新冠疫苗研发概述及中国生物产品简介
Covid-19 Vaccine R&D and CNBG's Product Portfolio

CNBG

中国生物技术股份有限公司
China National Biotec Group Company Limited

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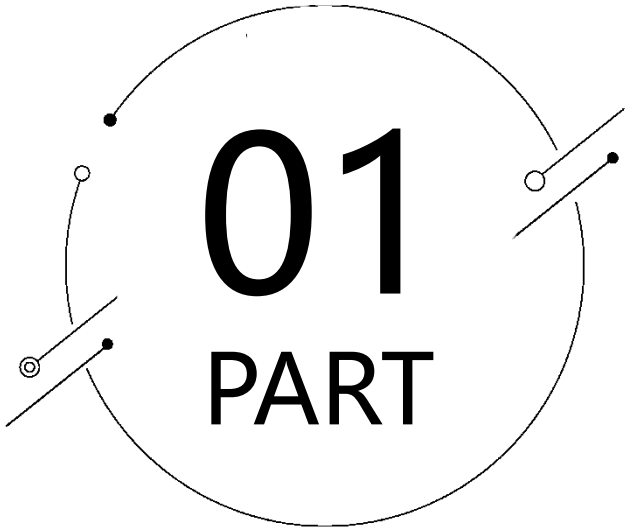


新冠病毒疫苗研发概述

COVID-19 Vaccine R&D Lanscape

新冠疫情概况
COVID-19 Pandemic Overview

- 截至10月28日，全球累计感染新冠病毒确诊病例达到43,341,451人，累计死亡1,157,509人。

Up until Oct. 28th, there have been 43,341,451 confirmed cases of COVID-19, including 1,157,509 deaths.

- 确诊人数已达每日35万人。

Daily confirmed cases exceed 30 thousand.

- 美国、印度、巴西确诊病例为全球最多。

The USA, India and Brazil have the most confirmed cases globally.

Cases by Country/Region/Sovereignty	
8,779,653	US
7,990,322	India
5,439,641	Brazil
1,537,142	Russia
1,244,242	France
1,116,738	Spain

全球新冠病毒疫苗概述
Overview of Global COVID-19 Vaccine R&D

截止2020年10月19日，根据WHO公布的数据，全球有44个候选疫苗进入临床阶段，154个进入临床前期阶段

Up until Oct. 19th, 2020, according to data from WHO, there are 44 candidate vaccines entered clinical phase and 154 entered preclinical phase

10个候选疫苗进入3期临床
Ten candidate vaccines entered Phase III clinical trials

疫苗企业 Vaccine Manufacturers	进入3期临床时间 Phase III Launching Time
中生武汉所 WIBP/Sinopharm	06/23
中生北京所 BIBP/Sinopharm	06/23
牛津大学/阿斯利康 University of Oxford/AstraZeneca	07/01
科兴生物 Sinovac	07/03
Moderna公司 Moderna	07/27
BioNTech/复星/辉瑞 BioNTech/Fosun Pharma/Pfizer	08/28
加马列亚研究所 Gamaleya Research Institute	09/02
康希诺 Cansino Biological	09/02
扬森 Janssen Pharmaceuticals	09/07
Novavax公司 Novavax	09/23

按技术路线分类
Classification by Technology Platforms

疫苗企业 Vaccine Manufacturers	疫苗技术路线 Vaccine Platform	疫苗类型 Type of Vaccine
中生武汉所 WIBP/Sinopharm	灭活 Inactivated	灭活 Inactivated
中生北京所 BIBP/Sinopharm	灭活 Inactivated	灭活 Inactivated
牛津大学/阿斯利康 University of Oxford/AstraZeneca	非复制性载体病毒 Non-replicating Viral Vector	ChAdOx1-5
科兴生物 Sinovac	灭活 Inactivated	灭活 Inactivated
Moderna公司 Moderna	RNA	LNP-encapsulated mRNA 脂质纳米粒包裹mRNA
BioNTech/复星/辉瑞 BioNTech/Fosun Pharma/Pfizer	RNA	3 LNP-mRNAs 3个脂质纳米粒mRNA
加马列亚研究所 Gamaleya Research Institute	非复制性载体病毒 Non-replicating Viral Vector	rAd26-S+rAd5-S
康希诺 Cansino Biological	非复制性载体病毒 Non-replicating Viral Vector	Adenovirus Type 5 Vector 腺病毒5型载体
扬森 Janssen Pharmaceuticals	非复制性载体病毒 Non-replicating Viral Vector	Ad26COVS1
Novavax公司 Novavax	蛋白质亚单位 Protein Subunit	Recombinant Glycoprotein Nanoparticle 重组糖蛋白纳米粒子

国内研发情况情况 R&D in China

01 品种及技术 Type and Technology

- 共25个候选疫苗
- 25 vaccine candidates
- 采取了4条技术路线
- 4 platforms
- 共使用了3种载体（腺病毒、痘苗、流感）
- 3 vectors (Adenovirus, vaccinia and flu)
- 重组蛋白疫苗10个、灭活疫苗7个、核酸疫苗5个、载体疫苗3个。
- 10 recombinant protein vaccines, 7 inactivated vaccines, 5 nucleic acid vaccines, 3 vector vaccines

02 研究单位 Developer

- 共24家研究单位
- 24 developers
- 分布在北京、天津、湖北、云南、上海、安徽、四川、福建、香港和台湾
- Located in Beijing, Tianjing, Hubei, Yunnan, Shanghai, Anhui, Sichuan, Fujian, Hongkong and Taiwan.

03 合作情况情况 Cooperation

- 国际合作9项
- 9 internationally collaborative projects

02
PART

中国生物新冠病毒疫苗介绍

CNBG’s COVID-19 Vaccine Product Portfolio

我们选择灭活疫苗
Why Inactivated Vaccine

- 通过化学方法使病毒失去感染性和复制力，但保持了能引起人体免疫应答活性而制备成的疫苗

By chemical methods, the virus loses its infectivity and replication, but keeps the activity to induce human immune response

- **灭活疫苗的优势 Advantages:**
  - 具备全病毒抗原，具有更全面的保护性；having whole virus antigen to provide broad protection
  - 传统的疫苗制备方式，全球已上市疫苗中,灭活疫苗品种最多；classic formulation with the largest number of listed products
  - 已上市多种灭活疫苗,市场多年验证安全性、有效性良好；excellent safety and efficacy profile validated by listed products
  - 同类制品在药典中有明确质控标准，易于建立指控标准和进行质量评价；having clear quality criteria in Pharmacopoeia to establish quality standards and evaluation
  - 研发生产技术体系非常成熟，研发速度快,可借鉴EV71,sIPV等的经验。mature R&D platform and fast R&D speed, referring to EV71 and sIPV vaccine

灭活疫苗的研发流程
R&D of Inactivated Vaccine

生产工艺研究
Production Process Studies

发酵工艺、灭活工艺、纯化工艺等 Fermentation, inactivation, purification

优化工艺参数 Optimization

质量研究 Quality Studies

- 建立全面的质量标准

Comprehensive quality standards

- 实行全过程质量控制

Comprehensive quality control

- 对全生命周期的质量负责

Responsible for entire life cycle

人体中的临床研究
Human in vivo clinical studies

- Ⅰ期：初步安全性

Phase I: preliminary safety

- Ⅱ期：安全性和剂量探索

Phase II: safety and dose exploration

- Ⅲ期：扩大的安全性和有效性

Phase III: expanded safety and efficacy

01 02 03 04 05

获取免疫原
Obtaining Antigen

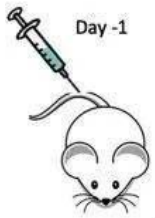
根据疫苗的原理不同：分为病毒、蛋白、基因片段、携带病毒基因的载体等 According to vaccine platform, it can be divided into virus, protein, gene fragment and viral vector gene

动物体内评价 Animal *in vivo* Evaluation

- 小鼠、大鼠、豚鼠、家兔、恒河猴、食蟹猴等

Mice, rats, guinea pigs, rabbits, rhesus monkeys, cynomolgus monkeys, etc

- 免疫原性、安全性、保护性 Immunogenicity, safety, efficacy



产品概况
Product Profile

- 0.5毫升/剂，1支/盒，2针免疫程序 0.5 ml/dose, 1 Syringe/box, 2 doses regimen.
- 储存条件：2-8摄氏度 Storage conditions: 2-8 ℃.
- Above 3 years old.

生产工艺研究和获得疫苗株
Production Process Studies & Obtaining Virus Strain

- 生产工艺研究 Production Process Studies:

细胞培养 Cell Culture | 病毒培养 Virus Culture | 收获灭活 Harvest Inactivation | 浓缩纯化 Concentration and Purification | 成品配置 Product Formulation

- 获得疫苗株 Obtaining Virus Strain：不同时间从不同地区获得多个样本，分离得到多个病毒株，经过形态学、免疫学、分子生物学、抗原性、遗传稳定性等的分析，最终确定1个生产株；经过三轮噬斑纯化获得高滴度病毒株，建立三级毒种库。

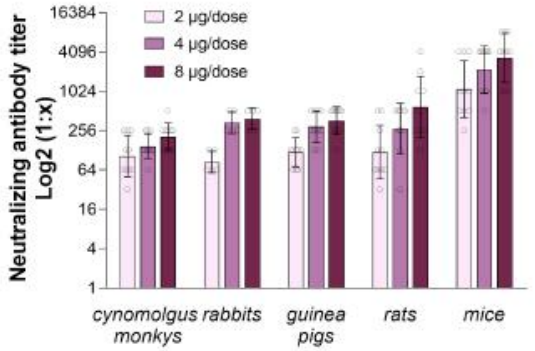
Collecting samples from different place at different time; separating samples to have multiple stains; by morphology, immunology, molecular biology, antigenicity and genetic stability studies, finalizing one manufacturing strain, after 3 rounds of plague purification, obtaining high titer virus strain, establishing Tier 3 virus bank.

质量标准研究
Quality Standard Studies

病毒收获液 Virus Harvest Solution	灭活病毒收获液 Inactivated Virus Harvest Solution	原液 Bulk	半成品 Final Bulk	成品 Finished Product
无菌检测 Sterility Test	抗原含量 Antigen Content	无菌检测 Sterility Test	无菌检测 Sterility Test	鉴别试验 Identification
支原体检查 Mycoplasma Test	病毒灭活验证试验 Inactivation Validation	蛋白质含量 Protein Content	pH值测定 pH Level	外观 Appearance
病毒滴度检查 Virus Titer Test		抗原含量 Antigen Content	氢氧化铝吸附效果测定 Aluminum Hydroxide Adsorption	装量 Filling Volume
		病毒灭活验证试验 Inactivation Validation	铝含量测定 Aluminum Content Test	pH值 pH Level
		牛血清白蛋白残留量 Bovine Serum Albumin Residual		铝含量测定 Aluminum Content Test
		宿主细胞残留DNA检测 Host Cell DNA Residual		无菌检查 Sterility Test
		宿主细胞残留蛋白检测 Host Cell Protein Residual		细菌内毒素检查 Endotoxin Test
		细菌内毒素检查 Endotoxin Test		异常毒性试验（小鼠试验、豚鼠试验） Abnormal Toxicity Test (mice, guinea pigs)
				抗原含量测定（体外相对效力实验） Antigen Content Test
				体内效力试验 in vivo Relative Potency Test
				渗透压摩尔浓度 Osmotic Pressure Molar Concentration

动物体内评价
Animal in vivo Evaluation

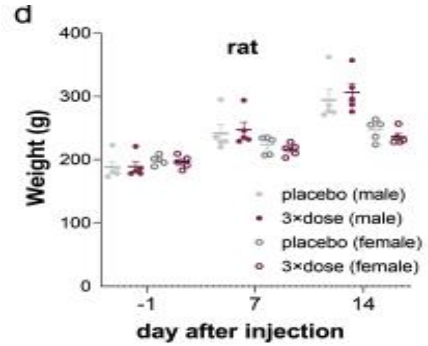
免疫原性 Immunogenicity

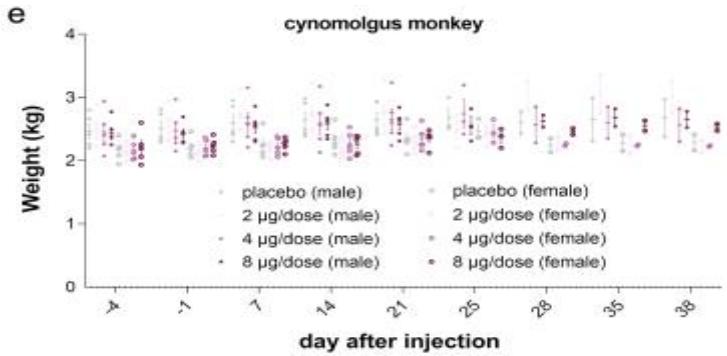


结论 Conclusion：

- 新冠灭活疫苗可诱导多种动物体内的免疫反应；Inactivated vaccine can induce immune response in many animals
- 不同种动物体内不同免疫剂量、免疫程序均能产生高滴度抗体；High titer antibody can be produced by different dosages, schedules in different animals
- 抗体水平与免疫针次、剂量呈正相关。The antibody level is positively related with the times and dose of immunization.

安全性 Safety





结论：

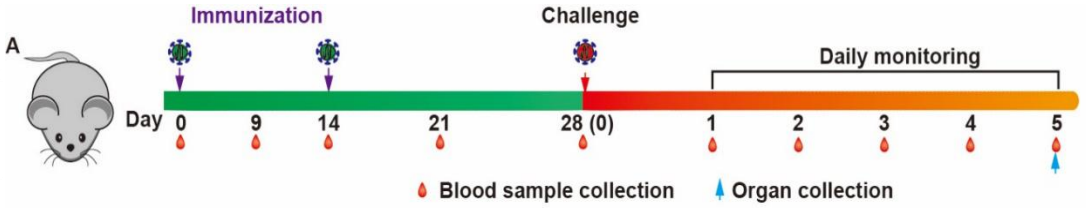
- 受试动物的生理指标、临床病理指标均未见明显异常，疫苗的安全性良好！

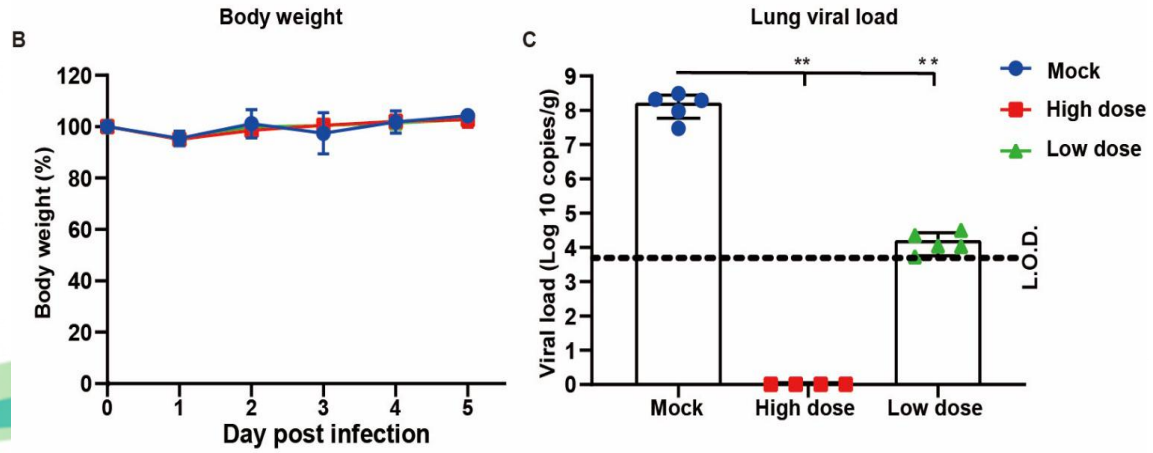
There is no obvious abnormality in the physiological and clinicopathological indexes of the tested animals, and the safety of the vaccine is good!

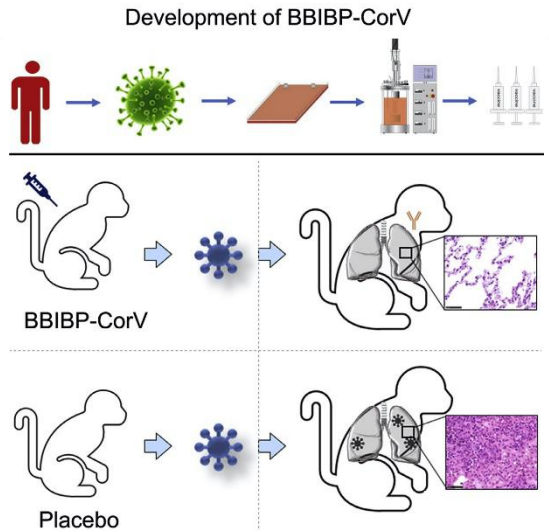
动物体内评价
Animal in vivo Evaluation

ACE2转基因小鼠 ACE2 Transgenic Mice

- 疫苗免疫（高、中、低剂量、0,7d，0,14d程序）
- Schedule: (high, medium, low dose, [0,7],[0,14] schedule
- 攻毒，观察保护效果 Challenge and observe efficacy







结论 Conclusion：

- 可以在动物体内产生高滴度的保护性抗体；

Induce high titer of protective antibody in animals

- 能够降低动物肺部的病毒载量；

Reduce the viral load in the lung of the animals

- 可以减轻新冠病毒造成的病理损伤，对新冠病毒的感染可起到一定的保护作用。

Alleviate the pathological damage and protect the infection of COVID-19.

人体内评价
Human in vivo Evaluation

1期临床和2期临床 Phase I and Phase II

- **已完成I、II期全部18岁以上2240名受试者的全程免疫**

All 2240 subjects over 18 years old have complete full immunization schedule in Phase I and Phase II

- **武汉公司I、II期临床结果已经发表在《JAMA》**

WIBP’s results of Phase I and Phase II have been published on ***JAMA***

- **北京公司I、II期临床结果发表在《柳叶刀》**

BIBP’s results of Phase I and Phase II have been published on ***the Lancet***

Research

JAMA | Preliminary Communication

Effect of an Inactivated Vaccine Against SARS-CoV-2 on Safety and Immunogenicity Outcomes

Interim Analysis of 2 Randomized Clinical Trials

Shengli Xia, BS; Kai Duan, PhD; Yuntao Zhang, PhD; Dongyang Zhao, BS; Huajun Zhang, PhD; Zhiqiang Xie, MD; Xinguo Li, MD; Cheng Peng, MD; Yanbo Zhang, MD; Wei Zhang, MD; Yunkai Yang, MD; Wei Chen, MSc; Xiaoxiao Gao, PhD; Wangyang You, MD; Xuewei Wang, MD; Zejun Wang, PhD; Zhengli Shi, PhD; Yanxia Wang, BS; Xuqin Yang, MD; Lianghao Zhang, MSc; Lili Huang, BS; Qian Wang, MD; Jia Lu, PhD; Yongli Yang, PhD; Jing Guo, PhD; Wei Zhou, PhD; Xin Wan, MD; Cong Wu, MD; Wenhui Wang, MD; Shihe Huang, PhD; Jianhui Du, MD; Ziyan Meng, MD; An Pan, PhD; Zhiming Yuan, PhD; Shuo Shen, PhD; Wanshen Guo, BS; Xiaoming Yang, MD

IMPORTANCE A vaccine against coronavirus disease 2019 (COVID-19) is urgently needed.

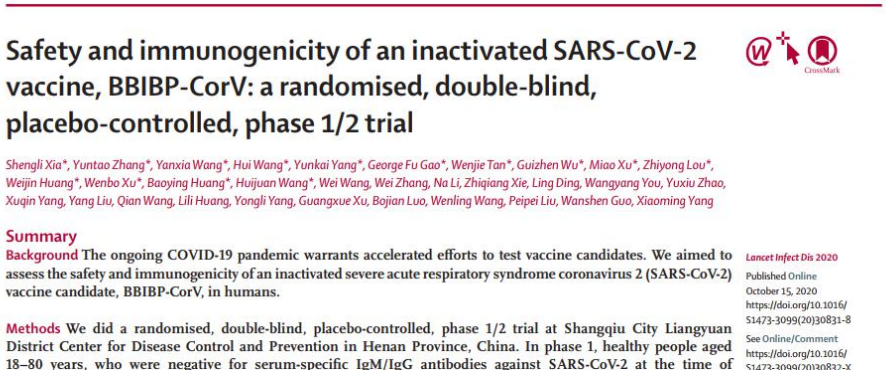
OBJECTIVE To evaluate the safety and immunogenicity of an investigational inactivated whole-virus COVID-19 vaccine in China.

INTERVENTIONS In the phase 1 trial, 96 participants were assigned to 1 of the 3 dose groups

Editorial

Supplemental content

Articles



Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: a randomised, double-blind, placebo-controlled, phase 1/2 trial

Shengli Xia, Yuntao Zhang*, Yanxia Wang*, Hui Wang*, Yunkai Yang*, George Fu Gao*, Wenjie Tan*, Guizhen Wu*, Miao Xu*, Zhiyong Lou*, Weijin Huang*, Wenbo Xu*, Baoying Huang*, Huijuan Wang*, Wei Wang, Wei Zhang, Na Li, Zhiqiang Xie, Ling Ding, Wangyang You, Yuxiu Zhao, Xuqin Yang, Yang Liu, Qian Wang, Lili Huang, Yongli Yang, Guangxue Xu, Bojian Luo, Wenling Wang, Peipei Liu, Wanshen Guo, Xiaoming Yang*

Summary

Background The ongoing COVID-19 pandemic warrants accelerated efforts to test vaccine candidates. We aimed to assess the safety and immunogenicity of an inactivated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine candidate, BBIBP-CorV, in humans.

Methods We did a randomised, double-blind, placebo-controlled, phase 1/2 trial at Shangqiu City Liangyuan District Center for Disease Control and Prevention in Henan Province, China. In phase 1, healthy people aged 18–80 years, who were negative for serum-specific IgM/IgG antibodies against SARS-CoV-2 at the time of

Lancet Infect Dis 2020

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See Online/Comment https://doi.org/10.1016/

人体内评价
Human in vivo Evaluation

武汉公司 WIBP		北京公司 BIBP	
安全性 Safety	有效性 Efficacy	安全性 Safety	有效性 Efficacy
• 疫苗组和安慰剂组见无显著差异，说明该灭活疫苗在人体安全性良好。 No significant difference between the vaccine group and the placebo group, indicating the inactivated vaccine is safe in human body.	• 中剂量两针免疫后14天，抗体阳转率97.6%； 14 days after the second injection, antibody serum conversion level reached 97.6% • 0，14天和0，21天两针免疫后第14天中和抗体GMT值分别为121和247。 14 days after the second injection, the GMT of [0,14] and [0,21] schedule are 121 and 247 respectively.	• 疫苗组和安慰剂组见无显著差异，说明该灭活疫苗在人体安全性良好。 No significant difference between the vaccine group and the placebo group, indicating the inactivated vaccine is safe in human body.	• 两针免疫后28天，抗体阳转率100%； 28 days after the second injection, antibody serum conversion level reached 100% • 2ug、4ug和8ug免疫后28天，GMT值分别为87，211和229 28 days after the second injection, the GMT of 2ug, 4ug and 8ug group are 87, 211 and 229 respectively.

人体内评价-3期临床
Human in vivo Evaluation-Phase III Clinical Trials

临床III期 Phase III clinical trials

- 进一步扩大的安全性和有效性确证；

Expanded safety and efficacy validation

- 需要根据流行病学统计出来的数据，在更大规模的样本中评价新的疫苗需要开展保护性临床研究。

To perform large scale efficacy studies according to epidemiology data

- 国际多中心临床试验，计划入组45,000人

Multi-center clinical trials, expected to recruit 45,000 subjects

- 6月23日，阿联酋项目正式启动

June 23rd clinical trial in UAE initiated

- 8月初，巴林、埃及、约旦、摩洛哥临床实验启动

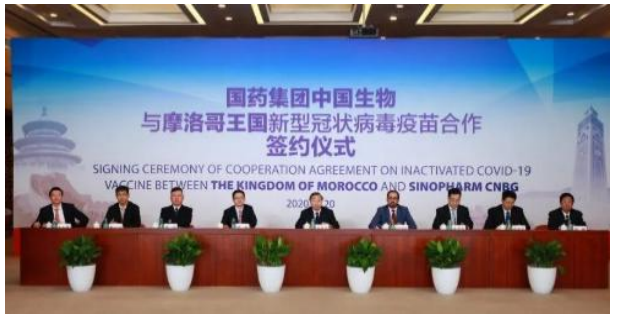
Trials in Bahrain, Egypt, Jordan and Morocco launched at the beginning of August

- 8月20日，秘鲁、阿根廷临床试验启动

Aug. 20th, trials in Peru and Argentina launched

- 截至10月17日，已入组5万余人

Up until Oct 17th , over 50,000 subjects have been recruited



规模化生产车间建设
Construction of Large-scale Manufacturing Facilities

- **产能 Capacity**：两车间合计可达3亿剂/年
- at least 300 million doses/annual for 2 facilities in total
- **生产许可 Manufacturing Licensure**：均已获得新冠疫苗生产许可证

Both received licensure to manufacture COVID-19 vaccine

- **生物安全认证 Biosafety Certificate**：
  - 均已经通过卫健委等多部委的生物安全认证

  Both received biosafety certificates from NHC and other ministries

感谢您的聆听！
THANKS FOR LISTENING

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