(TO BE PRINTED ON SITE HEADED PAPER)

Participant Information Sheet and Informed Consent Form

Study Title: A Phase II, randomised, double-blind, placebo-controlled clinical trial to assess the safety and efficacy of AZD1656 in diabetic patients hospitalised with suspected or confirmed COVID-19 (The ARCADIA Trial)

Protocol Number: SGS.1656.201

IRAS ID: 283686

Sponsor: St George Street Capital, 2a/2b Thrales End Business Centre, Thrales End Lane, Harpenden, AL5 3NS, United Kingdom

Principal Investigator Name and Address: XXXXXXXXX
Study Site Telephone No: XXXXXXXXX
Out of Office Hours No: XXXXXXXXX
Participant ID No: XXXXXXXXX

1 Why have I been invited to take part in this study?

We are asking you to take part in this research study because you have type 1 or type 2 diabetes mellitus and you are in hospital with suspected or confirmed COVID-19.

2 What is the medicine that is being tested?

This study will investigate a drug called AZD1656. This drug was developed as a treatment for diabetes. Approximately 960 people have taken this drug in 25 previous clinical trials. In these trials AZD1656 was shown to help control blood sugar levels for up to 4 months. As the effects did not persist beyond 4 months, it was not considered useful as a long-term treatment for diabetes. However, a short course of AZD1656 whilst you are in hospital with COVID-19 may help to better control your glucose levels.

In addition, AZD1656 may have a positive effect on your immune system, reducing excessive inflammation in the lungs and other organs, which is sometimes seen in patients with COVID-19. This effect has not yet been proven and will be studied in this trial.

AZD1656 has not yet been approved for use by any Competent Authority (the people responsible for authorising medicine approvals) such as the UK Medicines and Healthcare Products Regulatory Authority (MHRA).

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3 Who else is taking part and how long will I be in the study?

There will be approximately 150 patients taking part in the study at about 15 sites in the United Kingdom (UK). You will be in this study for a maximum of 30 days, comprising of up to 2 days for Screening, 21 days of treatment and 7 days of follow-up.

4 Do I have to take part in this study?

No. Your participation in this study is voluntary. You do not have to take part in this study if you do not want to. Your study doctor will discuss alternative treatment that may be available to you and their potential benefits and risks. Your decision to take part or not will in no way affect your current or future treatment. You will be given ample time and chance to ask questions about the details of this study and decide if you wish to take part. If you cannot sign the consent form, you can give verbal consent and an impartial witness can sign the form on your behalf.

You can decide to withdraw from the study at any time. You do not have to give a reason. If you decide to take part, you will be given a copy of this document to keep.

5 What will happen if I agree to take part?

Whether you agree to participate in this study or not, you will receive the usual care provided to all diabetic patients in hospital with COVID-19. If you do agree to participate and meet the entry requirements of the study, you will be assigned to one of two treatment groups. The treatment group that you will be in is selected by chance, like tossing a coin. Half of the study patients will receive AZD1656 (the active drug) and half will receive placebo (a dummy pill that looks the same as AZD1656 but does not contain the active drug). This study is "double-blinded". This means that neither you nor your study doctor will know whether you are taking AZD1656 or placebo. If required for a medical need, the doctor is able to find out which treatment you are receiving.

Each day whilst you are on the study, you will take two tablets with your breakfast and two tablets with your evening meal. The tablets must be taken with food because the medicine has been shown to possibly lower blood glucose levels. You must **not** take the tablets without food. If you miss a dose, take the next dose at the usual time. You will receive the study tablets for up to a maximum of 21 days. If your symptoms significantly improve (and you are to be discharged from hospital) or significantly worsen during this 21-day period, study treatment will be stopped.

Before you enter the study:

To ensure that you can safely enter the study it will be necessary for some blood tests and physical examinations to be taken by your doctor. The doctor will also ask for details of your health in the past and any medication which you are currently taking, including your diabetic medications and any over the counter medicines and supplements. The tests and examinations will include the following:

- Your demographic details, including ethnicity.
- Electrocardiogram (ECG) – this is a painless test which looks at the function of your heart. You will lie down for several minutes and have sensors taped to your arms, legs and chest. It takes approximately 5 minutes.

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- Blood pressure, pulse, temperature and oxygen levels (measured using a finger probe)
- Urine sample – tested with a dipstick including a pregnancy test only for women who can have children.
- Blood samples for a safety check - approximately 15 mL (or 3 teaspoons) in total.
- *COVID-19 test (sample of nasal secretion taken from the back of nose and throat)*

Once you have entered the study:

The study is trying to find out how the body and the immune system responds to the study medication and to find out how effective it is. Therefore, once you begin taking the study medication some blood tests and assessments will be taken at regular intervals until the day that you stop taking the medication. These are the following:

- Blood pressure, pulse, temperature and oxygen levels (measured using a finger probe)
- What type of breathing support you require, if any (e.g. Oxygen)
- Safety blood tests – a maximum of 40 mL (8 teaspoons) taken over 4 timepoints during the study
- Bloods tests to look at the following items:
    - Your Vitamin D levels – 5 mL (one teaspoon)
    - An assessment of your current glucose control – 5 mL (one teaspoon)
    - how the immune system is responding to the treatment – a maximum of 100 mL (20 teaspoons) taken over 4 timepoints during the study
    - the concentration of the study drug in the blood – a maximum of 3 mL (less than 1 teaspoon) taken over 3 timepoints during the study
    - the clotting of your blood (only if your study site has the facilities to store the samples for this test and if you agree to this test) – a maximum of 9 mL or (2 teaspoons) taken over 2 timepoints during the study.

For the entire study, a maximum total of 177mL (about 36 teaspoons) of blood is expected to be taken.

As long as you are taking the study medication your medical team will also check how you are feeling and monitor any other medications you are taking, including your diabetic medications. They will also decide if you need any other tests or examinations as part of your standard care.

Your doctor knows which medicines must be avoided during the study and will advise you accordingly. You should always check with your study doctor before you take any new medicines, including over the counter and herbal medicines. Tell the study doctor if you feel unwell in any way during the study. Give full details of your health in the past including any known allergies or side effects to medicines.

If you are a woman who could get pregnant, do not get pregnant while you are taking part in the study. A pregnancy test will be done at the first visit and at the End of Study visit.

If you are a sexually active man or woman, you **must** use a reliable form of birth control while taking part in this study and for 2 weeks after the study has finished. It is **very important** that you continue to use contraception for this time period. Highly effective contraceptive methods are combined or progestogen-only oral contraception, intrauterine device (coil), intrauterine hormone-releasing system (Mirena ™), bilateral tubal occlusion, vasectomised partner, and sexual abstinence, defined as true abstinence.

We do not know enough about the effects of the study medicine on the unborn child. This is why it is extremely important that effective contraception is used.

After you have completed the study treatment:

You will continue to be assessed up to 7 days after stopping study treatment. If you have been discharged from hospital you will receive a phone call 7 days after discharge to check on your health. (You will not need to revisit the hospital for this purpose.) This also includes questions on any other medications you have been taking during the last 7 days and on possible side effects.

6 What are the side effects and possible risks of taking part in this study?

As with all research studies, the study drug and study procedures may involve unknown risks.

In 25 prior clinical trials, approximately 960 men and women received AZD1656 for up to 6 months and no safety concerns have been raised in those trials. Overall, the proportion of patients reporting side effects on AZD1656 treatment was similar to those on placebo (the dummy pill). Mild headaches and lowered blood glucose were the most commonly reported side effects in the prior trials. No data is available on the effects of AZD1656 on pregnancy and breastfeeding in humans.

Some of the tests and procedures that will be done during the study may present risk or cause discomfort. While taking a sample to test for COVID-19 from the back of your nose and throat, you may gag a little and feel slightly uncomfortable, but it shouldn´t be painful. You may have a minor nosebleed afterwards.

When a blood sample is being taken from you, you may feel faint, or experience mild pain, bruising, irritation or redness at the injection site. In rare cases, you may get an infection.

For the ECG test, you may need to have small patches of your hair clipped on your chest, shoulders and hips. These sticky pads may cause some irritation and may be uncomfortable to remove.

It is not known whether treatment with AZD1656 may cause injury or harm to the unborn child if taken during pregnancy. If you are pregnant, you are unable to take part in this study. If you do fall pregnant, you will be monitored until the birth of your baby. When the baby is born, it must be

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examined for any abnormalities and, if these are present, your study doctor must be informed immediately. You must not breast feed your baby while participating in this study.

7 What are the possible benefits of taking part?

We cannot promise that the study drug will help you. Although you may not benefit yourself, your taking part in this study may provide new information about a new method of treatment for others who have the same condition as yourself.

8 Will my GP be informed about my study participation?

If you agree to take part in the study, with your permission, we will inform your GP about your participation in this study.

9 Will it cost me anything to be in this study?

There will be no cost to you for the study drug or the study-related procedures and examinations. You will not be paid for taking part in the study.

10 What happens if your study treatment is stopped?

Your study treatment may be stopped by your study doctor or by the sponsor without your consent at any time. If your study treatment is stopped, you will be asked to have the tests, examinations and follow-up questions described in the Visit Schedule table above to make sure that it is safe for you to stop the treatment. If your study doctor withdraws you from the study, your data will still be analysed, reported and provided to the sponsor.

Your study doctor will stop your study treatment if:

- your disease symptoms have significantly worsened or,
- your study doctor feels it is not safe for you to receive further study treatment because you have experienced serious side effects, taken prohibited medicines or,
- you become pregnant or,
- you cannot cooperate fully with the study requirements or the sponsor decides that the drug poses a hazard to your health.
- the sponsor decides to stop the study.
- your symptoms significantly improve, and you are to be discharged from hospital.

11 What happens if you withdraw your consent for the study?

You may withdraw your consent for the study at any time without giving a reason. If you decide to stop taking part, tell your study doctor immediately. This will not affect your care.

If you withdraw voluntarily, all treatments and study-related procedures will be stopped, and no further information will be collected on you. However, you will have some tests and examinations as described in the Visit Schedule table above and you will be asked follow-up questions before you leave the study. You have the right to choose not to answer these questions. You can also decline taking part in any tests or examinations once you withdraw from the study.

You will be asked to keep in contact with the study doctor for a follow-up to make sure you are all right.

If you withdraw consent, the sponsor may keep and continue to use any data collected before such a withdrawal of consent, unless you ask otherwise. You may request destruction of any samples taken and not tested, and your study doctor must note this in your study records.

12 What if new information becomes available?

Sometimes we receive new information about the treatment being studied. If this happens, your study doctor will tell you in a timely manner and discuss whether you should continue in the study. If you decide not to carry on, your study doctor will make arrangements for your care to continue. If you decide to continue in the study, your study doctor may ask you to sign an agreement outlining the discussion.

13 What will happen at the end of the study?

After the study is completed or you withdraw from the study, the study doctor will discuss with you your treatment options and your continued care.

After the study is completed, a summary of the results will be published on the Clintrials.gov website, https://clinicaltrials.gov and on the St George Street Capital website *(www.sgscapital.org)* for you to look at should you want to. You may also ask your study doctor to explain to you the results that come from the trial if you so wish.

14 What will happen to your data collected during the study?

The sponsor or other companies acting on their behalf will analyse the information gained via your participation in the study to see how and if the drug has worked. Certain statistical tests will be carried out on the data collected. The sponsor may forward the results to health authorities in other countries outside the UK and the European Union, including the USA, and the results may also be used in study reports, scientific presentations or publications. Your identity will never be disclosed.

15 What happens if something goes wrong?

The Sponsor will provide compensation for any injury caused by taking part in this study in accordance to the guidelines of the Association of British Pharmaceutical Industry (ABPI). The Sponsor will pay compensation where injury has resulted from a test or procedure you have received as part of the study. You should immediately contact your study doctor on the contact information provided on page 1 of this form in the event you experience any study-related illness or injury.

16 How will we use information about you?

We will need to use information from your medical records for this research project.

This information will include your:

- Demographic data, including ethnicity

- Medical history
- Results of procedures
- Results of tests on your blood and urine samples,
- Information on any side-effects you may have had during the study

People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure.

Some of your information may be sent to the USA. They must follow our rules about keeping your information safe.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

16.1 What are your choices about how your information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.
- If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study. This will only happen if study site has the facilities to freeze and store samples for future analysis. These future studies will be reviewed and approved by an Ethics Committee before they can take place.

16.2 Where can you find out more about how your information is used?

You can find out more about how we use your information:

- at www.hra.nhs.uk/information-about-patients/
- our leaflet available from the study team (Generic Patient Information Sheet)
- by asking one of the research team
- by sending an email to the Sponsor's Data Protection Officer at **info@sgscapital.org**
- by ringing us on the telephone number listed on page 1 of this document.

17 What will happen to any samples that have been taken?

Blood and urine samples will be taken as part of the study. These samples are needed to monitor your safety and to find out if the study drug is having an effect. All samples taken will be stored in tubes that have your participant identifier. They will not have your name and can only be linked to you via the participant identifier. Your study doctor and the study team will keep the list that links your name to your participant identifier. Your samples will be accessible only to authorised representatives of the sponsor.

If you decide to stop taking part in this study, your already collected samples will still be used in the ways that you agreed to when you started in the study. Once you have withdrawn your consent for participating in the study, no further data will be collected about you for the purposes of this study. Any unused samples that were collected can be destroyed at your request, but if the samples are no longer linked to you or if the samples were sent to a third party, this might not be possible.

In future, identifiers associated with your data and/or specimens could be removed from the data and specimens. The de-identified data and specimens could then be used for future research by the study team or other researchers without notifying you or asking your permission for this use.

Your samples will be stored at the study site. The samples will be analysed at:

York Bioanalytical Solutions, Cedar House, Northminster Business Park, Upper Poppleton, York YO26 6QR and Queen Mary University of London, Mile End Road, London E1 4NS.

Your samples for future clotting factor analyses will be stored at the study site and will be analysed at a laboratory (still to be identified) in the UK.

Your samples may be stored for up to 15 years after the study ends. Samples will then be destroyed by the laboratory according to the local instructions for destruction.

If new tests that were not foreseen when you gave your consent to participate need to be done on your kept samples, you will be informed and will have the option to refuse further testing, or you will have the opportunity to sign a new Informed Consent Form.

18 Who is organising and funding this study?

This study is designed and funded by the sponsor, St George Street Capital. The sponsor is also paying the study site to cover the costs of this study.

19 Who has reviewed this study?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee, to protect your interests. This study has been reviewed and given a favourable opinion by Leicester South Research Ethics Committee.

20 Who can you contact for further information?

If you have a concern about any aspect of this study, you should ask to speak to the study team who will do their best to answer your questions. Information on contact details are listed on page 1 of this

document. Once all the data from the study has been analysed the sponsor will publish the data so that it is publicly available.

If you have any questions or concerns about your rights as a research participant in this research study, and you would like to talk to someone other than the study doctor or study staff, please contact Patient Advice and Liaison Services (PALS) on _____ or (if applicable) the complaints department at your site on _____.

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PARTICIPANT INFORMED CONSENT FORM

Study Title: A Phase II, randomised, double-blind, placebo-controlled clinical trial to assess the safety and efficacy of AZD1656 in diabetic patients hospitalised with suspected or confirmed COVID-19 (The ARCADIA Trial)

Protocol Number: SGS.1656.201

IRAS ID: 283686

Sponsor: St George Street Capital

Principal Investigator Name and Address: XXXXXXXXX
Study Site Telephone No: XXXXXXXXX
Out of Office Hours No: XXXXXXXXX
Participant ID No: XXXXXXXXX

		Please initial each box
1.	I confirm that I have read and understand the patient information sheet (V1.1, 29JUL2020) for the above study and have had the opportunity to speak with a study doctor about the conduct of the study. All my questions have been answered to my satisfaction. I have been adequately informed and I have had sufficient time to make my decision.	
2.	I understand that my participation is voluntary and that I am free to withdraw at any time (verbally or in writing), without giving any reason, without my medical care or legal rights being affected.	
3.	I understand that relevant sections of any of my medical notes and data collected during the study may be monitored/audited at the site OR remotely by responsible individuals from the sponsor (or their representatives) and from Regulatory Authorities. I give permission for these individuals to have access to my records. I understand that I will not be identified by name in any reports or publications resulting from the study.	
4.	I understand that any information relating to my medical records and data collected during the study will be reported in a form that will not allow my identity to be disclosed. I also understand that since this information may be required in support of the registration of a medicinal product outside the European Union, that my data may be transferred outside that area, where the data protection laws might not be as stringent as in the European Union.	
5.	I understand that my GP will be informed of my participation in this study.	
6.	I agree to take part in the above study and follow all study procedures, including informing the study doctor of any changes in my medications.	

Please circle your answer to show whether or not you would like to take part in each option:

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SAMPLES FOR FUTURE CLOTTING FACTOR ANALYSIS:

If your study site has the facilities to freeze and store samples for future analysis and if you agree to have your blood collected for future analysis, please indicate below.

I agree to have my blood collected and I agree that my blood samples and related information may be used for future analysis of clotting factors

YES NO

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to voluntarily take part in the main study and any additional studies where I circled 'yes'

_____
Participant's Name

_____
Participant's signature

_____ _____
Date of signature Time of signature

_____
Impartial witness's Name

_____
Signature of impartial witness (if applicable)

_____ _____
Date of signature Time of signature

_____
Name of person conducting the informed consent discussion

_____
Signature of person conducting the informed consent discussion

_____ _____
Date of signature Time of signature

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