克尔来福™
CoronaVac™
新型冠状病毒灭活疫苗

SARS-CoV-2 Vaccine (Vero cell), Inactivated

科兴控股生物技术有限公司
SINOVAC BIOTECH LTD.

CONTENTS

克尔来福™ CoronaVac™
新型冠状病毒灭活疫苗

Our History &Products

We focuses on the Research, Development, Manufacture and Commercialization of vaccines for infectious diseases with significant unmet medical need.

2001

SINOVAC

Sinovac Beijing
Established

2002

Hepatitis A Vaccine, Inactivated
(WHO PQ , 2017)

致尔来福® Healive®
甲型肝炎灭活疫苗

2004

Inactivated SARS Vaccine
(Phase 1 Completed)

2005

Hepatitis A & Hepatitis B Combined Vaccine

倍尔来福® Bilive®
甲型乙型肝炎联合疫苗

2006

安尔来福® Anflu®
流感病毒裂解疫苗

Influenza Vaccine (Split Virion) , Inactivated

2008

Pandemic Influenza Vaccine, Inactivated (H5N1)

盼尔来福® Panflu®
大流行流感病毒灭活疫苗

2009

盼尔来福.1® Panflu.1®
甲型H1N1流感病毒裂解疫苗

H1N1 Influenza A Vaccine (Split Virion) , Inactivated

SINOVAC

Sinovac LifeSciences
Established

2010

Sinovac Dalian Established

SINOVAC

2012

腮腺炎减毒活疫苗
MUMPS VACCINE,LIVE

Mumps vaccine, Live

2016

Enterovirus Type 71 Vaccine , Inactivated

益尔来福® Inlive®
肠道病毒71型灭活疫苗

2020...

克尔来福™ CoronaVac™
新型冠状病毒灭活疫苗

水痘减毒活疫苗
VARICELLA VACCINE,LIVE

四价流感病毒裂解疫苗
Influenza Vaccine (Split Virion), Inactivated, Quadrivalent

克尔来福™ CoronaVac™
新型冠状病毒灭活疫苗

Varicella Vaccine, Live
Quadrivalent Influenza Vaccine
COVID-19 Vaccine
PPV23
Sabin-IPV

Provide Chinese Children with Top Quality Vaccines, Provide Children around the World with Vaccines Made in China

Production Sites

Area: 22,264.21 m²
Floorage: 14,200.38 m²

- HepA
- Influenza
- HepA&B combo
- PPV23

Hadian·Beijing (Headquater)

Dalian·Liaoning

克尔来福™
CoronaVac™
新型冠状病毒灭活疫苗

Area: 95,685.6m²
Floorage: 20,000m²

- Mumps
- Varicella

Area: 29,021m²
Floorage: 32,322m²

- EV71
- Sabin-IPV

Changping·Beijing

Daxing·Beijing

Area: 45,523 m²
Floorage: 69,124.5 m²

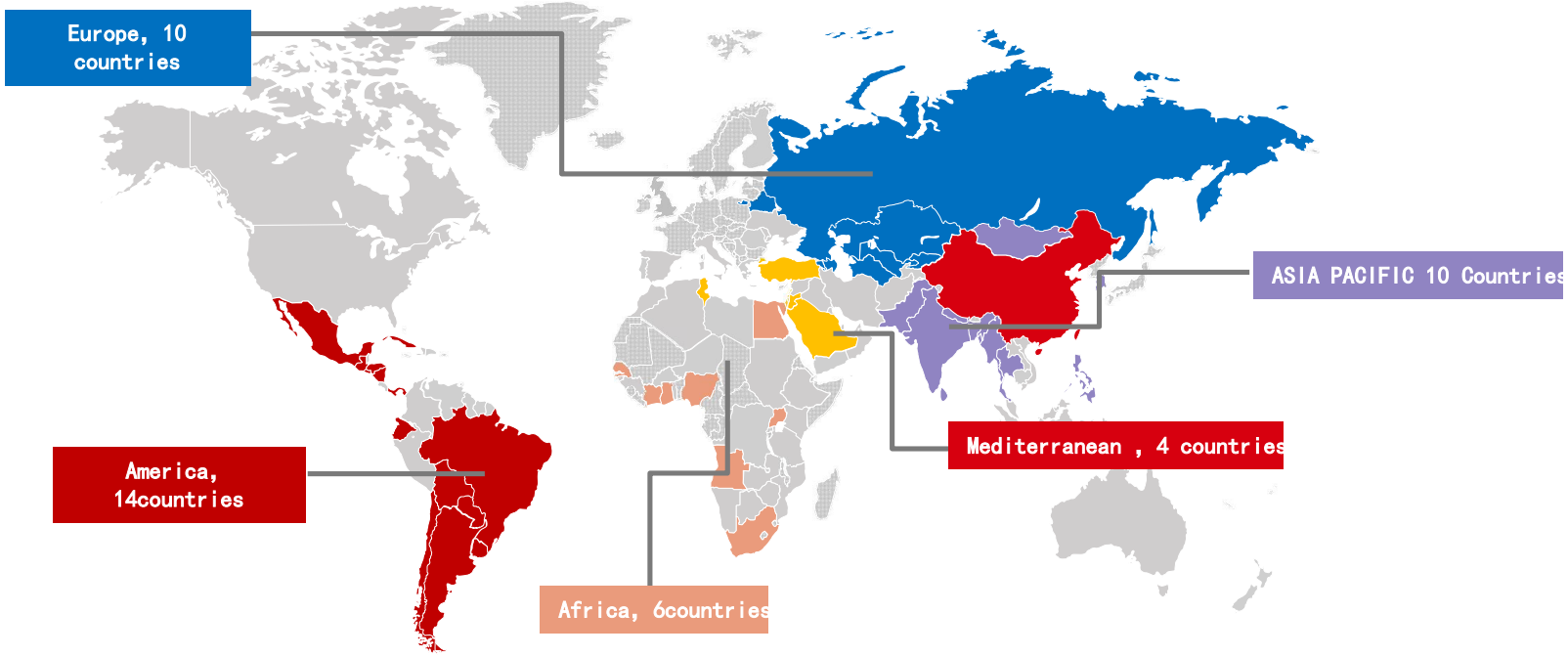
- Sars - Cov-2
- ……

- Beijing(Haidian, Changping, Daxing sites), and Dalian site. 4 sites in total
- Total Capacity: More than 400 million doses per year for more than 10 vaccines
- Total area:192,000m² Total floorage:136,000m²
- **SARS-COV-2 Vaccine Capacity: 300 million doses per year**

Worldwide Market & Footprint

克尔来福™ CoronaVac™ 新型冠状病毒灭活疫苗

- The cumulative global sales are nearly 160 million doses. In 2019, an average of 112 people per minute were vaccinated with Sinovac's vaccines to obtain immune protection.
- Sinovac's vaccine has been sold in 22 countries around the world, has been registered in 17 countries, and is being registered in 26 countries, covering 3.25 billion people 68 million newborns
- The hepatitis A vaccine Healive® ® is the first HepA vaccine in China to pass WHO-PQ, and is being exported to more than 10 "Belt and Road" countries and international organizations such as UNICEF and PAHO.



Quality Accreditation

克尔来福™ CoronaVac™ 新型冠状病毒灭活疫苗


China

Kazakhstan

Nepal

Nigeria

Argentina (PIC/s)

Turkey (PIC/s)

Thailand (PIC/s)

Cuba

MINISTÉRIO DA SAÚDE

AGÊNCIA NACIONAL DE VIGILÂNCIA SANITÁRIA

CERTIFICADO DE BOAS PRÁTICAS DE FABRICAÇÃO DE MEDICAMENTOS

LINHA DE INSUMOS FARMACÊUTICOS ATIVOS BIOLÓGICOS

A Agência Nacional de Vigilância Sanitária - ANVISA, por meio da Resolução RE nº 2.221, de 01/07/2020, publicada em Diário Oficial da União (DOU) na data de 06/07/2020, certifica que a empresa abaixo é periodicamente inspecionada e monitorada pelo Sistema Nacional de Vigilância Sanitária e que cumpre com as diretrizes de Boas Práticas de Fabricação dadas pela legislação brasileira, a qual está em consonância com as recomendações da Organização Mundial de Saúde.

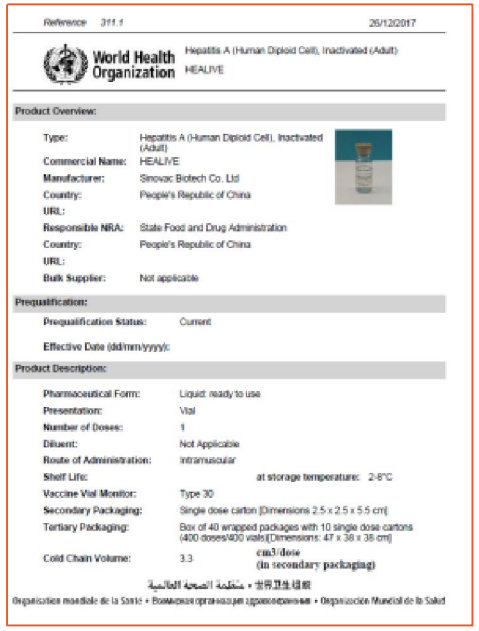
Fabricante: Sinovac Biotech CO. LTD.
Endereço: Nº 39, Shangdi Xi Road, Haidian District,100085, Beijing (Pequim)
País: República Popular da China Código Único: A.1404
Solicitante: Bio Medicamentos Ltda CNPJ: 15.268.466/0001-40
Autorização de Funcionamento: 1.14.586-7 Expediente(s): 0115791/20-5
Certificado de Boas Práticas de Fabricação de Medicamentos:
Insumos farmacêuticos ativos biológicos: vacina adsorvida hepatite A (inativada).

A presente certificação é válida até o dia 06/07/2022 e poderá ser cancelada, caso seja comprovado, pela autoridade sanitária competente, o não cumprimento dos requisitos preconizados pelas normas vigentes de Boas Práticas.

Documento assinado eletronicamente por **Ronaldo Lucio Ponciano Gomes**, **Gerente-Geral de Inspeção e Fiscalização Sanitária**, em 03/07/2020, às 09:36, conforme horário oficial de Brasília, com fundamento no art. 6º, § 1º, do Decreto nº 8.539, de 8 de outubro de 2015 http://www.planalto.gov.br/ccivil_03/_Ato2015-2018/2015/Decreto/D8539.htm.

A autenticidade deste documento pode ser conferida no site https://sei.anvisa.gov.br/autenticidade, informando o código verificador **1073069** e o código CRC **AF531C91**.

Brazil



Reference 3f1.1 26/12/2017

World Health Organization

Hepatitis A (Human Diploid Cell), Inactivated (Adult)
HEALIVE

Product Overview:

Type:	Hepatitis A (Human Diploid Cell), Inactivated (Adult)
Commercial Name:	HEALIVE
Manufacturer:	Sinovac Biotech Co. Ltd
Country:	People's Republic of China
URL:	
Responsible NRA:	State Food and Drug Administration
Country:	People's Republic of China
URL:	
Bulk Supplier:	Not applicable

Prequalification:

Prequalification Status:	Current
Effective Date (dd/mm/yyyy):	

Product Description:

Pharmaceutical Form:	Liquid: ready to use
Presentation:	Vial
Number of Doses:	1
Diluent:	Not Applicable
Route of Administration:	Intramuscular
Shelf Life:	at storage temperature: 2-8°C
Vaccine Vial Monitor:	Type 30
Secondary Packaging:	Single dose carton [Dimensions: 2.5 x 2.5 x 5.5 cm]
Tertiary Packaging:	Box of 40 wrapped packages with 10 single dose cartons (400 doses/400 vials)[Dimensions: 47 x 38 x 38 cm]
Cold Chain Volume:	3.3 cm3/dose (in secondary packaging)

منظمة الصحة العالمية • 世界卫生组织
Organisation mondiale de la Santé • Всемирная организация здравоохранения • Organización Mundial de la Salud

WHO PQ

Total GMPs: 11 Certificates

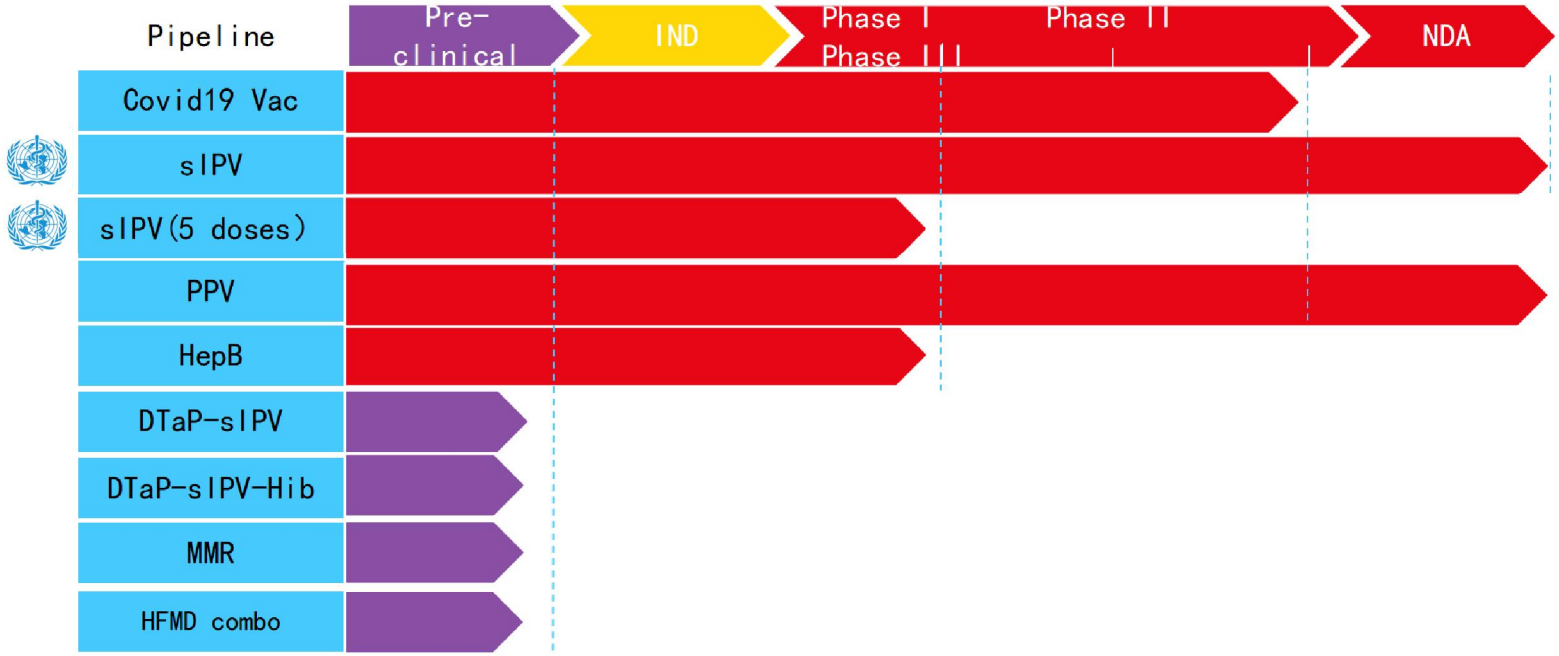
Total MAs : 33 product

Our Pipeline

克尔来福™ CoronaVac™ 新型冠状病毒灭活疫苗

Leveraging Our Proven Track Record in Vaccine Development,

SINOVAC's Future Growth is Driven by Advancement of Our Pipeline Product.



Total R&D: 9 projects

International Coordination

克尔来福 CoronaVac 新型冠状病毒灭活疫苗

dcvmn Developing Countries Vaccine Manufacturers Network & IFPMA International Federation of Pharmaceutical Manufacturers & Associations

Member

SINOVAC

Partnership

PAHO Pan American Health Organization

World Health Organization Americas

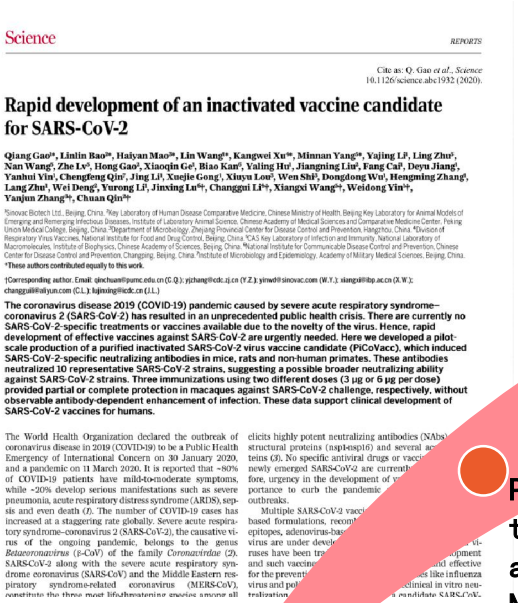
unicef | for every child

克尔来福™
CoronaVac™
新型冠状病毒灭活疫苗

SARS-COV-2 VACCINE (VERO CELL), INACTIVATED

Development Process

克尔来福™ CoronaVac™
新型冠状病毒灭活疫苗



Science REPORTS

Cite as: Q. Gao *et al.*, *Science* 10.1126/science.abc1932 (2020).

Rapid development of an inactivated vaccine candidate for SARS-CoV-2

Qiang Gao[1*], Linlin Bao[2*], Haiyan Mao[3*], Lin Wang[4*], Kangwei Xu[5*], Minnan Yang[6*], Yajing LI[7], Ling Zhu[2], Nan Wang[1], Zhe Lv[3], Hong Gao[2], Xiaoqin Ge[1], Biao Kan[8], Yaling Hu[1], Jiangning Liu[1], Fang Cai[9], Deyu Jiang[1], Yanhui Yin[1], Chengfeng Qin[2], Jing Li[3], Xuejie Gong[1], Xiuyu Lou[2], Wen Shi[2], Dongdong Wu[1], Hengming Zhang[1], Lang Zhu[1], Wei Deng[2], Yurong Li[2], Jinxing Lu[10], Changgui Li[10], Xiangxi Wang[4†], Weidong Yin[1†], Yanjun Zhang[4†], Chuan Qin[2†]

[1]Sinovac Biotech Ltd., Beijing, China. [2]Key Laboratory of Human Disease Comparative Medicine, Chinese Ministry of Health. Beijing Key Laboratory for Animal Models of Emerging and Reemerging Infectious Diseases, Institute of Laboratory Animal Science, Chinese Academy of Medical Sciences and Comparative Medicine Center, Peking Union Medical College, Beijing, China. [3]Department of Microbiology, Zhejiang Provincial Center for Disease Control and Prevention, Hangzhou, China. [4]Division of Respiratory Virus Vaccines, National Institute for Food and Drug Control, Beijing, China. [5]CAS Key Laboratory of Infection and Immunity, National Laboratory of Macromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing, China. [6]National Institute for Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Changping, Beijing, China. [7]Institute of Microbiology and Epidemiology, Academy of Military Medical Sciences, Beijing, China.
*These authors contributed equally to this work.

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The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome–coronavirus 2 (SARS-CoV-2) has resulted in an unprecedented public health crisis. There are currently no SARS-CoV-2-specific treatments or vaccines available due to the novelty of the virus. Hence, rapid development of effective vaccines against SARS-CoV-2 are urgently needed. Here we developed a pilot-scale production of a purified inactivated SARS-CoV-2 virus vaccine candidate (PiCoVacc), which induced SARS-CoV-2-specific neutralizing antibodies in mice, rats and non-human primates. These antibodies neutralized 10 representative SARS-CoV-2 strains, suggesting a possible broader neutralizing ability against SARS-CoV-2 strains. Three immunizations using two different doses (3 μg or 6 μg per dose) provided partial or complete protection in macaques against SARS-CoV-2 challenge, respectively, without observable antibody-dependent enhancement of infection. These data support clinical development of SARS-CoV-2 vaccines for humans.

The World Health Organization declared the outbreak of coronavirus disease in 2019 (COVID-19) to be a Public Health Emergency of International Concern on 30 January 2020, and a pandemic on 11 March 2020. It is reported that ~80% of COVID-19 patients have mild-to-moderate symptoms, while ~20% develop serious manifestations such as severe pneumonia, acute respiratory distress syndrome (ARDS), sepsis and even death (*1*). The number of COVID-19 cases has increased at a staggering rate globally. Severe acute respiratory syndrome–coronavirus 2 (SARS-CoV-2), the causative virus of the ongoing pandemic, belongs to the genus *Betacoronavirus* (β-CoV) of the family *Coronaviridae* (*2*). SARS-CoV-2 along with the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle Eastern respiratory syndrome-related coronavirus (MERS-CoV), constitute the three most life-threatening species among all

elicits highly potent neutralizing antibodies (NAbs) ... structural proteins (nsp1-nsp16) and several ac... teins (*3*). No specific antiviral drugs or vacci... newly emerged SARS-CoV-2 are currently ... fore, urgency in the development of ... portance to curb the pandemic ... outbreaks.

Multiple SARS-CoV-2 vacci... based formulations, recom... epitopes, adenovirus-bas... virus are under develo... ruses have been tra... opment and such vaccine... and effective for the prevent... like influenza virus and pat... clinical in vitro neu... candidate SARS-CoV-

Initial R&D of CIVID-19 vaccine on Jan 28, 2020

Phase I/II trials were approved by NMPA on April 13, 2020

Phase I and II was commenced on April 16, and May 3, 2020

Efficacy result on rhesus model published in *Science* on May 6, 2020

Phase III was approved by Brazil authority on July 3, and has started on July 21, 2020.

Started in Indonesia on 11th Aug, 2020

Also approved by Turkey and Bangladash

- This is a vaccine based on inactivated whole virion technology.
- Product capacity of over 300 million doses per year

PRECLINICAL STUDIES

克尔来福 CoronaVac 新型冠状病毒灭活疫苗

Summary of the studies

Studies performed by GLP compliant lab, results presented in the following slides.

Study design

	Item	Animal
Efficacy	Immunogenicity	Mice, Rat
	Virus Challenge*	Machaca Rhesus
	Cross-protection test	Mice, Guinea Pig, Rabbit, Rat, Sheep
Safety	Singe dose Toxicity/ Acute Toxicity	Rat
	Active Systemic Anaphylaxis	Guinea Pig
	Repeat Doses Toxicity (inc. local irritation)	Rat, Machaca Fascicularis

**. An animal model which has been successfully developed for COVID-19 vaccine evaluation, including hCAE2 mice and Rhesus is employed*
https://www.biorxiv.org/content/10.1101/2020.02.07.939389v3

GLP compliance

Virus Challenge test:
Institute of Laboratory Animal Sciences, Chinese Academy of Medical Sciences
- National Institution

Other safety tests:
JOINN Laboratories (Beijing)
- CFDA GLP Certified
- U.S.FDA GLP Inspected
- AAALAC Accredited
- OECD GLP Certified
- Korean MFDS GLP Inspected
- http://www.joinn-lab.com/

PRECLINICAL STUDIES

克尔来福™ CoronaVac™ 新型冠状病毒灭活疫苗

EFFICACY DATA PRESENTING - Design of Virus Challenge test

Focus of study

Vaccine group VS. Model group

(1) Routine observation

(2) Virus load for throat swab.

(3) Virus load for anal swab.

(4) Virus load on each lung.

(5) Pathology of lungtissue.

Difference between

(6) Correlation between neutralizing antibody and efficacy.

Design

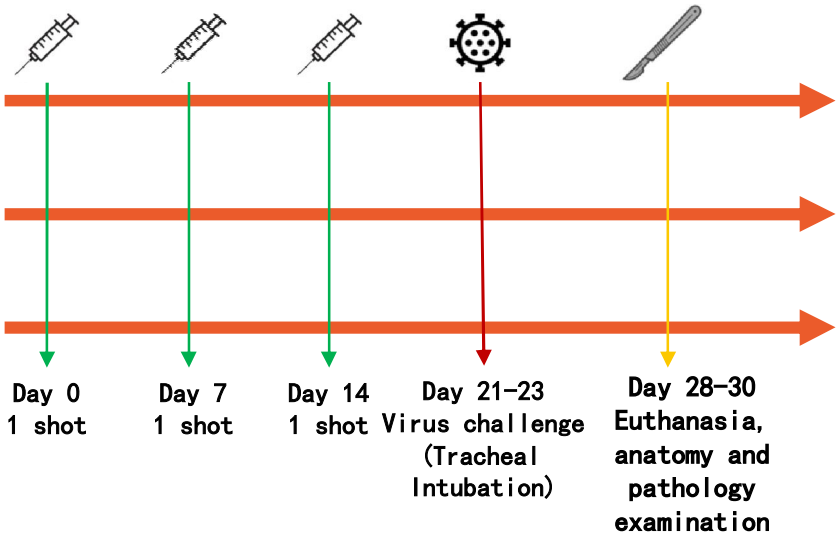
Model group (control) ×2

High dose group 1200SU/dose ×4

Medium dose group 600SU/dose ×4

Adjuvant group 0SU/dose ×2

Three dose schedule (0, 7, 14)

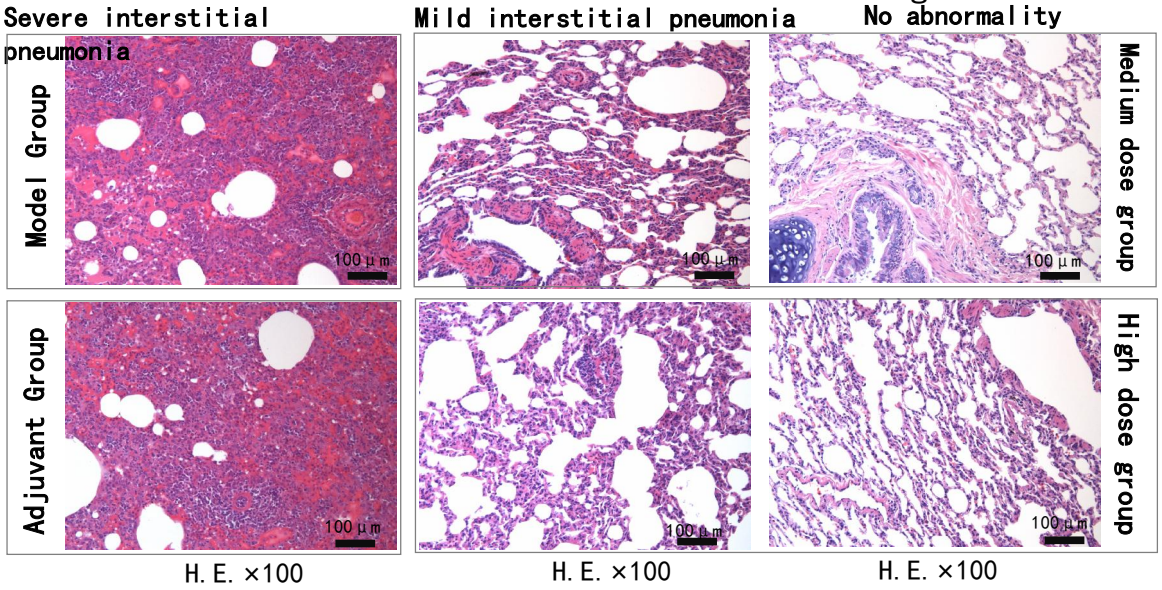


PRECLINICAL STUDIES

克尔来福™ CoronaVac™ 新型冠状病毒灭活疫苗

EFFICACY DATA PRESENTING - Results of Virus Challenge test

Pathology



Significant protective effect observed for medium dose vaccination

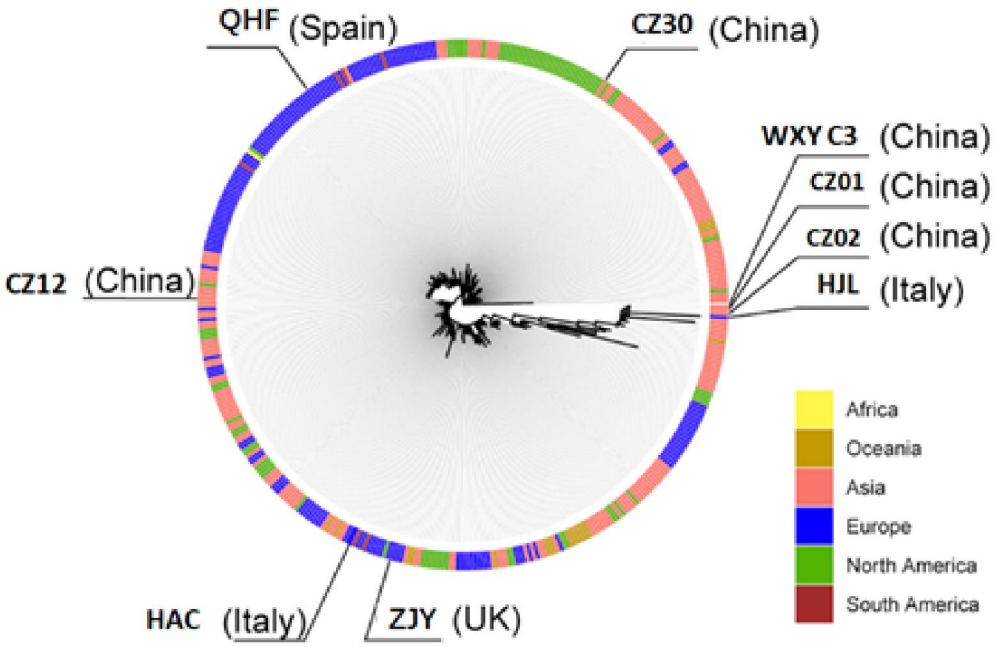
Significant protective effect observed for high dose vaccination

- **Model:** 2 cases (2/2) showed severe interstitial pneumonia with Vascular and peribranchial inflammatory cells infiltrate
- **Adjuvant:** 1 case (1/2) showed mild interstitial pneumonia; 1 case (1/2) showed Severe interstitial pneumonia with Vascular and peribranchial inflammatory cells infiltrate
- **High dose group:** 4 cases (4/4) showed mild interstitial pneumonia; Compare with model group and adjuvant group, the pulmonary pathological change of vaccine groups has been siganificantely reduced.
- **Medium dose group:** 4 cases (4/4) showed mild interstitial pneumonia; Compare with model group and adjuvant group, the pulmonary pathological change of vaccine groups has been siganificantely reduced.

PRECLINICAL STUDIES

EFFICACY DATA PRESENTING - Cross-protection test

Source of the strains	
Name	**Source**
CW01	Wuhan, China
WXY-C3	Zhejiang, China
CZ01	Zhejiang, China
CB01	AS-IV, China
V34	Chinese military academy of science, China
CZ12	Zhejiang, China
CZ30	Zhejiang, China
HAC	Imported from Italy
HJL	Imported from Italy
QHF	Imported from Spain
SSH	Imported from Switzerland
ZYF	Imported from Italy

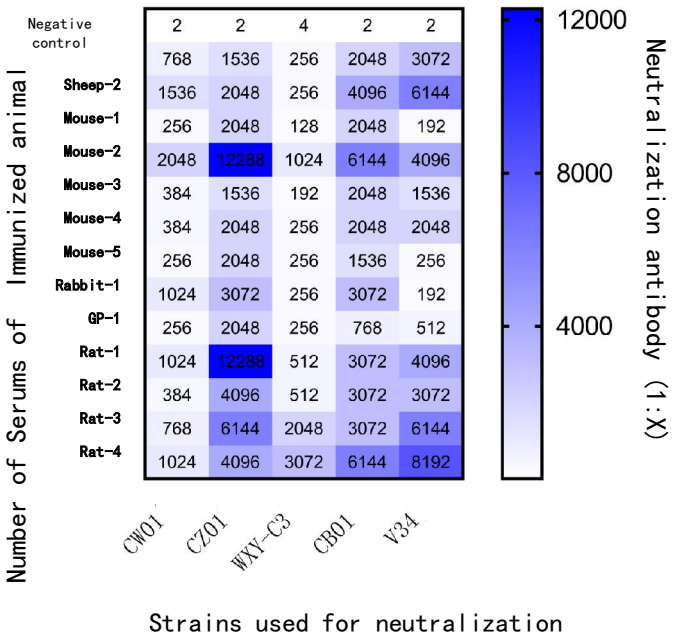


PRECLINICAL STUDIES

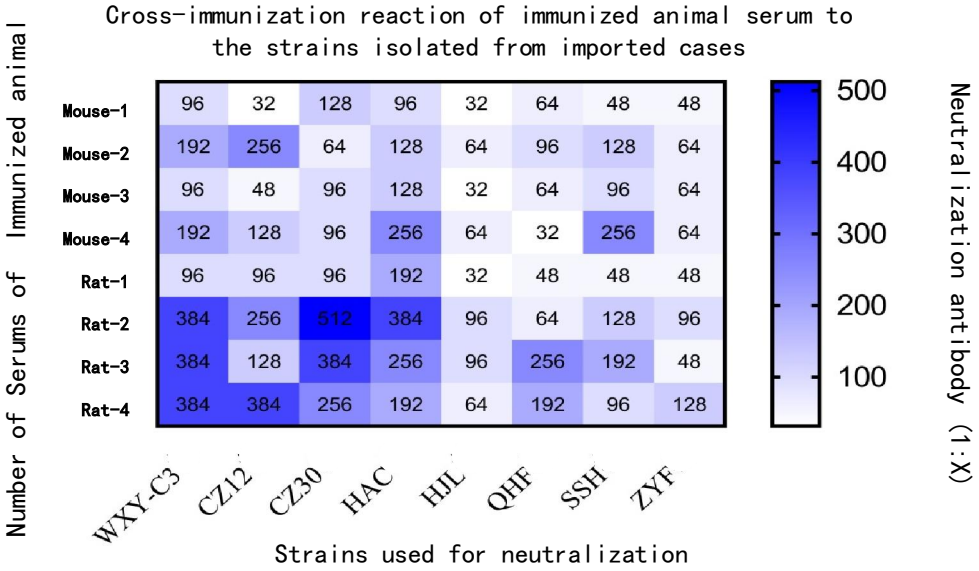
克尔来福™ CoronaVac™ 新型冠状病毒灭活疫苗

EFFICACY DATA PRESENTING - Cross-protection test

Cross-immunization reaction of immunized animal serum to the strains isolated in China



Cross-immunization reaction of immunized animal serum to the strains isolated from imported cases



CLINICAL STUDY PROTOCOLS

克尔来福™ CoronaVac™ 新型冠状病毒灭活疫苗

Volunteer Subjects: Phase I/II clinical trials in Healthy Adult Aged 18-59

Trial Design: Typical double blinded, randomized, placebo control

Schedule/ No. Volunteers	Phase I	Phase II
0, 14 day	72	300
0, 28 day	72	300
Total	**144**	**600**

Studies on elderlies are being carried on;
Studies on adolescents and pediatric groups are going to commence;

CLINICAL STUDY RESULT-Phase III Plan

克尔来福™ CoronaVac™ 新型冠状病毒灭活疫苗

- Phase III trials have been approved in Brazil, Indonesia, Turkey and Bangladesh
- Trials have commenced in Brazil and Indonesia
- Other phase III trials will be initiated in September
- Approximately 30,000 subjects will be enrolled in these phase III trials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