COVID-19 Vaccine

(Vero Cell), Inactivated

China National Biotec Group Company Limited
Beijing Institute of Biological Products Co., Ltd.

29 April, 2021
CONTENTS

01  Vaccine Characteristics
02  Pre-clinical Study
03  Clinical Study
04  Post-marketing Activities
Vaccine Characteristics

- Vaccine Portfolio
- Overall Progress
Basic Characteristics of Vaccines - Inactivated Whole Viron

COVID-19 Vaccine (Vero Cell), Inactivated

**Indications**
Prevention of COVID-19 caused by SARS-CoV-2

**Key Components**
Inactivated SARS-CoV-2 virus

**Dosage**
6.5 U/dose

**Adjuvant**
Aluminum hydroxide

**Packaging**
0.5ml/Pre-filled syringe/vial

**Storage and Transportation**
2~8°C

**Validity Period**
Tentatively 2 years

**Applicable population**
- 18 years old and above
- Study of the 3-17-year-old cohorts are completed.
Research and Development Process

Advanced Production Process Based on Basket Bioreactor

- Small/pilot scale process
- Process Scale-up and Site Transfer
- Large-scale production

Screening of Vaccine Strains and Pre-clinical Study
- Isolation of virus strains
- Production process establishment
- Animal study

Domestic/International Clinical Study
- Clinical Phase I/II
- Clinical Phase III
  - Immunobridging, three lots consistency = 2100
  - ≥ 60,000 subjects
- Vaccine efficacy evaluation
- Safety, Immunogenicity, Dose finding
- Production site and GMP compliance,
  Phase I/II clinical sites (Shangqiu, Yanjin),
  Third party testing institution (China CDC, Henan Jinyu),
  Phase III UAE Site (Remote)

- Obtain clinical trial approval 2020.4.27
- Initiate Phase III clinical study 2020.6.28
- On-site inspection 2020.9-2020.11
- Marketing authorization and Registration

2020.12
Pre-clinical Study

- Immunogenicity
- Safety
- Challenge study
Dosages
All produced high titer antibodies;
Antibody level is positively correlated with time;
The antibody level in the medium and low dose group reached its peak in 21 days;
The high dose group reached the peak in 14 days.

Immunization Schedules
(0/7, 0/14, 0/21) all produced high titer antibodies;
There was a positive correlation between the number of doses and the antibody level;
In the high and medium dose groups, 3 doses are better than 2 doses and 2 doses are better than 1 dose;
0/21 is better than 0/7 and 0/14.

The vaccine showed good immunogenicity in 6 species
The safety evaluation of acute toxicity, long term toxicity, reproductive toxicity and allergy has been completed, and no abnormal reaction has been observed.

<table>
<thead>
<tr>
<th>Study Item</th>
<th>Study Animal</th>
<th>Grouping</th>
<th>Route of administration</th>
<th>Time of administration</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute toxicity</td>
<td>Rat</td>
<td>High, medium dose, control</td>
<td>Intramuscular injection, single administration</td>
<td></td>
<td>No abnormal reaction observed</td>
</tr>
</tbody>
</table>
| Reproductive toxicity | 2 dose groups, control | Intramuscular injection, Multiple administrations | Male: D1/D15/D29/D43
Female: D1/D15/D29/GD6/PND7 |                              |                          |
| Long term toxicity  | Rat          | 4 dose groups, control            | Multiple administrations                        | D1/D15/D29/D43                |                                          |
|                     | Cynomolgus macaques | 3 dose groups, control            |                                                  | D1/D8/D15/D22                |                                          |
| Allergy             | Guinea pigs  | 2 dose groups, control            | Sensitize by intramuscular injection, stimulate by intravenous injection |                              |                                          |
Objective: To evaluate the active protection of the inactivated SAS-CoV-2 vaccine in rhesus monkeys and provide animal study data for clinical research.

Study showed that:
- The inactivated SARS-CoV-2 vaccine has good protective effect and no antibody-dependent enhancement effect (ADE) was observed.

<table>
<thead>
<tr>
<th>Group</th>
<th>Pathology</th>
<th>Viral load</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose group</td>
<td>Mild interstitial pneumonia (4/4)</td>
<td>The viral load was 0 (4/4)</td>
</tr>
<tr>
<td>Low dose group</td>
<td>Mild interstitial pneumonia (4/4)</td>
<td>The viral load was 0 (4/4)</td>
</tr>
<tr>
<td>Placebo Group</td>
<td>Severe interstitial pneumonia (2/2)</td>
<td>High viral load (2/2)</td>
</tr>
</tbody>
</table>

Clinical Studies

- Phase I and II Clinical Studies
- Phase III Clinical Studies
Study Objectives
Aimed to assess the safety and immunogenicity of an inactivated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine candidate

Phase I/II Study
Age Group: 3–5 years old, 6–12 years old, 13–17 years old, 18–59 years old, ≥ 60 years old
Dosage: High, Medium and Low doses
Immunization Schedules: D0 – D28 – D56

Phase II Study (middle doses)
Immunization Schedules: D0 – D28 – D56, D0 – D21 – D42, D0 – D14, D0 – D28, D0 (high doses)

Follow-up period

First dose (D0)
Second dose (D0/D14, D0/D21, D0/D28)
Third dose

• Location: Liangyuan District, Shangqiu City, Henan Province
• Randomized, placebo-controlled:
• High, medium and low dose groups
• Different age groups:
  18 ~ 59 years old group
  ≥ 60 years old group
  13-17 years old group
  6 ~ 12 years old group
  3 ~ 5 years old group

Pre-immunization: blood collection, neutralizing antibodies and binding antibodies testing.
After first dose of immunization:
Regular telephone calls, follow-up and observation of safety
Regular blood collection, determination of binding antibody, neutralizing antibody
Within 0-30 days after the whole course vaccination, the total adverse reaction rates of the low/medium/high/placebo groups in the 18-59 year-old group were 45.83%, 41.67%, 45.83% and 29.17%, respectively.

The total incidence of adverse reactions in low/medium/high/placebo group was 4.17%, 25%, 25% and 8.33% respectively in the group ≥ 60 years old.

The incidence of total adverse reactions in the group ≥ 60 years old was lower than that in the group 18-59 years old.
Within 0-30 days after the whole course vaccination, the total incidence of adverse reactions in the low/medium/high/placebo group of the 18-59 year-old group was 20%, 25%, 30% and 10%, respectively.

The total incidence of adverse reactions in low/medium/high/placebo group was 15%, 15%, 13.33% and 8.33% respectively in group ≥ 60 years old.

The incidence of total adverse reactions in the group ≥ 60 years old was lower than that in the group 18-59 years old.
The incidence of systemic adverse reactions was low, mainly fever, with 4.17%, 4.17%, 8.33% and 8.33% in the low/medium/high dose group and placebo group respectively in the population aged 18-59 years old.

The local adverse reactions were mainly pain, and the low/medium/high dose group and placebo group were 41.67%, 33.33%, 37.5% and 8.33% respectively.
The incidence of systemic adverse reactions is relatively low, mainly diarrhea and fever. The low/medium/high dose fever rates were 0%, 0%, and 5% respectively in the 18-59 year-old population, and 3.33%, 0%, and 1.67% respectively in the low/medium/high dose group and placebo group in the population aged ≥ 60 years old.

Local adverse reactions were mainly pain, with 10.00%, 0%, 18.75% and 1.67% in low/medium/high dose group and placebo group respectively for 18-59 years old. The low/medium/high dose groups were 3.33%, 11.67% and 5.00% respectively in the population aged ≥ 60 years old.

- The incidence of systemic adverse reactions is relatively low, mainly diarrhea and fever. The low/medium/high dose fever rates were 0%, 0% and 5% respectively in the 18-59 year-old population, and 3.33%, 0%, 1.67% and 3.33% respectively in the low/medium/high dose group and placebo group in the population aged ≥ 60 years old.

- Local adverse reactions were mainly pain, with 10.00%, 0%, 18.75% and 1.67% in low/medium/high dose group and placebo group respectively for 18-59 years old. The low/medium/high dose groups were 3.33%, 11.67% and 5.00% respectively in the population aged ≥ 60 years old.
There were 13 subjects developed 38 SAEs in total. They were all unrelated to vaccination.
The level of neutralizing antibody after two or three doses of immunization is significantly superior than that after one dose of immunization.

In the two-dose immunization schedule, the neutralizing antibody level at D0/D21 and D0/D28 schedule are significantly better than that at D0/D14.

After vaccination, population aged 60 and above can generate immune response.

The antibody level in the high/medium dose groups were higher than that in the low dose group.

GMT of neutralizing antibody maintained at high level.
No significant reduction was observed until D90 after the last dose.
Phase III Clinical Study

- Study Objectives
- Study Design
- Diagnostic Criteria
- Efficacy
- Safety
- Immunogenicity
Primary Objective

- Vaccine efficacy against COVID-19 among healthy population aged 18 years old and above

Secondary Objectives

- Vaccine efficacy against severe and death cases accompanied by COVID-19
- Immunogenicity
- Safety

Exploratory Objectives

- Protective efficacy of neutralizing antibody against COVID-19 (Immune surrogate Endpoint)
- Occurrence of ADE/VED after vaccination

Primary Endpoint

- Incidence of COVID-19 starting on day 15 after two doses of vaccination in healthy population aged 18 years and above.

Secondary Endpoint

- Severe and Death cases of COVID-19 starting on day 15 after 2nd dose of vaccination.
- Anti-SARS-CoV-2 neutralizing antibodies 4-fold rise, GMT
- Adverse events collected within day 0~7, 8~21/28days

Exploratory Efficacy Endpoint

- The vaccine efficacy of neutralizing antibodies of SARS-CoV-2 against COVID-19.
- The incidence of ADE / VED following vaccination of SARS-CoV-2 inactivated vaccine.
Overall Design: International Multi-center, Randomized, Double Blinded, Placebo Controlled Phase III Clinical Trial.

Protocol No.: CNBG2020003SQ.

Investigational Vaccine:
Name: COVID-19 Vaccine (Vero Cell), Inactivated
Manufacturer: Beijing Institute of Biological Products Co., Ltd., Wuhan Institute of Biological Products Co., Ltd., Wuhan Institute of Virus, Chinese Academy of Sciences.

Study Grouping: The total sample size of approx 45000 subjects were randomly assigned to vaccine group 1, vaccine group 2 and placebo groups according to the ratio of 1: 1: 1.

Immunization Schedule: According to the 0, 21 (+7) day immunization schedule, 2 doses of investigational vaccines or placebo are inoculated on the deltoid muscle of the upper arm. According to the results of immune persistence in Phase I/II clinical trials, the third dose (booster dose) will be vaccinated at an appropriate time.
**Immunization Schedule**

- **21 (+7) days**
  - First dose vaccination
  - Collection and evaluation of safety events after each dose of vaccine:
  - Second dose vaccination

- **0-21 (+7) days**
  - Collection and evaluation of safety events after each dose of vaccine:
  - Second dose vaccination

**Follow-up period**

- **14 days after 2 doses of vaccinations**
  - Collect cases
  - Long-term telephone follow-up

- **28 days after 2 doses of vaccinations**
  - Blood collection

- **After 2 doses of vaccinations**
  - Follow-up for one year

**Visit 10 completed**

**Established safety assessment**

**Long-term telephone follow-up**

- 3 months, 6 months, 9 months, and 12 months after 2 doses of immunization
  - Blood collection

**Fill in diary card and telephone follow-up**

- Day 0
  - First dose vaccination
  - Blood collection before immunization

- 0-21 (+7) days
  - Collection and evaluation of safety events after each dose of vaccine:
  - Second dose vaccination

- 14 days after 2 doses of immunization
  - Blood collection
Diagnostic Criteria

Suspected cases

• Have any of the epidemiological history, and have two or more A symptoms, or have one or more B symptoms;
• If there is no clear epidemiological history, they should have two or more A symptoms or one or more B symptoms and detectable SARS-CoV-2 specific IgM; or have two or more A symptoms and One or more B symptoms; or with imaging features of COVID-19

Clinical symptoms

• Symptoms A (presence for at least 2 days, ≥48h): fever (axillary temperature ≥37.5°C); chills; sore throat; fatigue; nasal congestion or runny nose; body pain, muscle pain; headache; nausea or vomiting; diarrhea.
• Symptoms B: Cough (presence for at least 2 days, ≥48h); new taste or smell disorders(presence for at least 2 days, ≥48h); shortness of breath or difficulty breathing;

Confirmed cases

• On the basis of the determination of the suspected case, the COVID-19 PCR detection result is positive.
<table>
<thead>
<tr>
<th><strong>Clinical Classification</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mild</strong></td>
</tr>
<tr>
<td>• The clinical symptoms were mild, and there was no sign of pneumonia on imaging.</td>
</tr>
<tr>
<td><strong>Moderate</strong></td>
</tr>
<tr>
<td>• Showing fever and respiratory symptoms with radiological findings of pneumonia.</td>
</tr>
<tr>
<td><strong>Severe</strong></td>
</tr>
<tr>
<td>• Respiratory distress (RR≥30 breaths/min);</td>
</tr>
<tr>
<td>• Oxygen saturation≤93% at rest;</td>
</tr>
<tr>
<td>• Arterial partial pressure of oxygen (PaO2)/ fraction of inspired oxygen (FiO2) ≤300mmHg (1mmHg=0.133kPa);</td>
</tr>
<tr>
<td>• The clinical symptoms progressively worsened, and the chest imaging showed &gt;50% obvious lesion progression within 24-48 hours.</td>
</tr>
<tr>
<td><strong>Critical</strong></td>
</tr>
<tr>
<td>• Respiratory failure and requiring mechanical ventilation;</td>
</tr>
<tr>
<td>• Shock;</td>
</tr>
<tr>
<td>• With other organ failure that requires ICU care;</td>
</tr>
<tr>
<td>• Death</td>
</tr>
</tbody>
</table>
CNBG’s COVID-19 Vaccine (Vero Cell), Inactivated, has been carrying out large-scale phase III efficacy clinical studies in the United Arab Emirates (UAE) and four other countries. As of December 31, 2020, nearly 45,000 people had been enrolled.

<table>
<thead>
<tr>
<th>Clinical Center</th>
<th>Recruitment</th>
<th>First Dose Subjects</th>
<th>Second Dose Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abu Dhabi, UAE</td>
<td>27,391</td>
<td>27,362</td>
<td>26,537</td>
</tr>
<tr>
<td>Sharjah, UAE</td>
<td>5,265</td>
<td>5,265</td>
<td>5,174</td>
</tr>
<tr>
<td>Bahrain</td>
<td>7,755</td>
<td>7,755</td>
<td>7,512</td>
</tr>
<tr>
<td>Egypt</td>
<td>3,000</td>
<td>2,991</td>
<td>2,828</td>
</tr>
<tr>
<td>Jordan</td>
<td>480</td>
<td>478</td>
<td>450</td>
</tr>
</tbody>
</table>
### Demographic Data and Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Statistics</th>
<th>HB02</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, n(%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 - 59 years</td>
<td>14338 (97.99)</td>
<td>14313 (98.00)</td>
<td></td>
</tr>
<tr>
<td>≥ 60 years</td>
<td>294 (2.01)</td>
<td>292 (2.00)</td>
<td></td>
</tr>
<tr>
<td><strong>Gender, n(%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>2293 (15.72)</td>
<td>2247 (15.42)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>12294 (84.28)</td>
<td>12327 (84.58)</td>
<td></td>
</tr>
<tr>
<td><strong>Populations, n(%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>12619 (86.23)</td>
<td>12702 (86.96)</td>
<td></td>
</tr>
<tr>
<td>Non-Asian</td>
<td>2015 (13.77)</td>
<td>1904 (13.04)</td>
<td></td>
</tr>
<tr>
<td><strong>Country, n(%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chinese</td>
<td>1837 (12.55)</td>
<td>1866 (12.78)</td>
<td></td>
</tr>
<tr>
<td>Non-Chinese</td>
<td>12740 (87.22)</td>
<td>12797 (87.45)</td>
<td></td>
</tr>
</tbody>
</table>

The median follow-up time was 112 days.
The second interim analysis is based on the data as of December 31, 2020.

According to the judgment of EAC and agreement among regulatory authorities, the total number of cases is 116, of which 95 were in placebo group, and 21 were in HB02 group. The number of cases required for the second interim analysis is 100.
Primary Efficacy Results (mFAS-1)

Vaccine efficacy against COVID-19 cases after 14 days post full course of immunization-based on person-year incidence

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>HB02</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Number of Subjects</td>
<td>13765</td>
<td>13765</td>
</tr>
<tr>
<td>Number of Cases</td>
<td>95</td>
<td>21</td>
</tr>
<tr>
<td>Person-Year Incidence (95%CI)</td>
<td>4.40%(3.60%, 5.38%)</td>
<td>0.96% (0.63%, 1.48%)</td>
</tr>
</tbody>
</table>

HB02 vs placebo (≥18 years old)

- The vaccine efficacy was 78.07%
- The two-sided 95% CI was (64.82%, 86.33%)
- Two-sided 95% CI lower limit is greater than 30%.
### Vaccine efficacy against COVID-19 cases after 14 days post full course of immunization-based on person-year incidence

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>HB02</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Number of Subjects</td>
<td>13765</td>
<td>13765</td>
</tr>
<tr>
<td>Number of Cases</td>
<td>94</td>
<td>20</td>
</tr>
<tr>
<td>Person-Year Incidence (95% CI)</td>
<td>4.35%(3.55%, 5.32%)</td>
<td>0.92% (0.59%, 1.42%)</td>
</tr>
</tbody>
</table>

**HB02 vs placebo (≥18 years old)**
- The vaccine efficacy was 78.89%
- The two-sided 95% CI was (65.79%, 86.97%)
- Two-sided 95% CI lower limit is greater than 30%.
## Efficacy against Severe Covid-19

Vaccine efficacy against COVID-19 severe cases after 14 days post full course of immunization-based on person-year incidence

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>HB02</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Number of Subjects</strong></td>
<td>13765</td>
<td>13765</td>
</tr>
<tr>
<td><strong>Number of Cases</strong></td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td><strong>Person-Year Incidence (95%CI)</strong></td>
<td>0.09%(0.01, 0.33)</td>
<td>0.00% (0.00, 0.17)</td>
</tr>
</tbody>
</table>

**HB02 vs placebo (≥18 years old)**

- The vaccine efficacy was 100.00%
- The two-sided 95% CI was (-430.26, 100.00)
## Primary Efficacy Results – Subgroup Analysis (mFAS-1)

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Placebo (N=13765)</th>
<th>HB02 (N=13765)</th>
<th>VE (%)</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-59</td>
<td>95</td>
<td>21</td>
<td>78.09</td>
<td>(64.85, 86.34)</td>
</tr>
<tr>
<td>60 and above</td>
<td>0</td>
<td>0</td>
<td>NE</td>
<td>NE</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>83</td>
<td>18</td>
<td>78.43</td>
<td>(64.09, 87.04)</td>
</tr>
<tr>
<td>Female</td>
<td>12</td>
<td>3</td>
<td>75.54</td>
<td>(13.34, 93.1)</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>89</td>
<td>18</td>
<td>79.76</td>
<td>(66.42, 84.81)</td>
</tr>
<tr>
<td>Chinese</td>
<td>0</td>
<td>0</td>
<td>NE</td>
<td>NE</td>
</tr>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgG Positive</td>
<td>1</td>
<td>0</td>
<td>100</td>
<td>(-3395.15, 100)</td>
</tr>
<tr>
<td>IgG Negative</td>
<td>83</td>
<td>16</td>
<td>80.79</td>
<td>(67.19, 88.75)</td>
</tr>
</tbody>
</table>
### Primary Efficacy Results – Subgroup Analysis (mFAS-1)

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Placebo</th>
<th>HB02</th>
<th>VE (%)</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMI≥30</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of participants</td>
<td>3080</td>
<td>3040</td>
<td>80.72</td>
<td>(56.67, 91.42)</td>
</tr>
<tr>
<td>No. of incident cases</td>
<td>36</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Asymptomatic Infection</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of participants</td>
<td>13765</td>
<td>13765</td>
<td>50.39</td>
<td>(-2.30, 75.94)</td>
</tr>
<tr>
<td>No. of incident cases</td>
<td>22</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Comorbidity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>4 (367)</td>
<td>0 (374)</td>
<td>100</td>
<td>(-100)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>6 (308)</td>
<td>2 (300)</td>
<td>63.71</td>
<td>(-79.79, 92.68)</td>
</tr>
<tr>
<td>CVDs</td>
<td>1 (67)</td>
<td>0 (73)</td>
<td>100</td>
<td>(-100)</td>
</tr>
</tbody>
</table>
The confirmed COVID-19 cases in placebo group were 138, which included 95 surveillance cases and 43 non-surveillance cases.

The confirmed COVID-19 cases in HB02 group were 48, which included 21 surveillance cases and 27 non-surveillance cases.

<table>
<thead>
<tr>
<th></th>
<th>Surveillance Period</th>
<th>Non-Surveillance Period</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo Group</td>
<td>95</td>
<td>43</td>
<td>138</td>
</tr>
<tr>
<td>HB02 Group</td>
<td>21</td>
<td>27</td>
<td>48</td>
</tr>
</tbody>
</table>
### Primary Efficacy Results (mFAS-1 Sensitivity Analysis)

#### Vaccine efficacy against COVID-19 cases after 1st dose-based on person-year incidence

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>HB02</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Number of Subjects</strong></td>
<td>14574</td>
<td>14587</td>
</tr>
<tr>
<td><strong>Number of Cases</strong></td>
<td>138</td>
<td>48</td>
</tr>
<tr>
<td><strong>Person-Year Incidence (95%CI)</strong></td>
<td>3.9%(3.3,4.61)</td>
<td>1.35%(1.02,1.79)</td>
</tr>
</tbody>
</table>

**HB02 vs placebo (≥18 years old)**

- The vaccine efficacy was 65.45%
- The two-sided 95% CI was (52.02,75.12)
Kaplan-Meier Estimates - Time to First Occurrence of COVID-19 since the First Dose of Vaccination

- Participants with confirmed COVID-19 (%)
  - 0.00
  - 0.25
  - 0.50
  - 0.75
  - 1.00
  - 1.25
  - 1.50

- Time since first dose (days)
  - 0
  - 25
  - 50
  - 75
  - 100
  - 125
  - 150

- HCO2
  - Participants: 14587
  - Time: 11810, 8153, 653, 0

- Placebo
  - Participants: 14574
  - Time: 13840, 13795, 11704, 8060, 665, 1
• The total cases of adverse events (times) in placebo group and HB02 vaccine group were 7,159 (17,547) and 6,570 (16,057) respectively, with the incidence rates of 49.01% and 44.90% respectively.
• Majority of the adverse reactions were grade 1.
• The incidence of Grade 1 adverse events in placebo group was higher than that in vaccine group, and the difference between groups was statistically significant. There was no significant difference between the two groups in other classifications.
The incidence of AE over 10% in age group 18-59 are local pain and fatigue.

The incidence of fatigue at the injection site was higher in the placebo group than in the vaccine group.

Adverse events were obviously concentrated in the solicited period.
• The incidence of AE over 10% is local pain
• The incidence of pain at the injection site was higher in the placebo group than in the vaccine group
• Adverse events were obviously concentrated in the solicited period
<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>HB02</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All AE</td>
<td>Related AE</td>
<td></td>
</tr>
<tr>
<td>Number of Cases</td>
<td>14297</td>
<td>14310</td>
<td></td>
</tr>
<tr>
<td>All AE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Cases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence (%)</td>
<td>0.01</td>
<td>0.01</td>
<td>0.9096</td>
</tr>
<tr>
<td>Hypersensitivity Reaction</td>
<td>48</td>
<td>42</td>
<td>0.34</td>
</tr>
<tr>
<td>Number of Cases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence (%)</td>
<td>0.34</td>
<td>0.29</td>
<td>0.9847</td>
</tr>
</tbody>
</table>

The vaccine-related AE incidence of allergic reaction in Placebo group and HB02 group were both 0.01, and there was no significant difference between two groups.
<table>
<thead>
<tr>
<th></th>
<th>Placebo (N=14606)</th>
<th></th>
<th></th>
<th>HB02 (N=14634)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Times</td>
<td>Cases</td>
<td>Incidence(%)</td>
<td>Times</td>
<td>Cases</td>
<td>Incidence(%)</td>
</tr>
<tr>
<td>Total SAEs</td>
<td>114</td>
<td>80</td>
<td>0.55</td>
<td>129</td>
<td>59</td>
<td>0.40</td>
</tr>
<tr>
<td>Related to Investigational Vaccine</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
<td>6</td>
<td>2</td>
<td>0.01</td>
</tr>
<tr>
<td>Unrelated to Investigational Vaccine</td>
<td>114</td>
<td>80</td>
<td>0.55</td>
<td>123</td>
<td>57</td>
<td>0.39</td>
</tr>
</tbody>
</table>
### Summary of SAEs after Vaccination among Different Ages and Different Populations (SS)

<table>
<thead>
<tr>
<th></th>
<th>Placebo (N=14606)</th>
<th></th>
<th></th>
<th>HB02 (N=14634)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Times</td>
<td>Cases</td>
<td>Incidence (%)</td>
<td>Times</td>
<td>Cases</td>
<td>Incidence (%)</td>
</tr>
<tr>
<td>18-59 Years Old</td>
<td>113</td>
<td>79</td>
<td>0.55</td>
<td>129</td>
<td>59</td>
<td>0.41</td>
</tr>
<tr>
<td>60 Years Old and above</td>
<td>1</td>
<td>1</td>
<td>0.34</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Asian</td>
<td>103</td>
<td>72</td>
<td>0.57</td>
<td>113</td>
<td>52</td>
<td>0.41</td>
</tr>
<tr>
<td>Baseline PCR Positive</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Chinese</td>
<td>3</td>
<td>3</td>
<td>0.16</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
</tr>
</tbody>
</table>
## Pregnancy Event Incidence (SS)

<table>
<thead>
<tr>
<th></th>
<th>Placebo (N=14631)</th>
<th>HB02 (N=14630)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pregnancy Subject (%)</strong></td>
<td>8 (0.05%)</td>
<td>5 (0.03%)</td>
</tr>
<tr>
<td><strong>Pregnancy Times</strong></td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td><strong>Delivery(%)</strong></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Non-delivery(%)</strong></td>
<td>8 (0.03%)</td>
<td>5 (0.03%)</td>
</tr>
</tbody>
</table>
Neutralizing Antibody GMT:
- 14 days after 2 doses, the anti-SARS-CoV-2 neutralizing antibody GMT in HB02 group is 156.
- Anti-SARS-CoV-2 neutralizing antibody have obvious increase.

Binding Antibody GMT:
- 14 days after 2 doses, the anti-SARS-CoV-2 binding antibody GMT in HB02 group is 1366.1.
- Anti-SARS-CoV-2 binding antibody have obvious increase.
Neutralizing Antibody GMT:
- 14 days after 2 doses, the anti-SARS-CoV-2 neutralizing antibody GMT in HB02 group for population aged 18-59 and 60 and above are 156.2 and 109.7 respectively.
- Anti-SARS-CoV-2 neutralizing antibody for two different aged groups have obvious increase.

Binding Antibody GMT:
- 14 days after 2 doses, the anti-SARS-CoV-2 binding antibody GMT in HB02 group for population aged 18-59 and 60 and above are 1374.4 and 1218.2 respectively.
- Anti-SARS-CoV-2 binding antibody for two different aged groups have obvious increase.
Neutralizing Antibody GMT:
- 14 days after 2 doses, anti-SARS-CoV-2 neutralizing antibody GMT in HB02 group for population aged 18-58 and 60 and above are 156.2 and 114.1 respectively.
- Anti-SARS-CoV-2 neutralizing antibody for two different aged groups have obvious increase.
Neutralizing Antibody GMT:
- 14 days after 2 doses, anti-SARS-CoV-2 neutralizing antibody GMT in HB02 group for male and female are 158.5 and 146.3 respectively.
- Anti-SARS-CoV-2 neutralizing antibody for different genders have obvious increase.

Binding Antibody GMT:
- 14 days after 2 doses, anti-SARS-CoV-2 binding antibody GMT in HB02 group for male and female are 1389 and 1280 respectively.
- Anti-SARS-CoV-2 binding antibody for different genders have obvious increase.
The GMT Level of Serum Neutralizing Antibody in Each Subset 14 Days after Immunization

- Female: 146.3
- Male: 158.5
- Non-chinese population: 160.9
- Chinese population: 134.2
- Non-Asian population: 167.7
- Asian population: 154.8
- Aged 60 and above: 109.7
- Aged 18-59: 156.2

Comparison between post-immunization and pre-immunization levels.

(post-immunization: orange, pre-immunization: grey)
Phase I-III clinical serum:
Has high cross neutralization activity against multiple prevalent SARS-CoV-2 strains, showing broad cross protection.
Cross-Neutralization against 501Y.V2

Inactivated vaccine (BBIBP-CorV)

- x 1.6
- P=0.12
- P=0.92
- P=0.25

50% Neutralization titer

- HB02 (WT)
- BJ01(D614G)
- GDPCC (501Y.V2)
Summary of Phase III Second Interim Analysis

◆ Vaccine Efficacy
• The vaccine efficacy based on the person-year incidence rate of population aged 18 years old and above reached 78.89%, achieved the primary efficacy endpoint.
• The vaccine efficacy against severe cases of COVID-19 in population aged 18 years old and above is 100%, achieved the secondary efficacy endpoint.

◆ Safety
• Within 28 days after the second vaccination, placebo group and HB02 group had an AE incidence of 49.01% and 44.90%, respectively.
• Population aged 60 (29.25%) and above had lower AE incidence than population aged 18-59 (45.22%) after 2 doses of vaccination.
• Adverse event was mainly concentrated on grade 1 AE, and the grade 3 AE had an incidence of 0.77%. No grade 4 vaccine related AE.

◆ Immunogenicity
• After 14 days following 2 doses of immunization, the positive seroconversion rate (4 fold growth rate), GMT and GMI of anti-SARS-CoV-2 neutralizing antibody were 100%, 156.0 and 68.689 respectively, which were significantly higher than those of placebo group.
◆ Cross-Neutralization Protection Effect of Subject Serum

- The results of the true virus cross-neutralization test by blindly drawing serum samples from the subjects in this phase III clinical trial showed that, the serum of HB02 groups at 28 days after whole immunization had good cross-neutralization ability with 10 SARS-CoV-2 strains epidemic at domestic and abroad.

- The positive seroconversion rate of neutralizing antibody in HB02 groups can reach 100%, and there is no significant difference in antibody titers among these strains. The vaccines have extensive cross neutralization reactions to the current domestic and abroad epidemic or representative SARS-CoV-2 Wild Viruses.
Post-marketing activities

- Post-marketing surveillance
- Post-marketing clinical studies
As of 31 March 2021, AEFI reports from 65.58 million people vaccinated have been obtained;

- **Common reactions:** 7355 cases reported (11.22 /100,000)
- **Local reactions:** redness, swelling, and induration; mainly mild
- **Systemic reactions:** fever, fatigue, headache, dizziness

- **Abnormal (rare) reactions:** 1617 reported (2.47 /100,000) were reported
- **Most common reactions** were allergic rash, other allergic reactions, and urticarial

- **Male:** 37.4%; **female:** 62.58%
- **Age:** majority are 18-59 years old, ≥60 years:79 cases
As of March 31, 2021, a total of 1,123,413 doses of BIBP COVID-19 vaccine have been administered to people 60 years of age or older in China, 79 cases aged 60 and above were reported;

• Among the 79 cases, 35 cases were mainly general reactions, accounting for 44.30%;
• Followed by coincidental events, with a total of 19 cases, accounting for 24.05%;
• 86% cases have improved or been recovered.

From the age distribution, the age of the majority of recipients is concentrated in the range of 60-69 years old:
• among them, the age group of 65-69 years old is the most (30 cases); Followed by 70-74 years old group, with 15 cases in total;
• Fewer cases were reported in the age group 75 years and above.

The 79 AEFI cases reported 125 adverse reaction;
• among which dizziness was the most, with 23 cases;
• Followed by headache and fatigue, with 9 cases each;
• The terms reported more than 5 cases were nausea (7 cases), fever (6 cases), vomiting (6 cases), allergic dermatitis (6 cases), rash (5 cases), palpitation (5 cases),
• the other AEs reported less than 5 cases;
AEFI cases are mainly general reactions, followed by abnormal reactions and coincidental diseases.

The known adverse reactions are mainly dizziness, fever, allergic dermatitis, fatigue, etc. The reporting rate of serious adverse reactions is less than 0.1%, which is very rare.

To sum up, the safety profile of Covilo-BIBP in this reporting period are basically consistent with the safety data in the package insert, with good benefits/risks. The company will continue to pay attention to the safety monitoring of this product.
## Post-marketing Clinical Studies

<table>
<thead>
<tr>
<th>Study Code</th>
<th>Subjects</th>
<th>purpose</th>
<th>Location(s)</th>
<th>sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNBG-RWS-001</td>
<td>aged 18 years and above</td>
<td>effectiveness; safety</td>
<td>low and middle income countries</td>
<td>At least 526 subjects (70% efficacy)</td>
</tr>
<tr>
<td>CNBG-RWS-002</td>
<td>aged 18 years and above</td>
<td>1. safety monitoring (active surveillance); 2. Special population, Co-morbidities.</td>
<td>China;</td>
<td>1) 105,000 subjects (safety) 2) 42,000 subjects ≥60Y; 3) 2,250 subjects with comorbidity (hypertension and diabetes);</td>
</tr>
<tr>
<td>CNBG-RWS-003</td>
<td>aged 18 years and above</td>
<td>1)Immunogenicity 2)safety 3) Special populations</td>
<td>China;</td>
<td>1,000 subjects</td>
</tr>
<tr>
<td>CNBG-CIP-004</td>
<td>aged 18 years and above</td>
<td>Co-administration; Immunogenicity; safety; Immune interventions;</td>
<td>China;</td>
<td>1,152 subjects</td>
</tr>
<tr>
<td>CNBG-RWS-005</td>
<td>aged 18 years and above</td>
<td>safety (Passive safety monitoring); rare/very rare AR; potential ADE/VED;</td>
<td>China;</td>
<td>1,000,000 subjects</td>
</tr>
<tr>
<td>IVI-006</td>
<td>aged 18 years and above</td>
<td>protective efficacy; Safety, Immunogenicity; Special populations; Co-administration vaccination;</td>
<td>Mozambique</td>
<td>9,800 subjects</td>
</tr>
<tr>
<td>BIBP2020004CN</td>
<td>aged 3 years and above</td>
<td>Safety, Immunogenicity; immune-persistency of different schedules;</td>
<td>China;</td>
<td>4400 subjects</td>
</tr>
</tbody>
</table>
Thanks to our collaborators, investigators, subjects and your kindly attention!

- National Medical Products Administration (NMPA)
- Center for Drug Evaluation, NMPA
- Joint Prevention and Control Mechanism of the State Council
- National Health Commission, PRC
- Ministry of Science and Technology, PRC
- National Institutes for Food and Drug Control
- Center for Food and Drug Inspection of NMPA
- Chinese Center for Disease Control and Prevention (CDC)
- Institute of Laboratory Animal Sciences, Cams & Pumc

- People's Government of Beijing Municipality Management Committee of Beijing Economic and Technological Development Zone
- Beijing Municipal Drug Administration
- Henan Center for Disease Control and Prevention
- G42 group
- Al Qarain Primary Healthcare Center
- Shaikh Khalifa Medical City
- Beijing Contrico Statistical Technology Co., Ltd
- Beijing Zhaoyan New Drug Research Center Co. Ltd
Thank you!