INFORMED CONSENT FORM
For Subject Participation in a Clinical Research Study

Principal Investigator:
Site Name:
Address:
24-Hour Site Phone Number:
IRB/Ethics Committee Protocol #:
Sponsor study #: NAPc-201/301
Phase 2b/3 (Phase 2b consent only)
Version Date: 07 July 2021

Study Title: Assessing Safety, Hospitalization and Efficacy of rNAPc2 in COVID-19 (ASPEN-COVID-19)

Some people in this study may have a medical condition or a disability that does not allow them to make important decisions for themselves. If you have been asked to decide for someone else whether they should be in this study, please read this consent form carefully. You will be asked to sign this form if you agree that they should be in this study.

In this form, we use the words "you" and "your." If you are reading this form and deciding for someone else, the words 'you' and 'your' refer to that person, not to you.

You are being asked to be in a clinical research study. This form provides you with information about the study. A member of the research team will describe this study to you and answer all of your questions. Please read the information below and ask questions about anything you don't understand before deciding whether or not to participate. Once you understand the study and the other options that are available, you will be asked to sign this form if you wish to be in this study. You will be given a signed copy of this form to keep.

Why is this study being done?

People with COVID-19 infection (caused by the SARS-CoV-2 virus) are at high risk for problems caused by blood clotting too easily. When your blood clots too easily, it can form clots inside blood vessels that keep blood from reaching important body parts. These blood clots can be dangerous and even life-threatening. This study plans to learn more about the effects of rNAPc2, an investigational drug (study drug) that makes blood thinner and keeps it from clotting easily in people in the hospital with COVID-19 infection. This study will compare the study drug to heparin, a standard blood thinning medicine, to see if the study drug decreases the measures of blood clotting risk, health problems from blood clotting and the time to recover from COVID-19 infection.

You are being asked to be in this clinical research study because you are in the hospital due to COVID-19 infection and your blood tests show that you have an increased risk of blood clotting.

How many subjects will take part in the study?

About 160 people at approximately 20 international sites will be in this study.

How long will I be in the study?

Your participation will last up to 40 days.

What happens if I join this study?

If you join the study, the study doctor will first look at your medical records to make sure your blood tests show a high risk for blood clotting, interview you and conduct a physical exam to make sure you are eligible to continue in the study.

If you are eligible to continue, you will be assigned to one of two different groups of research subjects. To decide which group you will be in, we will use a method of chance. This method is like flipping a coin. You will have an equal chance of being assigned to one group or the other group, and each group will get slightly different care:

One group will receive the study drug as an injection just under the skin. If you are in this group, you will be assigned to receive one of two doses of the study drug. This decision will also be made by chance, like flipping a coin.

The other group will receive heparin, a blood thinning medicine used as standard of care, as an injection just under the skin or through an IV line, as determined by the usual practice at your hospital.

You will be given your assigned study drug or heparin while you are in the hospital. The different study groups have different dose schedules, and you might not receive a dose every day you are in the hospital.

You will not be told which treatment group you are in. Your study doctor *will* know. In research studies treatment assignment information is usually kept secret to avoid the influence of that knowledge on the study results.However, we can give this information out if you have medical emergency.

If an emergency arises, make sure you tell the emergency staff about this study. They can contact us, and we will give them all relevant information.

While you are in the hospital, we will look at your medical records to collect information about your health.

Schedule of activities for the clinical research study:

Activity	Screening Day -7 to 1	Baseline Day 1	Day 2 (24h ± 2h)	Day 3±1d	Day 5±1d	Day 8±1d	Day of hospital discharge	Day 30±3d
Informed Consent	X							
Assess Eligibility	X	X						
Study Drug/Heparin						*	*	*
Medical History, Physical Exam, Vital Signs, Height and Weight		X						
Review Medications	X	X	X	X	X	X	X	X
Blood Draw	X	X	X	X		X**	X**	X
Urine Pregnancy Test, if applicable		X						
Health Status Questions		X	X	X	X	X	X	X

*After Day 8, subjects assigned study drug may begin standard of care medication to prevent blood clotting, while heparin subjects will continue to receive treatment at the study doctor's discretion.

**Blood draw will be performed at either Day 8 or Day of Discharge for subjects who leave the hospital prior to the Day 8 visit.

Health Status Questions: You will be asked questions about your health, and about any changes in your health since your last assessment. For example, whether you visited any hospitals or health care providers, whether you needed oxygen or had any problems, or whether you needed any assistance with your daily activities.

Blood draws: Blood will be drawn on Days 1, 2, 3, 8 and 30 after you enter the study. Some of these blood draws will be done for the research and are not part of your hospital care. Blood will be drawn to check your general health and risk for blood clotting; and for research purposes including how much study drug is in your blood, certain measures of blood clotting, and whether the study drug causes antibody production. Antibodies are proteins that are part of the body's natural defense system, called the immune system. The immune system can produce antibodies to remove unwanted substances such as bacteria, viruses or drugs. In this study we are interested in knowing whether the body produces antibodies related to the study drug. In addition, optional samples are requested which will be retained for future research use. If you leave the hospital before these blood draw days, your study doctor will arrange a way to collect this blood. This might mean you will be asked to come to the hospital from home on those days to have your blood drawn.

If you are no longer in the hospital at Day 30, your study doctor will still check on your health and draw your blood. You might be asked to come to the hospital to see the study doctor for a visit, or the visit might be conducted over the phone.

It is important that we monitor your health through Day 30. You will be receiving blood thinning medication as part of this study, and this information will help us monitor the safety and effects of these treatments. If we are not able to reach you by phone for the required follow up visit, we

will use other methods to monitor your health. These methods might include contacting you through public records or social media, looking at your medical records, speaking with your primary health care provider, or speaking with a family member that you identify as a close contact.

What are the possible discomforts or risks?

Discomforts you may experience while in this study include the following:

Bleeding. Because the **study drug and heparin** are both designed to thin your blood, bleeding is the main risk. Bleeding can be minor, like bruising, it can lead to low red blood cell counts, or it can be severe and life-threatening. Bleeding risk can also be further increased if other drugs that thin your blood are given at the same time. Being on these drugs can also increase the risk of bleeding from other medical procedures you might need. It is important to tell your study doctor about any bleeding you notice.

Additional risks of the study drug:

- **Fever**
- **Allergic reaction** which could be severe or life-threatening
- **Immune reaction.** It is possible that your immune system will make antibodies to attack the study drug, which could make the study drug less effective at thinning your blood or cause allergic reactions.

Additional risks of heparin medications (standard blood thinner):

- **Low platelets.** Heparin can cause your blood platelet levels to fall. Platelets help the blood clot. Low platelets can increase the chance of bleeding, but sometimes these low levels also are caused by increased clotting. Platelet levels usually go back to normal after stopping heparin.
- **Allergic reaction** which could be severe or life-threatening
- **Immune reaction.** It is possible that your immune system will make antibodies to attack the drug, which could make this drug less effective at thinning your blood.

Blood Draws

In this study we will collect between 0.3 and 2.6 tablespoons (5.4 to 38.9 ml) of blood from you during each blood draw. We will get blood by putting a needle into one of your veins and letting the blood flow into a glass tube. We will draw the blood through your existing intravenous (IV) line when possible. You may feel some pain when the needle goes into your vein. A day or two later, you may have a small bruise where the needle went under the skin.

Other Risks
There is a risk that people outside of the research team will see your research information. We will do all that we can to protect your information, but it can not be guaranteed.

You cannot participate in this study if you are pregnant. If you are a woman who can become pregnant, you must have a negative urine pregnancy test before starting study drug and must be willing to avoid sex or use an effective method of contraception for the duration of the study. If you become pregnant, the treatment or procedures involved in the study may involve risks to the embryo or fetus, which are not currently known.

Male patients must agree to avoid partner pregnancy and sperm donation for at least 90 days after last dose of study medication.

The study may include risks that are unknown at this time.

Measures Taken to Minimize Risks, Discomforts, and Inconveniences

You will be closely monitored to identify and minimize any side effects throughout the clinical research study. The study team will tell you about new findings or other information that may affect your health, welfare, or willingness to stay in the study.

What are my responsibilities?

By taking part in this clinical research study you agree to follow the study schedule and procedures. You agree to follow-up with your study doctor or study staff at the required times. You agree to report any signs of bleeding and any changes in health to your doctor or study staff.

What are the possible benefits of the study?

This study is designed for the researcher to learn more about the effects of the study drug in people with COVID-19 infection. However, there is no guarantee that your health will improve if you join this study. Also, there could be risks to being in this study. These risks are described in the section describing the discomforts or risks.

Are there alternative treatments?

There may be other ways of treating the high risk of blood clotting associated with COVID-19. These other ways include blood thinning medications which are currently approved and available outside of this study. You could also choose to get no treatment at all.

You should talk to your doctor about your choices. Make sure you understand all of your choices before you decide to participate in this study. You may leave this study at any time and still have these other choices available to you.

Who is paying for this study?

This research is being sponsored by ARCA biopharma, Inc. ("Sponsor"), the manufacturer of the study drug.

Will I be paid for being in the study?

You will not be paid to be in the study. [Ex-US Countries – if subjects' transportation will be paid for follow up clinic visits for blood collection or if they'll be compensated for visits, specify here]

Will I have to pay for anything?

There are some medical treatments that you would have to get for your condition whether you were in this study or not. You will have to pay for these. There are other medical treatments that you will get because you are in this clinical research study. The Sponsor will pay for those. Those medical treatments are the study drug, and the blood tests that are for research purposes only. [For Ex-US Countries update per the agreement with the Sponsor.]

Is my participation voluntary?

Taking part in this study is voluntary. You have the right to choose not to participate in this study. If you choose to participate, you have the right to stop at any time. If you refuse or decide to withdraw later, you will not lose any benefits or rights to which you are entitled.

If you leave this study, you will still receive your normal medical care. The only medical care that you will lose is the medical care you are getting as part of this study. You might be able to get that same kind of medical care outside of the study. Ask your study doctor.

Can I be removed from this study?

The study doctor may decide to stop your participation without your permission if the study doctor thinks that being in the study may cause you harm, or for any other reason. Also, the Sponsor may stop the study at any time.

What happens if I am injured or hurt during the study?

If you have an injury while you are in this study, you should call *<insert name>* immediately. *[His/Her]* phone number is *<insert phone number>*.

If you are injured as a direct result of the study drug or any properly performed procedure (carried out according to the protocol), the Sponsor will pay for reasonable costs related to your treatment that is not covered by your health insurance, if your injury or illness is "research related". The term "research-related injury" means physical injury caused by drugs or procedures required by the study that are different from the medical treatment you would have received if you had not participated in the clinical study. The Sponsor and the study doctor will determine if your injury or illness is research-related. Treatment must be authorized by the study doctor except in

the event of an emergency (in which case the study doctor should be notified as soon as possible). Payment for lost wages, disability, discomfort, etc., due to injury is not available.

Who do I call if I have questions?

The researcher carrying out this clinical research study is *<investigator name>*. You may ask any questions you have now. If you have questions, concerns, or complaints later, you may call *<investigator name>* at *<investigator phone number>*. You will be given a copy of this form to keep.

You may have questions about your rights as someone in this clinical research study. You can call *<investigator name>* with questions. You can also call the responsible Institutional Review Board /Independent Ethics Committee. You can call them at *<IRB phone number>*.

A description of this clinical research study will be available on https://clinicaltrials.gov/, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Who will see my research information?

The *<institution>* and its affiliated health systems have rules to protect information about you. Federal and state laws including the Health Insurance Portability and Accountability Act (HIPAA) also protect your privacy. [Ex-US Countries– replace with appropriate language] This part of the consent form tells you what information about you may be collected in this study and who might see or use it.

The institutions involved in this study include: (*list only **local** institutions) Institution/Covered Entity name*

We cannot do this study without your permission to see, use and give out your information. You do not have to give us this permission. If you do not agree, then you may not join this study.

We will see, use and disclose your information only as described in this form or other privacy notices provided to you; however, people outside the *[local institution]* and its affiliate hospitals may not be covered by this obligation.

We will do everything we can to maintain the confidentiality of your personal information, but confidentiality cannot be guaranteed.

The use and disclosure of your information has no time limit. You can cancel your permission to use and disclose your information at any time by writing to the study's Principal Investigator, at the name and address listed below. If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in this study.

PI Name
Mailing Address

Both the research records that identify you and the consent form signed by you may be looked at by others who have a legal right to see that information, such as:

- Federal offices such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP) that protect research subjects like you
- The Institutional Review Board/Independent Ethics Committee that is responsible for overseeing this research
- The study doctor and the rest of the study team
- ARCA biopharma, Inc., who is the company paying for this clinical research study, and companies working for ARCA biopharma, Inc., to help run the study
- Officials at the institution where the research is conducted and officials at other institutions involved in this study who are in charge of making sure that we follow all of the rules for research
- *<add any other groups or entities that are applicable; this section is only for entities that have the legal right to audit study records>*

By signing this form, you are allowing the Sponsor, it's related companies or independent companies monitoring the clinical research study and auditing results on behalf of the Sponsor, to have access to your original medical records for the purpose of collecting data, verifying the data are correct and checking that the clinical research study is conducted properly without violating the confidentiality of your records to the extent permitted by applicable laws and regulations. In addition, the Sponsor's employees, its related companies and other companies working with the Sponsor, the study doctor and study staff, the ethics committee and others responsible for overseeing research studies, and domestic and foreign regulatory authorities will have access to your study data in a form that does not mention your name in order to complete the research including the processing, analyzing, using, and storing data.

We might talk about this clinical research study at meetings. We might also print the results of this clinical research study in relevant journals. But we will always keep the names of the research subjects, like you, private.

You have the right to request access to your personal health information from the study doctor. To ensure proper evaluation of test results, your access to these study results may not be allowed until after the study is completed.
You have the right to request correction of data if they are inaccurate or incomplete.

The study doctor or staff acting on behalf of the study doctor, will use your information for the research outlined in this consent form. They will also make *all or some* **of the following health information about you collected in this study available to:** ARCA biopharma, Inc. (contact phone number 720-940-2100) and entities working for ARCA biopharma Inc., including University of Colorado Anschutz Medical Center, and CPC Clinical Research, an Academic Research Organization helping to conduct the clinical research study.

Information about you that will be seen, collected, used and disclosed in this study, as allowed by local regulations:

- Name and Demographic Information (age, sex, race, ethnicity, address, phone number, etc.)
- Portions of your previous and current medical records that are relevant to this study, including but not limited to diagnosis(es), History and Physical, laboratory or tissue studies, radiology studies, procedure results
- Research Visit and Research Test records
- Blood samples and the data associated with the samples

What happens to Data and Specimens that are collected in this clinical research study?

Scientists at ARCA biopharma, Inc. and the University of Colorado Anschutz Medical Center work to find the causes and cures of disease. The data and specimens collected from you during this clinical research study are important to this study and to future research. If you join this study:

- The data and other specimens given by you to the study doctor for this research no longer belong to you.
- Both the study doctor and the Sponsor of this research may study your data and other specimens collected from you.
- If data or other specimens are in a form that identifies you, the University or the health systems involved in this study may use them for future research only with your consent or Institutional Review Board approval.
- Any product or idea created by the researchers working on this study will not belong to you.
- There is no plan for you to receive any financial benefit from the creation, use or sale of such a product or idea.

Optional Consent for Data and Sample Banking for Future Research

ARCA biopharma, Inc., would like to keep some of the data and blood that is taken during the clinical research study to be used for other tests. If you agree, the data and samples will be kept and may be used in future research to learn more about COVID-19 or the study drug.

- The research that is done with your data and samples is not designed to specifically help you. Reports about research done with your data and samples will not be given to you or your doctor. These reports will not be put in your health records. The research using your data and samples will not affect your care.
- The choice to let the Sponsor keep the data and samples for future research is up to you. No matter what you decide to do, it will not affect the care that you will receive as part of the

study. If you decide now that your data and samples can be kept for research, you can change your mind at any time and contact your study doctor to let him or her know that you do not want the Sponsor to use your data and samples any longer, and they will no longer be used for research. Otherwise, they may be kept until they are used up, or until the Sponsor decides to destroy them.

- Your data and samples might be given to other researchers in the future. When this happens, the Sponsor will not give them your name, address, phone number or any other information that will let the researchers know who you are.
- Data and samples will be used for genetic research (about diseases that are passed on in families). Even if your data and samples are used for this kind of research, the results will not be told to you and will not be put in your health records.
- We may share data from our research with other researchers or data banks. One such data bank is called dbGAP, which collects genetic and other data and is sponsored by the National Institutes of Health (USA). By sharing data in data banks like this, we can make our discoveries more accessible to other researchers. Information which directly identifies you will not be sent to these data banks. Because your genetic information is unique to you, there is a small risk that someone could connect the information back to you. Also, genetic research and broadly sharing data may involve risks to you or people like yourself that are unknown at this time.
- Your data and samples will only be used for research and will not be sold. The research done with your data and samples may help to develop new products in the future, but there is no plan for you to be paid.

The possible benefits of research from your data and samples include learning more about what causes COVID-19 and other diseases, how to prevent them and how to treat them. The greatest risk to you is the release of your private information. The Sponsor will protect your records so that your medical information related to the study will be kept private. The chance that this information will be given to someone else is very small. There will be no cost to you for any data or sample collection and storage by the Sponsor. Please read each sentence below and think about your choice.

After reading each sentence, write your initials on the line next to "Yes" or "No." If you have questions, please talk to your doctor or nurse. No matter what you decide to do about the storage and future use of your data and samples, you may still participate in the study.

1. I give my permission for my data and blood samples to be kept by ARCA biopharma, Inc., for use in future research to learn more about how to prevent, detect, or treat COVID-19 and how people respond to the study drug:
   Yes_____ No_____

2. I give my permission for my data, blood and tissue samples to be used for research about other health problems (for example, causes of heart disease, osteoporosis, diabetes):
   Yes_____ No_____

Agreement to be in this study and use my data

I have read this document about the clinical research study or it was read to me. I understand the possible risks and benefits of this study and my responsibilities. I understand and authorize the access, use and disclosure of my information as stated in this form. I know that being in this study is voluntary. I choose to be in this study.

Signature of Subject:_____ Date: _____

Subject's Printed Name:_____

Signature of Legally Authorized Representative (LAR) **OR** Proxy Decision Maker (if applicable):

_____ Date: _____

LAR's **OR** Proxy Decision Maker's Printed Name:_____

(Select one: □ *Legally Authorized Representative* **OR** □ *Proxy Decision Maker*)

Signature of Person Obtaining Consent: _____ Date:_____

Printed Name of Person Obtaining Consent: _____

----------Use the following only if applicable----------

Witness's Signature: _____ Date: _____

Witness's Printed Name:_____

Witness of signature □
Witness of consent process □