cancer

Dr. Robert Kamen
Venture Partner at Third Rock Ventures
Former President & Unit Head of Abbott Bioresearch Centre

Dr. Shivaani Kummar
Director, Phase 1 Clinical Research Program, Division of Oncology Stanford School of Medicine
Professor of Medicine & Radiology at Stanford University Medical Centre
Specialty Sarcoma

Dr. John M Kirkwood
Distinguished Service Professor Medicine, University of Pittsburg
Usher Professor of Medicine, Dermatology, Clinical and Translational Science at The University of Pittsburg School of Medicine
Specialty Global Melanoma and Skin Cancer
HBM4003-A Next Generation Anti-CTLA-4 Fully Human Heavy-Chain-Only Antibody with Enhanced ADCC for Treg Depletion

- The HCAb molecules have only 2 heavy chains linked by disulfide bonds. Each heavy chain consists of 1 heavy chain variable region and 2 heavy chain constant regions (CH2 and CH3) without the CH1 region

- The potential features of HCAb include unique binding epitopes, high affinity, and high tissue/tumor penetration

- HBM4003 demonstrated near dose-proportional pharmacokinetics (PK), extended pharmacodynamic (PD) effect, and low immunogenicity
**HBM4003 Preclinical Data: Superior Treg Depletion Activity (100x More Potent Than Ipilimumab Analogue)**

**Treg Depletion by HBM4003 in Primary Human PBMCs in in vitro ADCC Assay**

Superior Treg depletion activity in comparison to ipilimumab analogue as measured in vitro via ADCC killing assay

In Vivo T_{reg} (%) in Tumor, Spleen, and Blood in MC38-Bearing hCTLA-4 KI Mice (3 mice per group)

Samples were collected 24hrs post 2nd dosing and analyzed by FACS
HBM4003 Preclinical Data: Comparable Mean Survival Time At 1/6 Of Dose Compared to Ipilimumab, and Predicted Human Exposure Is Much Lower (~1/35 of AUC)

Survival Prolongation (Mean Survival Time)

![Graph showing survival prolongation with different treatments](image)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean Survival Time (MST)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ipilimumab 10 mg/kg</td>
<td>23 Days</td>
</tr>
<tr>
<td>ipilimumab 1 mg/kg</td>
<td>19 Days</td>
</tr>
<tr>
<td>HBM4003 5.4 mg/kg</td>
<td>40 Days</td>
</tr>
<tr>
<td>HBM4003 3.054 mg/kg</td>
<td>28 Days</td>
</tr>
<tr>
<td>HBM4003 1.5 mg/kg</td>
<td>21 Days</td>
</tr>
</tbody>
</table>

Simulated PK exposure at steady state

<table>
<thead>
<tr>
<th></th>
<th>AUC(_{0-tau}) (μg*day/ml)</th>
<th>Cmax (μg/ml)</th>
<th>Cmin (μg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ipilimumab</td>
<td>1942.7</td>
<td>744.9</td>
<td>576.3</td>
</tr>
<tr>
<td>HBM4003 1.5 mg/kg</td>
<td>54.27</td>
<td>40.26</td>
<td>2.50</td>
</tr>
</tbody>
</table>

Ipilimumab (10mg/kg q3w)

HBM4003 (1.5mg/kg q3w)
Agenda

01 Company Overview

02 HBM4003 Phase I Data Readout
   Section 2: Phase 1 study Design & Patient Features

03 HBM4003 Outlook
**HBM4003 Mono Therapy: Study4003.1 Overall Design Outline**
Includes Two Parts and the Abstract of Part 1 Has Been Submitted to ESMO 2021

**Part 1:**
Dose escalation in previously treated (including anti-PD-1 therapy) advanced solid tumors

- **Primary endpoint:**
  - Proportion of patients with DLT

- **Dose Regimens:**
  - 0.6 mg/kg Q3W
  - 0.45 mg/kg Q3W
  - 0.3 mg/kg QW

**Primary endpoint:**
• Proportion of patients with DLT

**Secondary endpoints:**
• ORR
• DOR, DCR, DDC, maximum tumor shrinkage

**HBM4003 IV QW or Q3W**

**Part 2:**
Dose expansion

- **Primary endpoint:**
  - ORR

- **Secondary endpoints:**
  - DOR, DCR, DDC, maximum tumor shrinkage

Melanoma, HCC, RCC...

**HBM4003 IV Q3W**
### Key Patient Features and Demographics

- 20 patients with advanced solid tumors, at 4 Australian sites
- Heavily pre-treated population
  - 13 out of 20 patients (65%) having received 2 or more prior regimens
  - 8 out of 20 patients (40%) were treated previously with immune checkpoint inhibitor
  - The average age of subjects is **62.5** (SD= 11.5)

<table>
<thead>
<tr>
<th>Age, mean (SD)</th>
<th>0.3mg/kg QW (N=7)</th>
<th>0.45mg/kg Q3W (N=7)</th>
<th>0.6mg/kg Q3W (N=6)</th>
<th>Total (N=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>67.6 (8.3)</td>
<td>62.3 (10.2)</td>
<td>56.8 (15.0)</td>
<td>62.5 (11.5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ECOG PS, n(%)</th>
<th>3 (42.9)</th>
<th>3 (42.9)</th>
<th>3 (50.0)</th>
<th>9 (45.0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>3 (42.9)</td>
<td>3 (42.9)</td>
<td>3 (50.0)</td>
<td>9 (45.0)</td>
</tr>
<tr>
<td>1</td>
<td>4 (57.1)</td>
<td>4 (57.1)</td>
<td>3 (50.0)</td>
<td>11 (55.0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>N of Previous Treatment Lines, n(%)</th>
<th>2 (28.6)</th>
<th>0</th>
<th>0</th>
<th>2 (10.0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2 (28.6)</td>
<td>0</td>
<td>0</td>
<td>2 (10.0)</td>
</tr>
<tr>
<td>1</td>
<td>2 (28.6)</td>
<td>2 (28.6)</td>
<td>1 (16.7)</td>
<td>5 (25.0)</td>
</tr>
<tr>
<td>2 or more</td>
<td>3 (42.8)</td>
<td>5 (71.4)</td>
<td>5 (83.3)</td>
<td>13 (65.0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Previous PD-1/PD-L1 Therapies, n(%)</th>
<th>2 (28.6)</th>
<th>3 (42.9)</th>
<th>3 (50.0)</th>
<th>8 (40.0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2 (28.6)</td>
<td>3 (42.9)</td>
<td>3 (50.0)</td>
<td>8 (40.0)</td>
</tr>
<tr>
<td>1</td>
<td>2 (28.6)</td>
<td>2 (28.6)</td>
<td>1 (16.7)</td>
<td>5 (25.0)</td>
</tr>
<tr>
<td>2 or more</td>
<td>3 (42.8)</td>
<td>5 (71.4)</td>
<td>5 (83.3)</td>
<td>13 (65.0)</td>
</tr>
</tbody>
</table>

### Tumor Type

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Safety Assessment (n)</th>
<th>Post-Treatment Data for Anti-tumor Assessment (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrial Carcinoma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>PRCC</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>ccRCC</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Prostate Cancer</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>HCC</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Penile Cancer</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Testicular cancer</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Esophageus Cancer</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Colorectal Cancer</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Breast Cancer</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Bladder Cancer</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>HNSCC</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>NSCLC</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Mesothelial Cancer</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>20</strong></td>
<td><strong>15</strong></td>
</tr>
</tbody>
</table>
Agenda

01 Company Overview

02 HBM4003 Phase I Data Readout
   Section 3: Safety Data Readout

03 HBM4003 Outlook
HBM 4003 Were Well Tolerated

- No toxicity was reported related to lung, kidney, heart or endocrine system

- No treatment-related serious adverse event (TRSAE) was reported at 0.45 mg/kg Q3W

- No TRAE was > Grade 3
  - Grade 3 TRAEs included diarrhea, and 1 case of abnormal liver function test who has HCC. All were manageable and reversible

- The most common TRAE of any grade was diarrhea/enterocolitis
  - The most common irAEs were diarrhea/enterocolitis and skin rash

- Maximum tolerated dose (MTD) was not achieved
  - No DLT was observed in any Q3W dose level
  - 1 DLT was reported at 0.3mg/kg QW due to Grade 3 diarrhea which was well managed with the SOC

- 0.45 mg/kg Q3W was recommended as the phase II dose (RP2D) for dose expansion
Differentiated Safety Profile Were Indicated From Preliminary Data

- More severe baseline conditions - more prior treatments (including PD-1), higher ECOG, broad range of solid tumors mixed with cold tumors vs > 1 line melanoma
- irAE & G3 TRAE focused on diarrhea vs broad involvement with vital organs

<table>
<thead>
<tr>
<th></th>
<th>HBM4003 0.45mg/kg Q3W, n(%)</th>
<th>Ipilimumab 3mg/kg Q3W, n(%)</th>
<th>Ipilimumab 3mg/kg Q3W, n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No. patients</td>
<td>7</td>
<td>111 (pooled)</td>
<td>137/131 (AE)</td>
</tr>
<tr>
<td>Tumor types</td>
<td>Solid tumors</td>
<td>melanoma</td>
<td>melanoma</td>
</tr>
<tr>
<td>Prior treatment lines</td>
<td>≥2: 5(71.4) Prior PD-(L)1 Therapy: 3(42.9)</td>
<td>Prior systemic anti-cancer therapy(&gt;1):100(90.1) Prior IO Therapy: 61(55.0)</td>
<td>Prior systemic anti-cancer therapy(&gt;1):137(100)</td>
</tr>
<tr>
<td>ECOG</td>
<td>0: 3(42.9) 1: 4(57.1)</td>
<td>-</td>
<td>0: 72(52.6) 1: 64(46.7) 2: 1(0.7)</td>
</tr>
<tr>
<td>TRAE</td>
<td>4 (57.1)</td>
<td>88(79.3)</td>
<td>105(80.2)</td>
</tr>
</tbody>
</table>

**irAE**
- **Total: 2 (28.6)**
  - Enterocolitis 1(14.3)
  - Hepatic 1(14.3)
- **Total: 68(61.3)**

**G ≥3 irAE**
- **Total: 1(14.3)**
  - Hepatic 1(14.3)
- **Total: 16(14.4)**
  - Diarrhea 3(2.7)
  - Colitis 3(2.7)
- **Total: 19(14.5)**
  - Diarrhea 6(4.6)
  - Colitis 7 (5.3)
  - Dermatologic 2(1.5)
  - Endocrine 5(3.8)
  - Other 3(2.3)

Agenda

01 Company Overview

02 HBM4003 Phase I Data Readout
   Section 4: Efficacy & PD Marker Data

03 HBM4003 Outlook
Preliminary Efficacy Data Are Encouraging For HBM 4003 In This Monotherapy Dose Escalation Study

• 2 clinical responders
  • 1 patient with HCC who was pre-treated with Sorafenib, Lenvatinib and anti-PD-1 had confirmed partial response (PR)
  • 1 patient with CRPC had PSA response for > 26 weeks with SD in RECIST assessment

• 9 patients had stable disease (SD 60%)
  • 15 patients had at least 1 post-treatment tumor assessment
  • tumor shrinkage were reported with 3 patients

• Efficacy is assessed according to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1.
• An independent imaging reading group was hired to review CT scan and RECIST assessment for responders
Encouraging Preliminary Efficacy Have Been Observed with HBM 4003 Monotherapy - FIH with Dose Escalation, Heavily Pre-treated (including PD-1), Broad Range of Solid Tumors

Best Overall Response, n (%)

<table>
<thead>
<tr>
<th></th>
<th>0.3mg/kg QW (N=7)</th>
<th>0.45mg/kg Q3W (N=7)</th>
<th>0.6mg/kg Q3W (N=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>PR</td>
<td>0 (0.0)</td>
<td>1 (14.3)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>SD</td>
<td>5 (71.4)</td>
<td>0 (0.0)</td>
<td>4 (66.7)</td>
</tr>
<tr>
<td>PD</td>
<td>1 (14.3)</td>
<td>3 (42.9)</td>
<td>1 (16.7)</td>
</tr>
</tbody>
</table>

Abbreviations: CR: complete response; PR: partial response; SD: stable disease; PD: progressive disease

Tumor types (from left to right): breast cancer; colorectal cancer; clear cell renal cell carcinoma; esophagus cancer; breast cancer; clear cell renal cell carcinoma; mesothelial cancer; prostate cancer; prostate cancer; bladder cancer; papillary renal cell carcinoma; head and neck squamous cell carcinoma; endometrial carcinoma; hepatocellular carcinoma
HCC Patient: Confirmed PR in Target Lesion

**Patient background**
- 64-year-old man, Asian, HBV infected
- Prior treatments: sorafenib, lenvatinib and anti-PD-1
- HBM 4003, 0.45 mg/kg Q3W

**Strong & durable efficacy observed**
- Tumor reduction reached 64.4% for target lesions and non-target lesions were no longer detectable 16 weeks after the last dose

<table>
<thead>
<tr>
<th>Location</th>
<th>Baseline</th>
<th>6 W</th>
<th>12 W</th>
<th>16 W</th>
<th>24 W</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non target Lesions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung, LN, Left Liver</td>
<td>NA</td>
<td></td>
<td>Non PD/Non CR</td>
<td>Not detectable</td>
<td></td>
</tr>
<tr>
<td>Target lesions (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right Superior Liver, Right Kidney</td>
<td>225</td>
<td>175</td>
<td>115</td>
<td>105</td>
<td>80</td>
</tr>
<tr>
<td>Change from baseline</td>
<td>N/A</td>
<td>22.2%</td>
<td>48.9%</td>
<td>53.3%</td>
<td>64.4% PR</td>
</tr>
<tr>
<td>AFP u/L</td>
<td>170</td>
<td>5</td>
<td>5</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>Overall response</td>
<td>NA</td>
<td>SD</td>
<td>PR</td>
<td>PR</td>
<td>PR</td>
</tr>
</tbody>
</table>

HCC: hepatocellular carcinoma; PR: partial response
Note: The target lesion was measured at the longest diameter
CRPC Patient: SD by RECIST 1.1 with PSA Response

- **Patient profile**
  - 80-year-old man, HBM 4003 0.6 mg/kg Q3W
  - Prior treatments: docetaxel, cabazitaxel and bicalutamide

- **PSA response**
  - more than 50% reduction in PSA level from baseline at 6 week

- **Extended clinical benefits**
  - The PSA response still remained at week 45 from first dose, 26 weeks after the last dose
  - The SD of adrenal and axillary lymph node by RECIST 1.1 continued until week 45

<table>
<thead>
<tr>
<th>May 2020</th>
<th>Jun 2020</th>
<th>July 2020</th>
<th>Apr 2021</th>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSA (ng/ml)</td>
<td>240</td>
<td>92</td>
<td>89</td>
<td>58</td>
</tr>
<tr>
<td>Sum of Diameter (mm)</td>
<td>70</td>
<td>71</td>
<td>63</td>
<td>ND</td>
</tr>
<tr>
<td>% Change Baseline</td>
<td>NA</td>
<td>1</td>
<td>-10</td>
<td>NA</td>
</tr>
</tbody>
</table>

CRPC: castration-resistant prostate cancer; SD: stable disease; PI: principal investigator; PSA: prostate-specific antigen
**Tumor Biopsy**

- **Treg depletion** is selective and sustained in tumor microenvironment comparing to peripheral blood.
- Increase of CD8+ Teff cells is observed in tumor microenvironment and peripheral blood.

**Consistent with preclinical data**

- Subject 89301, 48y, Male, Chromophobe RCC, HBM4003 0.45mg/kg Q3W
- 6w tumor assessment: SD

**Peripheral Blood**

- Proliferated CD8+ Teff (CD8+Ki67+)
- Treg (CD4+CD25+CD127low/-)

**Biopsy collection time**

- C2D21

**CD8+ Teff**

<table>
<thead>
<tr>
<th>Time point</th>
<th>Ratio to Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1D1</td>
<td>0.7 folds</td>
</tr>
<tr>
<td>C1D2</td>
<td></td>
</tr>
<tr>
<td>C1D4</td>
<td></td>
</tr>
<tr>
<td>C1D8</td>
<td></td>
</tr>
<tr>
<td>C1D15</td>
<td></td>
</tr>
<tr>
<td>C2D1</td>
<td></td>
</tr>
<tr>
<td>C2D8</td>
<td></td>
</tr>
<tr>
<td>C3D1</td>
<td></td>
</tr>
<tr>
<td>C3D8</td>
<td></td>
</tr>
<tr>
<td>C4D1</td>
<td></td>
</tr>
</tbody>
</table>

**CD8+ Tm**

<table>
<thead>
<tr>
<th>Time point</th>
<th>Ratio to Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1D1</td>
<td>6.0 folds</td>
</tr>
<tr>
<td>C1D2</td>
<td></td>
</tr>
<tr>
<td>C1D4</td>
<td></td>
</tr>
<tr>
<td>C1D8</td>
<td></td>
</tr>
<tr>
<td>C1D15</td>
<td></td>
</tr>
<tr>
<td>C2D1</td>
<td></td>
</tr>
<tr>
<td>C2D8</td>
<td></td>
</tr>
<tr>
<td>C3D1</td>
<td></td>
</tr>
<tr>
<td>C3D8</td>
<td></td>
</tr>
<tr>
<td>C4D1</td>
<td></td>
</tr>
</tbody>
</table>
Conclusion--The Preliminary Data from This Phase 1 Trial Demonstrate Encouraging Activity across a Range of Tumors with Improved Tolerability for HBM 4003 Vs Ipilimumab

- HBM4003 is the next generation anti-CTLA-4 fully human HCAb with enhanced ADCC for Treg depletion and the first HCAb under clinical development

- The novel MOA of strong Treg depletion has been validated by both pre-clinical and clinical biopsy data

- HBM 4003 is well tolerated
  - The most common TRAE of any grade was diarrhea/enterocolitis
  - No toxicity was reported related to lung, kidney, heart or endocrine system
  - No TRAE was > Grade 3
  - Maximum tolerated dose (MTD) was not achieved

- Preliminary efficacy data is encouraging for HBM 4003 monotherapy
  - 9(out of 15) patients achieved SD
  - 1 patient pre-treated by all SOCs (including PD-1) was confirmed as PR, 1 patient had PSA response with SD by RECIST

- 0.45 mg/kg Q3W was recommended as the phase II dose (RP2D) for dose expansion
Agenda

01. Company Overview
02. HBM4003 Phase I Data Readout
03. HBM4003 Outlook
## Global Development Kicked Off for HBM4003 Aiming to Unlock Potential of Broad Tumor Setting With Multiple Exciting Catalysts In 2022

<table>
<thead>
<tr>
<th>Study Regimen</th>
<th>Clinical Development Programs</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBM4003 mono</td>
<td>27. Pivotal studies in 1L melanoma (China), 1L RCC (China), 2L HCC, 2L NEN</td>
</tr>
<tr>
<td>HBM4003 + PD-1</td>
<td>27. Pivotal study in 1L NSCLC (PD-L1 &lt;1%)</td>
</tr>
<tr>
<td>HBM4003 + bevacizumab</td>
<td>27. Pivotal study in 1L NSCLC regardless of PD-L1 expression</td>
</tr>
</tbody>
</table>

### Study Regimen
- HBM4003 mono
- HBM4003 + PD-1
- HBM4003 + bevacizumab

### Clinical Development Programs
- Ph Ib, HBM4003 + Toripalimab
- Ph Ib, HBM4003 + Pembrolizumab (HBM4003 + Pembrolizumab + platinum chemo)
- Ph Ib/II, HBM4003 + bevacizumab (HBM4003 + PD-(L)1 + bevacizumab)

### Abbreviations:
- ESCC: esophageal squamous cell carcinoma
- GC: gastric cancer
- HCC: hepatocellular carcinoma
- HNSCC: head and neck squamous cell carcinoma
- NET/NEC: neuroendocrine neoplasms
- NPC: nasopharyngeal carcinoma
- NSCLC: non-small cell lung carcinoma
- TNBC: triple-negative breast cancer

### Exciting Catalysts Expected in a Year
- ✓ POC data for Mono for melanoma, HCC, RCC
- ✓ POC data for PD-1 combination for melanoma, HCC, RCC, NEN, NSCLC
- ✓ Initiation of POC study for VEGFR combination

### Global Development
1. Global, simultaneous development on POC
2. 5 trials ongoing including 3 basket trials
3. Mono & combo treatment
4. Various solid tumors – melanoma, HCC, NET/NEC, RCC, NSCLC (HNSCC, ESCC, TNBC...)

**Note:**
- Ph: Phase
- Pivotal: POC (Proof of Concept)
- (L): L1 (mitogen-activated protein kinase)
- NSCLC: non-small cell lung carcinoma
- PD-L1: programmed death-ligand 1
- HCC: hepatocellular carcinoma
- RCC: renal cell carcinoma
- NEN: neuroendocrine neoplasms
- NPC: nasopharyngeal carcinoma
- TNBC: triple-negative breast cancer
HBM 4003’s Development Receives Continuous Strong Support from Global Investigators & Advisor Board Members

**Shivaani Kummar**
Director, Phase 1 Clinical Research Program, Division of Oncology Stanford School of Medicine
Professor of Medicine & Radiology at Stanford University Medical Centre
Specialty: Sarcoma

**John M Kirkwood**
Distinguished Service Professor Medicine, University of Pittsburgh
Usher Professor of Medicine, Dermatology, Clinical and Translational Science at The University of Pittsburgh School of Medicine
Specialty: Global Melanoma and Skin Cancer

**Paul de Souza**
Professor, St George Private Hospital, Kogarah, NSW, Australia

**Ren Zhenggang**
Director of Department of Hepatic Medical Oncology, Zhongshan Hospital, Fudan University

**Shukui Qin**
Deputy Dean of General Hospital of Eastern Theater Command; Secretary-general of Chinese Society of Clinical Oncology (CSCO)

**Hao Jihui**
Deputy Dean of Tianjin Medical University Cancer Institute & Hospital

**Jin Li**
Vice President of Federation Asian Alliance Clinical Oncology (FACO), Board Chairman of Chinese Society of Clinical Oncology (CSCO)

**Ye Dingwei**
Deputy Dean of Fudan University Shanghai Cancer Center, Director of Department of Urology Surgery

**Shen Lin**
Deputy Dean of Peking University Cancer Hospital, Director of Department of Gastrointestinal Oncology
HBM4003 Represents Significant Clinical Needs with Potential to be Backbone of Next Gen IO Therapy

- CTLA4 a clinically validated I/O target
- Novel design, heavy chain Ab and Treg depletion
- Significant improvement of efficacy and safety profile to achieve therapy breakthrough with Monotherapy
- Enhanced combination therapy with broad applications and extended benefits

- Significant Improvement of Clinical Outcomes
- Unlock Potential of Immuno-Oncology Therapy