Informed consent for the clinical trial of the recombinant novel coronavirus vaccine

(for low-dose group)

The purpose of this informed consent is to invite you to participate in a phase I clinical trial evaluating the safety and effect of the recombinant novel coronavirus vaccine. Before you decide whether or not to participate in the study, this informed consent will allow you to understand the details of the entire study, the risks and benefits, and what you need to do. Please read the following information carefully and consult the doctor of the study if you have any questions. This study has been registered for clinical study review and approved for clinical trial.

Study title: A phase I clinical trial of the recombinant novel coronavirus vaccine (adenovirus type 5 vector)

Protocol version: 1.2

Protocol Date: March 14, 2020

Sponsor: Beijing Institute of Biotechnology and CanSino Biologics Inc.

Study institutions: Jiangsu Provincial Center for Disease Control and Prevention and Hubei Provincial Center for Disease Control and Prevention

Principal investigators: Feng-cai Zhu, Xu-hua Guan, Wei Wang

This informed consent consists of two parts, namely, the information notice about the

study and the signature part proving that you agree to participate in the study. This informed consent is made in duplicate and you will receive one copy.

1. Information about this study

1.1. Background

COVID-19 has caused a global public health emergency since its outbreak in December 2019. By March 14, 2020, China had reported 81,029 confirmed cases and a total of 3,194 deaths. China's 31 provinces have announced the initiation of a public health emergency level 1 response to COVID-19, adopting the highest level of mandatory measures, including blocking public transportation, canceling gatherings, and extending the Spring Festival holiday to reduce the mobility of the population. At present, although this epidemic has been brought under control to some extent, there are no specific therapeutic drugs or preventive vaccines. China is still at a critical juncture in the prevention and control of COVID-19. To develop a safe and effective vaccine is the key to overcome COVID-19.

1.2. Introduction of the recombinant novel coronavirus vaccine

The recombinant novel coronavirus vaccine (adenovirus type 5 vector) was jointly developed by the Beijing Institute of Biotechnology and CanSino Biologics Inc., to prevent COVID-19 caused by SARS-CoV-2 infection. The vaccine uses replication-defective human adenovirus type 5 as vector and express the specific S protein of SARS-CoV-2, which is prepared by amplification and purification.

Preclinical studies suggest that both humoral and cellular immune responses play important roles in protective immunity.

1.3. Investigational vaccine

The investigational vaccine used in this study is a novel recombinant coronavirus vaccine (adenovirus type 5 vector) jointly developed by Beijing Institute of Biotechnology and CanSino Biologics Inc.

The investigational vaccine is a liquid formulation, using replication-defective human adenovirus type 5 as a vector, and express the specific S protein of the SARS-CoV-2. The low, middle and high doses were 5×10^{10}vp (0.5ml), 1×10^{11}vp (1.0ml), and 1.5×10^{11}vp (1.5ml), and the quality is in line with the “recombinant new coronavirus vaccine manufacturing and verification regulations (draft)". The investigational vaccine has got certification from National Institutes for Food and Drug Control.

1.4. Study objectives

To evaluate the safety and tolerability of the recombinant novel coronavirus vaccine (adenovirus type 5 vector) in healthy adults aged 18 to 60 years, and to preliminarily evaluate its immune effect.

1.5. Study groups and vaccination schedule

The study included three dose groups of 36 participants each. As the first group of participants, you will be vaccinated with the 5×10^{10}vp recombinant novel coronavirus

vaccine (adenovirus type 5 vector).

After passing the screening test, you will be vaccinated once with the investigational vaccine, which will be injected intramuscular into the lateral deltoid muscle of the upper arm.

1.6. Study process and visits

According to the requirements of the protocol, each participant in this study will complete a pre-enrollment visit within 7 days before the first dose of vaccination, and a study visit at day 0 (the day of vaccination), day 3, day 7, day 10, day 14, day 28, month 3 and month 6, respectively, for a total of 9 visits. It will take about 6 months to complete the whole study. If you agree to participate in this study, you need to cooperate with us to complete the following visits:

– If you can understand the methods and requirements of this study and are willing to participate, please sign the informed consent.
– Within 7 days before vaccination, we will conduct relevant physical examination for you at an optional time, including nucleic acid detection (throat swab/sputum and anal swab), HIV voluntary declaration and antibody detection against SARS-CoV-2. The study physician will determine whether you are eligible to participate in the study based on the results of the above physical examinations and your previous health and medical history.
– At day 0, we will provide you some physical examinations before vaccination, to evaluate whether you are fit to participate in this study, the physical

examinations include blood routine, blood biochemistry, height, weight, blood pressure, underarm body temperature, antibody detection against SARS-CoV-2, nucleic acid detection (pharyngeal swab/sputum and anal swab), CT examination, HIV antibody test, and pregnancy test for women of child-bearing age. The study physician will determine whether you are eligible to participate in the study based on the above results.

- If you pass the screening, we will vaccinate you once with the investigational vaccine.
- We will observe you at the study site for 6 hours after vaccination.
- From 6 hours to 14 days after vaccination, you need to live in the hotel of the study site for observation. During this period, we will arrange staff to follow up with you every day to guide you to complete the safety observation and recording.
- From day 15 to day 28 after vaccination, you need to observe at home. Please observe and record all adverse reaction symptoms, health status, medical history, drug and other vaccine use according to the requirements in the diary card we sent to you. 28 days after vaccination, we will interview you and review the record in the diary card.
- Blood samples will be collected twice before (day 0) and 7 days after vaccination for blood routine and biochemical testing. Fingertip blood will be collected twice before (day 0) and 6 months after vaccination for HIV antibody testing. The aim is to evaluate whether the vaccination has an impact on your health. 2ml of blood

will be collected for each routine blood test and 3ml for each biochemical blood test.

- During the whole study period (within 6 months after vaccination), if you have: 1. Any illness, injury, disability or life-threatening health event requiring hospitalization; 2. Respiratory symptoms such as fever and/or cough; 3. Any serious disease or symptoms, please contact us in time.
- Within 7 days before vaccination, at day 0, day 14, day 28, month 3 and month 6, 6 neutralizing antibody detections against SARS-CoV-2 and Ad5 will be conducted. In addition to 5ml in the first blood collection (within 7 days before vaccination), 10ml in each of the subsequent 5 blood collections will be used to evaluate the humoral immune effect of the vaccine.
- Specific CD4+ T cell and CD8+ T cell response detections will be performed for 4 times at day 0, day 14, day 28 and month 6, and 20ml of blood will be collected for each time to evaluate the cellular immune effect of the vaccine.
- The preferred blood sampling site is the cubital vein, followed by the wrist or dorsal hand vein.
- If you can participate in the whole study, you will be collected with blood in 7 times. The amount of blood collected each time is between 5 and 35ml, and the total amount of blood collection is about 145ml.
- If you have serious adverse reactions during the study, or if you are not healthy enough to continue to participate in the study, or if you violate the study protocol requirements, we may terminate your study in advance and inform you of the

relevant situation in a timely manner.

1.7. Risks and compensation

In this study, the physician will help you understand the basic knowledge and preventive measures of COVID-19. If you are vaccinated with the recombinant novel coronavirus vaccine (adenovirus type 5 vector), you may have antibody against SARS-CoV-2, but there is no guarantee that you will be 100% free from COVID-19 after vaccination.

Risks you may face after vaccination:

Possible risks of injection: redness, induration, swelling and itching at the injection site. These adverse reactions are generally mild, do not need special treatment, and can be alleviated or disappeared spontaneously. If necessary, contact with the doctor for symptomatic treatment, but the possibility of infection is very low.

Possible risk of blood collection: blood collection site may appear petechial spots and mild pain. Although syncope during blood collection and site infection are rare, they could occur.

Risk of allergy: a severe allergic reaction after vaccination is very rare, but can be life-threatening. Therefore, during the observation after vaccination, you will be monitored and evaluated by a special medical staff. If anaphylaxis occurs, symptomatic treatment will be given immediately.

Risk of receiving the investigational vaccine: as a novel vaccine, this is the first time the investigational vaccine has been vaccinated in human. No safety data in human

are available. But based on the results of previous animal experiments, the investigational vaccine is safe. We will closely observe the occurrence of adverse reactions after vaccination. The investigational vaccine may cause fever, pain at the injection site, joint pain and other adverse reactions.

Women who were pregnant, breast-feeding or planning to become pregnant during the study period were not allowed to participate in the study. Once the female participants have completed the vaccination, they should take effective contraceptive measures during the whole study period. If pregnancy occurs, please inform the investigators immediately, and independently choose whether to continue the pregnancy based on your own conditions. After the investigators were informed of the pregnancy event, they will be followed until the end of the pregnancy. It is recommended that those who choose to continue their pregnancy should receive routine pregnancy examinations and contact the investigators if any abnormality is found. Follow-up is usually conducted within six to eight weeks after the baby's due date, whether the baby is full-term or premature.

Foreign studies have suggested that adenovirus vector vaccines may increase the potential risk of HIV infection, which has not yet been confirmed. Therefore, during the study period, please try to avoid high-risk behaviors that can lead to HIV infection.

If an adverse event or serious adverse event occurs during the safety observation period, you will receive timely treatment. If the adverse event is proved by provincial experts to be related to the vaccination, Beijing Institute of Biotechnology and

CanSino Biologics Inc. will bear the reasonable diagnosis and treatment expenses and the corresponding economic compensation.

Your compensation for participating in this study:

You will not have to pay any fees to participate in this study, including physical examination, vaccination and scheduled visits. In order to thank you for contributing to the prevention and control of COVID - 19 in China, as well as the sacrifices (including nutrition fees, etc.) and risks you take in the process of participating in this study, we will give you 800 RMB in cash at the end of each blood collection visit. If you can complete the 7 blood sampling visits for the whole study, you will get 5600 RMB in total.

1.8. Right to withdraw from our study

Your participation in this study is completely voluntary, and you may withdraw from this study without any reason before or at any time after the study, and your withdrawal will not be subject to any penalty or loss of interest. If you have an adverse reaction, your withdrawal will not affect your treatment. If you decide not to participate in the study or to withdraw from the study at any time after the study has begun, please contact us.

1.9. Preventive measures other than the investigational vaccine

Currently, there is no specific therapeutic drug for COVID-19, and many domestic and foreign vaccines are being developed, but no licensed vaccine is available. If the

risk of SARS-CoV-2 infection is increasing, it can be prevented by strengthening personal protection against contact with a patient or the patient's body fluids, secretions and contaminants.

1.10. Confidentiality of the data

All materials and any information related to your identity will be confidential and you will be assigned a code to identify you in this study. Your name and other information will be kept strictly confidential. Your name will not appear in any published information or reports on this study. The detection results during the study will only be used for the analysis of this study and will not be used in other studies and will not be disclosed to others. The monitors and inspectors appointed by the sponsor, as well as the ethics review committee of the Jiangsu Provincial Center for Disease Control and Prevention and the representatives of National Medical Products Administration, may examine the original data with your personal information to verify the accuracy of the collected data. All of your personal information will be hided when the investigators submit the materials to the sponsor (Beijing Institute of Biotechnology and CanSino Biologics Inc.).

1.11. Feedback of results

Your personal information will not be marked on the blood samples, the results of the test will not be fed back to you, and will not be recorded in your physical examination or medical book. During the study, unless we find abnormal indicators that may

endanger your health, the results in this study will not be actively reported to you. However, if you need to, you can ask us for feedback of the results, and we will give you the feedback of the results you need at an appropriate time.

1.12. Preservation of blood samples and future studies

The blood samples you donate in this study will be properly preserved according to the preservation requirements of the blood products for the detections specified in the protocol. The blood samples may be exported to other countries for further analysis in the future. The export of blood samples will be conducted after obtaining the import and export approval documents of blood and blood products from the office of human genetic resources management of China.

1.13. Other matters

If there is any new information that may affect your decision to continue to participate in the study, we will inform you in a timely manner and communicate with you again.

1.14. Contact information of the investigator

In this study, if you have any adverse reactions or injuries that may be related to this study, or if you have any questions related to this study, please contact Dr. Wang at the 24-hour contact number 13476011311.

1.15. Contact information of ethics review committee of Jiangsu Provincial Center for

Disease Control and Prevention

In this study, if you have any adverse reactions or injuries that may be related to this study, or if you have any questions related to this study, or if you find any violation of ethics in this study, you may contact the ethics review committee of Jiangsu Provincial Center for Disease Control and Prevention. Contact: Miss Cai. Tel: 025-83759406 (8:30-17:30 at working days).

2. Sign the informed consent

If you or your approved witness sign this informed consent, it indicates that the investigator has explained the study to you, answered all your questions about the study, that you have understood all the information, and that you have given full consideration and agreed to participate in the study. You have learned that you can withdraw from the study at any time without any reason and that your withdrawal from the study will not affect your current or future healthcare services.

2.1. Signature of participant

Name of participant: _____ (completed by the investigator)

Signature of participant: _____ Date: ___ ___ ___ ___ ___ (completed by participant)

year/month/day/hour/minute

Since the participant cannot read the content of the informed consent correctly, the investigator has informed the participant that he/she has understood all the content of the informed consent and agreed to participate in this study. I hereby certify that I

have witnessed the whole process of informed consent as a third party!

Name of witness: _____ (completed by the investigator)

Signature of witness: _____ Date: ___ ___ ___ ___ ___ (completed by witness)

year/month/day/hour/minute

2.2. Statement of investigator

I confirm that I have explained the content of informed consent to the participant in detail, and have given adequate answers to the questions raised by the participant.

Signature of investigator: _____ Date: ___ ___ ___ ___ ___ (completed by investigator)

year/month/day/hour/minute

Informed consent for the clinical trial of the recombinant novel coronavirus vaccine

(for middle-dose group)

The purpose of this informed consent is to invite you to participate in a phase I clinical trial evaluating the safety and effect of the recombinant novel coronavirus vaccine. Before you decide whether or not to participate in the study, this informed consent will allow you to understand the details of the entire study, the risks and benefits, and what you need to do. Please read the following information carefully and consult the doctor of the study if you have any questions. This study has been registered for clinical study review and approved for clinical trial.

Study title: A phase I clinical trial of the recombinant novel coronavirus vaccine (adenovirus type 5 vector)

Protocol version: 1.2

Protocol Date: March 14, 2020

Sponsor: Beijing Institute of Biotechnology and CanSino Biologics Inc.

Study institutions: Jiangsu Provincial Center for Disease Control and Prevention and Hubei Provincial Center for Disease Control and Prevention

Principal investigators: Feng-cai Zhu, Xu-hua Guan, Wei Wang

This informed consent consists of two parts, namely, the information notice about the

study and the signature part proving that you agree to participate in the study. This informed consent is made in duplicate and you will receive one copy.

1. Information about this study

1.1. Background

COVID-19 has caused a global public health emergency since its outbreak in December 2019. By March 14, 2020, China had reported 81,029 confirmed cases and a total of 3,194 deaths. China's 31 provinces have announced the initiation of a public health emergency level 1 response to COVID-19, adopting the highest level of mandatory measures, including blocking public transportation, canceling gatherings, and extending the Spring Festival holiday to reduce the mobility of the population. At present, although this epidemic has been brought under control to some extent, there are no specific therapeutic drugs or preventive vaccines. China is still at a critical juncture in the prevention and control of COVID-19. To develop a safe and effective vaccine is the key to overcome COVID-19.

1.2. Introduction of the recombinant novel coronavirus vaccine

The recombinant novel coronavirus vaccine (adenovirus type 5 vector) was jointly developed by the Beijing Institute of Biotechnology and CanSino Biologics Inc., to prevent COVID-19 caused by SARS-CoV-2 infection. The vaccine uses replication-defective human adenovirus type 5 as vector and express the specific S protein of SARS-CoV-2, which is prepared by amplification and purification.

Preclinical studies suggest that both humoral and cellular immune responses play important roles in protective immunity.

1.3. Investigational vaccine

The investigational vaccine used in this study is a novel recombinant coronavirus vaccine (adenovirus type 5 vector) jointly developed by Beijing Institute of Biotechnology and CanSino Biologics Inc.

The investigational vaccine is a liquid formulation, using replication-defective human adenovirus type 5 as a vector, and express the specific S protein of the SARS-CoV-2. The low, middle and high doses were 5×10^{10}vp (0.5ml), 1×10^{11}vp (1.0ml), and 1.5×10^{11}vp (1.5ml), and the quality is in line with the “recombinant new coronavirus vaccine manufacturing and verification regulations (draft)". The investigational vaccine has got certification from National Institutes for Food and Drug Control.

1.4. Study objectives

To evaluate the safety and tolerability of the recombinant novel coronavirus vaccine (adenovirus type 5 vector) in healthy adults aged 18 to 60 years, and to preliminarily evaluate its immune effect.

1.5. Study groups and vaccination schedule

The study included three dose groups of 36 participants each. As the second group of participants, you will be vaccinated with the 1×10^{11}vp recombinant novel coronavirus

vaccine (adenovirus type 5 vector).

After passing the screening test, you will be vaccinated once with the investigational vaccine, which will be injected intramuscular into the lateral deltoid muscle of the upper arm.

1.6. Study process and visits

According to the requirements of the protocol, each participant in this study will complete a pre-enrollment visit within 7 days before the first dose of vaccination, and a study visit at day 0 (the day of vaccination), day 3, day 7, day 10, day 14, day 28, month 3 and month 6, respectively, for a total of 9 visits. It will take about 6 months to complete the whole study. If you agree to participate in this study, you need to cooperate with us to complete the following visits:

– If you can understand the methods and requirements of this study and are willing to participate, please sign the informed consent.
– Within 7 days before vaccination, we will conduct relevant physical examination for you at an optional time, including nucleic acid detection (throat swab/sputum and anal swab), HIV voluntary declaration and antibody detection against SARS-CoV-2. The study physician will determine whether you are eligible to participate in the study based on the results of the above physical examinations and your previous health and medical history.
– At day 0, we will provide you some physical examinations before vaccination, to evaluate whether you are fit to participate in this study, the physical

examinations include blood routine, blood biochemistry, height, weight, blood pressure, underarm body temperature, antibody detection against SARS-CoV-2, nucleic acid detection (pharyngeal swab/sputum and anal swab), CT examination, HIV antibody test, and pregnancy test for women of child-bearing age. The study physician will determine whether you are eligible to participate in the study based on the above results.

- If you pass the screening, we will vaccinate you once with the investigational vaccine.
- We will observe you at the study site for 6 hours after vaccination.
- From 6 hours to 14 days after vaccination, you need to live in the hotel of the study site for observation. During this period, we will arrange staff to follow up with you every day to guide you to complete the safety observation and recording.
- From day 15 to day 28 after vaccination, you need to observe at home. Please observe and record all adverse reaction symptoms, health status, medical history, drug and other vaccine use according to the requirements in the diary card we sent to you. 28 days after vaccination, we will interview you and review the record in the diary card.
- Blood samples will be collected twice before (day 0) and 7 days after vaccination for blood routine and biochemical testing. Fingertip blood will be collected twice before (day 0) and 6 months after vaccination for HIV antibody testing. The aim is to evaluate whether the vaccination has an impact on your health. 2ml of blood

will be collected for each routine blood test and 3ml for each biochemical blood test.

- During the whole study period (within 6 months after vaccination), if you have: 1. Any illness, injury, disability or life-threatening health event requiring hospitalization; 2. Respiratory symptoms such as fever and/or cough; 3. Any serious disease or symptoms, please contact us in time.
- Within 7 days before vaccination, at day 0, day 14, day 28, month 3 and month 6, 6 neutralizing antibody detections against SARS-CoV-2 and Ad5 will be conducted. In addition to 5ml in the first blood collection (within 7 days before vaccination), 10ml in each of the subsequent 5 blood collections will be used to evaluate the humoral immune effect of the vaccine.
- Specific CD4+ T cell and CD8+ T cell response detections will be performed for 4 times at day 0, day 14, day 28 and month 6, and 20ml of blood will be collected for each time to evaluate the cellular immune effect of the vaccine.
- The preferred blood sampling site is the cubital vein, followed by the wrist or dorsal hand vein.
- If you can participate in the whole study, you will be collected with blood in 7 times. The amount of blood collected each time is between 5 and 35ml, and the total amount of blood collection is about 145ml.
- If you have serious adverse reactions during the study, or if you are not healthy enough to continue to participate in the study, or if you violate the study protocol requirements, we may terminate your study in advance and inform you of the

relevant situation in a timely manner.

1.7. Risks and compensation

In this study, the physician will help you understand the basic knowledge and preventive measures of COVID-19. If you are vaccinated with the recombinant novel coronavirus vaccine (adenovirus type 5 vector), you may have antibody against SARS-CoV-2, but there is no guarantee that you will be 100% free from COVID-19 after vaccination.

Risks you may face after vaccination:

Possible risks of injection: redness, induration, swelling and itching at the injection site. These adverse reactions are generally mild, do not need special treatment, and can be alleviated or disappeared spontaneously. If necessary, contact with the doctor for symptomatic treatment, but the possibility of infection is very low.

Possible risk of blood collection: blood collection site may appear petechial spots and mild pain. Although syncope during blood collection and site infection are rare, they could occur.

Risk of allergy: a severe allergic reaction after vaccination is very rare, but can be life-threatening. Therefore, during the observation after vaccination, you will be monitored and evaluated by a special medical staff. If anaphylaxis occurs, symptomatic treatment will be given immediately.

Risk of receiving the investigational vaccine: as a novel vaccine, this is the first time the investigational vaccine has been vaccinated in human. Previously, 36 participants

have been vaccinated with the 5×10^{10}vp recombinant novel coronavirus vaccine (adenovirus type 5 vector), and the investigational vaccine is safe after preliminary observation. Combined with the results of previous animal experiments, the investigational vaccine is considered to be safe. We will closely observe the occurrence of adverse reactions after vaccination. The investigational vaccine may cause fever, pain at the injection site, joint pain and other adverse reactions.

Women who were pregnant, breast-feeding or planning to become pregnant during the study period were not allowed to participate in the study. Once the female participants have completed the vaccination, they should take effective contraceptive measures during the whole study period. If pregnancy occurs, please inform the investigators immediately, and independently choose whether to continue the pregnancy based on your own conditions. After the investigators were informed of the pregnancy event, they will be followed until the end of the pregnancy. It is recommended that those who choose to continue their pregnancy should receive routine pregnancy examinations and contact the investigators if any abnormality is found. Follow-up is usually conducted within six to eight weeks after the baby's due date, whether the baby is full-term or premature.

Foreign studies have suggested that adenovirus vector vaccines may increase the potential risk of HIV infection, which has not yet been confirmed. Therefore, during the study period, please try to avoid high-risk behaviors that can lead to HIV infection.

If an adverse event or serious adverse event occurs during the safety observation

period, you will receive timely treatment. If the adverse event is proved by provincial experts to be related to the vaccination, Beijing Institute of Biotechnology and CanSino Biologics Inc. will bear the reasonable diagnosis and treatment expenses and the corresponding economic compensation.

Your compensation for participating in this study:

You will not have to pay any fees to participate in this study, including physical examination, vaccination and scheduled visits. In order to thank you for contributing to the prevention and control of COVID - 19 in China, as well as the sacrifices (including nutrition fees, etc.) and risks you take in the process of participating in this study, we will give you 800 RMB in cash at the end of each blood collection visit. If you can complete the 7 blood sampling visits for the whole study, you will get 5600 RMB in total.

1.8. Right to withdraw from our study

Your participation in this study is completely voluntary, and you may withdraw from this study without any reason before or at any time after the study, and your withdrawal will not be subject to any penalty or loss of interest. If you have an adverse reaction, your withdrawal will not affect your treatment. If you decide not to participate in the study or to withdraw from the study at any time after the study has begun, please contact us.

1.9. Preventive measures other than the investigational vaccine

Currently, there is no specific therapeutic drug for COVID-19, and many domestic and foreign vaccines are being developed, but no licensed vaccine is available. If the risk of SARS-CoV-2 infection is increasing, it can be prevented by strengthening personal protection against contact with a patient or the patient's body fluids, secretions and contaminants.

1.10. Confidentiality of the data

All materials and any information related to your identity will be confidential and you will be assigned a code to identify you in this study. Your name and other information will be kept strictly confidential. Your name will not appear in any published information or reports on this study. The detection results during the study will only be used for the analysis of this study and will not be used in other studies and will not be disclosed to others. The monitors and inspectors appointed by the sponsor, as well as the ethics review committee of the Jiangsu Provincial Center for Disease Control and Prevention and the representatives of National Medical Products Administration, may examine the original data with your personal information to verify the accuracy of the collected data. All of your personal information will be hided when the investigators submit the materials to the sponsor (Beijing Institute of Biotechnology and CanSino Biologics Inc.).

1.11. Feedback of results

Your personal information will not be marked on the blood samples, the results of the

test will not be fed back to you, and will not be recorded in your physical examination or medical book. During the study, unless we find abnormal indicators that may endanger your health, the results in this study will not be actively reported to you. However, if you need to, you can ask us for feedback of the results, and we will give you the feedback of the results you need at an appropriate time.

1.12. Preservation of blood samples and future studies

The blood samples you donate in this study will be properly preserved according to the preservation requirements of the blood products for the detections specified in the protocol. The blood samples may be exported to other countries for further analysis in the future. The export of blood samples will be conducted after obtaining the import and export approval documents of blood and blood products from the office of human genetic resources management of China.

1.13. Other matters

If there is any new information that may affect your decision to continue to participate in the study, we will inform you in a timely manner and communicate with you again.

1.14. Contact information of the investigator

In this study, if you have any adverse reactions or injuries that may be related to this study, or if you have any questions related to this study, please contact Dr. Wang at the 24-hour contact number 13476011311.

1.15. Contact information of ethics review committee of Jiangsu Provincial Center for Disease Control and Prevention

In this study, if you have any adverse reactions or injuries that may be related to this study, or if you have any questions related to this study, or if you find any violation of ethics in this study, you may contact the ethics review committee of Jiangsu Provincial Center for Disease Control and Prevention. Contact: Miss Cai. Tel: 025-83759406 (8:30-17:30 at working days).

2. Sign the informed consent

If you or your approved witness sign this informed consent, it indicates that the investigator has explained the study to you, answered all your questions about the study, that you have understood all the information, and that you have given full consideration and agreed to participate in the study. You have learned that you can withdraw from the study at any time without any reason and that your withdrawal from the study will not affect your current or future healthcare services.

2.1. Signature of participant

Name of participant: _____ (completed by the investigator)

Signature of participant: _____ Date: ___ ___ ___ ___ ___ (completed by participant)

year/month/day/hour/minute

Since the participant cannot read the content of the informed consent correctly, the

investigator has informed the participant that he/she has understood all the content of the informed consent and agreed to participate in this study. I hereby certify that I have witnessed the whole process of informed consent as a third party!

Name of witness: _____ (completed by the investigator)

Signature of witness: _____ Date: ___ ___ ___ ___ ___ (completed by witness)

year/month/day/hour/minute

2.2. Statement of investigator

I confirm that I have explained the content of informed consent to the participant in detail, and have given adequate answers to the questions raised by the participant.

Signature of investigator: _____ Date: ___ ___ ___ ___ ___ (completed by investigator)

year/month/day/hour/minute

Informed consent for the clinical trial of the recombinant novel coronavirus vaccine

(for high-dose group)

The purpose of this informed consent is to invite you to participate in a phase I clinical trial evaluating the safety and effect of the recombinant novel coronavirus vaccine. Before you decide whether or not to participate in the study, this informed consent will allow you to understand the details of the entire study, the risks and benefits, and what you need to do. Please read the following information carefully and consult the doctor of the study if you have any questions. This study has been registered for clinical study review and approved for clinical trial.

Study title: A phase I clinical trial of the recombinant novel coronavirus vaccine (adenovirus type 5 vector)

Protocol version: 1.2

Protocol Date: March 14, 2020

Sponsor: Beijing Institute of Biotechnology and CanSino Biologics Inc.

Study institutions: Jiangsu Provincial Center for Disease Control and Prevention and Hubei Provincial Center for Disease Control and Prevention

Principal investigators: Feng-cai Zhu, Xu-hua Guan, Wei Wang

This informed consent consists of two parts, namely, the information notice about the

study and the signature part proving that you agree to participate in the study. This informed consent is made in duplicate and you will receive one copy.

1. Information about this study

1.1. Background

COVID-19 has caused a global public health emergency since its outbreak in December 2019. By March 14, 2020, China had reported 81,029 confirmed cases and a total of 3,194 deaths. China's 31 provinces have announced the initiation of a public health emergency level 1 response to COVID-19, adopting the highest level of mandatory measures, including blocking public transportation, canceling gatherings, and extending the Spring Festival holiday to reduce the mobility of the population. At present, although this epidemic has been brought under control to some extent, there are no specific therapeutic drugs or preventive vaccines. China is still at a critical juncture in the prevention and control of COVID-19. To develop a safe and effective vaccine is the key to overcome COVID-19.

1.2. Introduction of the recombinant novel coronavirus vaccine

The recombinant novel coronavirus vaccine (adenovirus type 5 vector) was jointly developed by the Beijing Institute of Biotechnology and CanSino Biologics Inc., to prevent COVID-19 caused by SARS-CoV-2 infection. The vaccine uses replication-defective human adenovirus type 5 as vector and express the specific S protein of SARS-CoV-2, which is prepared by amplification and purification.

Preclinical studies suggest that both humoral and cellular immune responses play important roles in protective immunity.

1.3. Investigational vaccine

The investigational vaccine used in this study is a novel recombinant coronavirus vaccine (adenovirus type 5 vector) jointly developed by Beijing Institute of Biotechnology and CanSino Biologics Inc.

The investigational vaccine is a liquid formulation, using replication-defective human adenovirus type 5 as a vector, and express the specific S protein of the SARS-CoV-2. The low, middle and high doses were 5×10^{10}vp (0.5ml), 1×10^{11}vp (1.0ml), and 1.5×10^{11}vp (1.5ml), and the quality is in line with the “recombinant new coronavirus vaccine manufacturing and verification regulations (draft)". The investigational vaccine has got certification from National Institutes for Food and Drug Control.

1.4. Study objectives

To evaluate the safety and tolerability of the recombinant novel coronavirus vaccine (adenovirus type 5 vector) in healthy adults aged 18 to 60 years, and to preliminarily evaluate its immune effect.

1.5. Study groups and vaccination schedule

The study included three dose groups of 36 participants each. As the third group of participants, you will be vaccinated with the 1.5×10^{11}vp recombinant novel

coronavirus vaccine (adenovirus type 5 vector).

After passing the screening test, you will be vaccinated once with the investigational vaccine, which will be injected intramuscular into the lateral deltoid muscle of the upper arm.

1.6. Study process and visits

According to the requirements of the protocol, each participant in this study will complete a pre-enrollment visit within 7 days before the first dose of vaccination, and a study visit at day 0 (the day of vaccination), day 3, day 7, day 10, day 14, day 28, month 3 and month 6, respectively, for a total of 9 visits. It will take about 6 months to complete the whole study. If you agree to participate in this study, you need to cooperate with us to complete the following visits:

– If you can understand the methods and requirements of this study and are willing to participate, please sign the informed consent.
– Within 7 days before vaccination, we will conduct relevant physical examination for you at an optional time, including nucleic acid detection (throat swab/sputum and anal swab), HIV voluntary declaration and antibody detection against SARS-CoV-2. The study physician will determine whether you are eligible to participate in the study based on the results of the above physical examinations and your previous health and medical history.
– At day 0, we will provide you some physical examinations before vaccination, to evaluate whether you are fit to participate in this study, the physical

examinations include blood routine, blood biochemistry, height, weight, blood pressure, underarm body temperature, antibody detection against SARS-CoV-2, nucleic acid detection (pharyngeal swab/sputum and anal swab), CT examination, HIV antibody test, and pregnancy test for women of child-bearing age. The study physician will determine whether you are eligible to participate in the study based on the above results.

- If you pass the screening, we will vaccinate you once with the investigational vaccine.
- We will observe you at the study site for 6 hours after vaccination.
- From 6 hours to 14 days after vaccination, you need to live in the hotel of the study site for observation. During this period, we will arrange staff to follow up with you every day to guide you to complete the safety observation and recording.
- From day 15 to day 28 after vaccination, you need to observe at home. Please observe and record all adverse reaction symptoms, health status, medical history, drug and other vaccine use according to the requirements in the diary card we sent to you. 28 days after vaccination, we will interview you and review the record in the diary card.
- Blood samples will be collected twice before (day 0) and 7 days after vaccination for blood routine and biochemical testing. Fingertip blood will be collected twice before (day 0) and 6 months after vaccination for HIV antibody testing. The aim is to evaluate whether the vaccination has an impact on your health. 2ml of blood

will be collected for each routine blood test and 3ml for each biochemical blood test.

- During the whole study period (within 6 months after vaccination), if you have: 1. Any illness, injury, disability or life-threatening health event requiring hospitalization; 2. Respiratory symptoms such as fever and/or cough; 3. Any serious disease or symptoms, please contact us in time.
- Within 7 days before vaccination, at day 0, day 14, day 28, month 3 and month 6, 6 neutralizing antibody detections against SARS-CoV-2 and Ad5 will be conducted. In addition to 5ml in the first blood collection (within 7 days before vaccination), 10ml in each of the subsequent 5 blood collections will be used to evaluate the humoral immune effect of the vaccine.
- Specific CD4+ T cell and CD8+ T cell response detections will be performed for 4 times at day 0, day 14, day 28 and month 6, and 20ml of blood will be collected for each time to evaluate the cellular immune effect of the vaccine.
- The preferred blood sampling site is the cubital vein, followed by the wrist or dorsal hand vein.
- If you can participate in the whole study, you will be collected with blood in 7 times. The amount of blood collected each time is between 5 and 35ml, and the total amount of blood collection is about 145ml.
- If you have serious adverse reactions during the study, or if you are not healthy enough to continue to participate in the study, or if you violate the study protocol requirements, we may terminate your study in advance and inform you of the

relevant situation in a timely manner.

1.7. Risks and compensation

In this study, the physician will help you understand the basic knowledge and preventive measures of COVID-19. If you are vaccinated with the recombinant novel coronavirus vaccine (adenovirus type 5 vector), you may have antibody against SARS-CoV-2, but there is no guarantee that you will be 100% free from COVID-19 after vaccination.

Risks you may face after vaccination:

Possible risks of injection: redness, induration, swelling and itching at the injection site. These adverse reactions are generally mild, do not need special treatment, and can be alleviated or disappeared spontaneously. If necessary, contact with the doctor for symptomatic treatment, but the possibility of infection is very low.

Possible risk of blood collection: blood collection site may appear petechial spots and mild pain. Although syncope during blood collection and site infection are rare, they could occur.

Risk of allergy: a severe allergic reaction after vaccination is very rare, but can be life-threatening. Therefore, during the observation after vaccination, you will be monitored and evaluated by a special medical staff. If anaphylaxis occurs, symptomatic treatment will be given immediately.

Risk of receiving the investigational vaccine: as a novel vaccine, this is the first time the investigational vaccine has been vaccinated in human. Previously, 36 participants

have been vaccinated with the 5×10^{10}vp and 36 participants have been vaccinated with the 1×10^{11}vp recombinant novel coronavirus vaccine (adenovirus type 5 vector), the investigational vaccine is safe after preliminary observation. Combined with the results of previous animal experiments, the investigational vaccine is considered to be safe. We will closely observe the occurrence of adverse reactions after vaccination. The investigational vaccine may cause fever, pain at the injection site, joint pain and other adverse reactions.

Women who were pregnant, breast-feeding or planning to become pregnant during the study period were not allowed to participate in the study. Once the female participants have completed the vaccination, they should take effective contraceptive measures during the whole study period. If pregnancy occurs, please inform the investigators immediately, and independently choose whether to continue the pregnancy based on your own conditions. After the investigators were informed of the pregnancy event, they will be followed until the end of the pregnancy. It is recommended that those who choose to continue their pregnancy should receive routine pregnancy examinations and contact the investigators if any abnormality is found. Follow-up is usually conducted within six to eight weeks after the baby's due date, whether the baby is full-term or premature.

Foreign studies have suggested that adenovirus vector vaccines may increase the potential risk of HIV infection, which has not yet been confirmed. Therefore, during the study period, please try to avoid high-risk behaviors that can lead to HIV infection.

If an adverse event or serious adverse event occurs during the safety observation period, you will receive timely treatment. If the adverse event is proved by provincial experts to be related to the vaccination, Beijing Institute of Biotechnology and CanSino Biologics Inc. will bear the reasonable diagnosis and treatment expenses and the corresponding economic compensation.

Your compensation for participating in this study:

You will not have to pay any fees to participate in this study, including physical examination, vaccination and scheduled visits. In order to thank you for contributing to the prevention and control of COVID - 19 in China, as well as the sacrifices (including nutrition fees, etc.) and risks you take in the process of participating in this study, we will give you 800 RMB in cash at the end of each blood collection visit. If you can complete the 7 blood sampling visits for the whole study, you will get 5600 RMB in total.

1.8. Right to withdraw from our study

Your participation in this study is completely voluntary, and you may withdraw from this study without any reason before or at any time after the study, and your withdrawal will not be subject to any penalty or loss of interest. If you have an adverse reaction, your withdrawal will not affect your treatment. If you decide not to participate in the study or to withdraw from the study at any time after the study has begun, please contact us.

1.9. Preventive measures other than the investigational vaccine

Currently, there is no specific therapeutic drug for COVID-19, and many domestic and foreign vaccines are being developed, but no licensed vaccine is available. If the risk of SARS-CoV-2 infection is increasing, it can be prevented by strengthening personal protection against contact with a patient or the patient's body fluids, secretions and contaminants.

1.10. Confidentiality of the data

All materials and any information related to your identity will be confidential and you will be assigned a code to identify you in this study. Your name and other information will be kept strictly confidential. Your name will not appear in any published information or reports on this study. The detection results during the study will only be used for the analysis of this study and will not be used in other studies and will not be disclosed to others. The monitors and inspectors appointed by the sponsor, as well as the ethics review committee of the Jiangsu Provincial Center for Disease Control and Prevention and the representatives of National Medical Products Administration, may examine the original data with your personal information to verify the accuracy of the collected data. All of your personal information will be hided when the investigators submit the materials to the sponsor (Beijing Institute of Biotechnology and CanSino Biologics Inc.).

1.11. Feedback of results

Your personal information will not be marked on the blood samples, the results of the test will not be fed back to you, and will not be recorded in your physical examination or medical book. During the study, unless we find abnormal indicators that may endanger your health, the results in this study will not be actively reported to you. However, if you need to, you can ask us for feedback of the results, and we will give you the feedback of the results you need at an appropriate time.

1.12. Preservation of blood samples and future studies

The blood samples you donate in this study will be properly preserved according to the preservation requirements of the blood products for the detections specified in the protocol. The blood samples may be exported to other countries for further analysis in the future. The export of blood samples will be conducted after obtaining the import and export approval documents of blood and blood products from the office of human genetic resources management of China.

1.13. Other matters

If there is any new information that may affect your decision to continue to participate in the study, we will inform you in a timely manner and communicate with you again.

1.14. Contact information of the investigator

In this study, if you have any adverse reactions or injuries that may be related to this study, or if you have any questions related to this study, please contact Dr. Wang at the

24-hour contact number 13476011311.

1.15. Contact information of ethics review committee of Jiangsu Provincial Center for Disease Control and Prevention

In this study, if you have any adverse reactions or injuries that may be related to this study, or if you have any questions related to this study, or if you find any violation of ethics in this study, you may contact the ethics review committee of Jiangsu Provincial Center for Disease Control and Prevention. Contact: Miss Cai. Tel: 025-83759406 (8:30-17:30 at working days).

2. Sign the informed consent

If you or your approved witness sign this informed consent, it indicates that the investigator has explained the study to you, answered all your questions about the study, that you have understood all the information, and that you have given full consideration and agreed to participate in the study. You have learned that you can withdraw from the study at any time without any reason and that your withdrawal from the study will not affect your current or future healthcare services.

2.1. Signature of participant

Name of participant: _____ (completed by the investigator)

Signature of participant: _____ Date: ___ ___ ___ ___ ___ (completed by participant)

year/month/day/hour/minute

Since the participant cannot read the content of the informed consent correctly, the investigator has informed the participant that he/she has understood all the content of the informed consent and agreed to participate in this study. I hereby certify that I have witnessed the whole process of informed consent as a third party!

Name of witness: _____ (completed by the investigator)

Signature of witness: _____ Date: ___ ___ ___ ___ ___ (completed by witness)

year/month/day/hour/minute

2.2. Statement of investigator

I confirm that I have explained the content of informed consent to the participant in detail, and have given adequate answers to the questions raised by the participant.

Signature of investigator: _____ Date: ___ ___ ___ ___ ___ (completed by investigator)

year/month/day/hour/minute