AGILE: Seamless Phase I/IIa Platform for the Rapid Evaluation of Candidates for COVID-19 treatment

Patient Information Sheet

CST-2 EIDD-2801 – Phase I

IRAS ID 282781

Candidate-Specific Trial-2: A Randomized, Multicentre, Seamless, Adaptive, Phase I/II Platform Study to Determine the Optimal Dose, Safety and Efficacy of EIDD-2801 for the Treatment of COVID-19

Invitation to participate
We are inviting adults who have suspected or confirmed COVID-19 and are within 5 days of symptom onset to consent to join this research study assessing possible treatments. Different treatments will be assessed in different arms of the study. This form gives information about one arm of the study (CST-2 EIDD-2801) including the aims, risks and benefits of taking part.

WHAT YOU SHOULD KNOW ABOUT THIS RESEARCH STUDY:

1) Why is this research being done?
Your doctors suspect that you have a lung disease called COVID-19. This condition is caused by a type of virus called SARS-CoV-2, or coronavirus for short.

This Study is the first time the Study Drug is being given to people with Covid-19.

The Study Drug has been tested extensively in animals at doses higher than the highest dose planned for this Study, with no serious side effects. A full description of the risks associated with the Study Drug is provided in Section 11 of this document.

There are no drugs of proven value against COVID-19 although there are several which may turn out to be helpful when added to the usual standard of care. This study aims to find out whether any of these additional treatments are of any help.

2) What is the purpose of this study?

The AGILE study aims to assess several different treatments that may be useful for patients with COVID-19. These treatments have been recommended for testing by a team of experts (The AGILE Scientific Advisory Board) based on strict criteria.

The aims of this Study are to determine, in people with COVID-19, the following:

- The safety of the Study Drug and any side effects that might be associated with it
- How much of the Study Drug gets into the bloodstream
- How quickly the body removes the Study Drug and its breakdown product
- How well the study drug might be able to reduce complications of COVID-19

Although these treatments show promise, nobody knows if any of them will turn out to be more effective in helping patients recover than the standard of care at home as recommended by their doctor (which all patients currently receive).

The treatment being assessed in this arm of the study is **EIDD-2801.**
At present, we don't know whether EIDD-2801 is effective in treating COVID-19. It has been given to healthy volunteers so we do have some limited information about potential side effects of this treatment. Side effects are any unwanted, or sometimes unpleasant reactions that may result from taking a drug or having a procedure. More information about this is explained further on in this information sheet.

The AGILE study for CST-2 EIDD-2801 is being done in two parts (phase 1 and 2) **You are being invited to take part in Phase I.**

Phase I: First, we need to establish which dose is safest to use in patients with COVID-19. A small group of patients will participate in the phase I component of the study where they will receive different doses of EIDD-2081 dependent on what groups (cohort) they are in. The doses chosen have already been used safely in a group of healthy volunteers.

3) What are the Treatment options?

The treatment options for the study are either the standard of care, or the drug under investigation (EIDD-2801).

Patients will be randomly split into two groups. The control group will receive the standard of care and the treatment group will receive EIDD-2801. Both you and your doctor will know which group you are in – this means that the trial is known as 'open label' or 'unblinded'.

All patients in the treatment group will be given a dose of EIDD-2801 which was shown to be safe in the healthy volunteer study. This is to check that the dose is also safe in patients who have COVID-19.

4) Do I have to take part?

Taking part in the study is entirely voluntary and if you do not wish to participate this will not affect the standard of your treatment in any way. It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and asked to sign a consent form.

If you decide to take part you are still free to withdraw at any time without giving a reason. This will not affect the standard of care you receive. If you do not wish to take part in this study, you will be offered whatever treatment your doctor thinks is best for you.

5) What is the drug that is being tested?

EIDD-2801 is an anti-viral drug which is currently being studied as a treatment for a number of viruses including COVID-19.

The study drug (EIDD-2801) is provided as a capsule that you swallow. If you are randomly assigned to the treatment group, you will receive the study drug treatment for dosing on days 1-5 depending on timing of first dose. Ten doses will be administered, (one dose in the morning and one dose again in the evening). You will be administered the first dose of study drug in the clinic and given the remainder of the study drug for you to take twice each day at home. You will return to the clinic on Days 3 and 5, with your study medication so that the research team can check you have taken the correct amount of capsules. You will receive a dose of study drug in the clinic on Day 5 and the remaining dose(s) of study drug will be sent home with you for self-administration.

You must have fasted for 2 hours before taking the study treatment, and one hour after. This is so that your stomach is empty before taking the capsule; and the one hour after allows drug to be absorbed without any food interference. When the capsule is given in clinic, 240ml of water will also be given. When taken at home, please take with water; no specific volume is required.

Please try and take the capsules at the same time each day.

If you are late taking a dose, you can still take it within six hours of your usual time. If it is longer than six hours, leave that dose out and take the next dose at your usual time. Please record any missed doses, as the research team will need to know. Any un-used doses should be returned to the research team.

6) Who is doing the study?

The study is being conducted by researchers at the Universities of Southampton and Liverpool. University of Liverpool is the Sponsor for the research. This means that they have overall responsibility for making sure the research is conducted in accordance with the relevant regulations.

7) Who is being included in the study?

You have been invited to consider taking part in this study because you may meet the criteria for taking part. We first need to ask you some questions; this is called screening. You must answer all the screening questions completely and truthfully. You must mention all past and present medical conditions, including any allergies. You must also mention any medications you are taking currently or have taken recently, including prescription and non-prescription/over-the-counter medications and vitamins/supplements.
To be eligible for the Study, you must meet the following criteria:

- Either over the age of 60 **or** over the age of 50 and have at least one well-controlled medical condition.
- Have someone aged 16 years or older living in the same household during the dosing period. (This is so medical help can be requested urgently in case of an anaphylactic reaction).

You must let the research team know about any other clinical studies you have taken part in or are currently taking part in. If you pass the screening assessments, we may invite you to take part in the Study. You must be able to comply with all study procedures and attend clinic visits. If you decide to join, you will be asked to sign the consent form.

Women of childbearing potential (WOCBP) and male patients who are sexually active with WOCBP must agree to use two methods of contraception, one of which must be highly effective. For women the contraception must be used from the first administration of trial treatment, and throughout the trial and up to 50 days after the last follow up visit (50 days after day 29). For men with female partners of child bearing potential, the contraception must be used from the first administration of trial treatment until 100 days after the last follow up visit (100 days after day 29). Further information is provided in section 13 of this Patient Information Sheet.

8) Design of the study

If you are given the study drug, you will be asked to take ten doses, two a day for five days (including the morning of day 6 if you had only one dose on day 1). Before receiving the Study Drug, you will be informed of how many days of dosing and how often you will be dosed.

The dose levels of Study Drug will be based on the results of the previously completed parts of the Study. It is planned to continue increasing the dose tested in the cohorts up to a dose level that is considered to be safe. The dose levels to be studied in the remaining groups will depend upon the results from the previous groups. Before receiving the Study Drug, you will be informed of the dose level your assigned group is to receive.

The Study compares the study drug with routine standard of care. The treatment group will receive the EIDD-2801 medication and the control group will receive the standard of care at home as explained by your doctor. This means that some participants will receive the Study Drug and some will not. Whether you receive Study Drug will be determined by a process called randomisation. The randomisation for this phase of the study will be done in a 2:1 ratio. This means that for every 3 patients who enter the study, 2 patients will receive the study drug 1 patient will receive normal standard of care. The only way to make sure that the two groups of patients are as similar as possible is to have your treatment decided by chance. Therefore, neither you nor your doctors can choose which of these options you will be allocated.

9) Study visits

During the Study, you will visit the Clinic on at least 9 occasions over a period of approximately 40 days. These visits will include the Screening visit, 2 in-clinic visits lasting approximately 6 hours and 6 in-clinic visits lasting approximately 2 hours. The specific visits are detailed below.

Visit 1	**Screening Visit**
Details	The purpose of the Screening visit is to determine if you are eligible and willing to participate in the Study. Before any procedures are performed, we will ask you to sign the Informed Consent Form at the end of this document. The visit will last approximately 2 hours.
Procedures Performed	• Written informed consent • Review of Study eligibility criteria • Demographic information (for example, age, sex, race) • Review of medical history (asking about current and previous medical conditions) and medications you are taking currently or have taken recently • Measurement of height and weight; calculation of body mass index (BMI) • Targeted physical examination

	• Vital signs, including blood pressure, pulse rate, oxygen saturations, breathing rate, and oral body temperature • Nose and throat swab to confirm coronavirus diagnosis. You will only be eligible to take part in the study if the laboratory test confirms you have coronavirus. This is not an NHS test for coronavirus but a research test, however this result will be reported to Public Health England and current guidelines will be followed. If the coronavirus test comes back as negative, you will not be eligible to take part in the study but you will still need to follow the government guidance regarding social distancing and self-isolation. • This must be performed within 5 days of the onset of your symptoms • Blood samples will be collected: o for routine lab tests (to check your liver, kidneys and other body systems are working normally) o blood sample for storage for future scientific research • Questions about how you're feeling • If you have had a chest x-ray we will review this • An ECG (electrocardiogram) recording of the electrical activity of your heart is also part of screening and will be carried out at the Clinical Research Unit on or before Day 1 (pre-dose).
Additional Information	After your Screening visit, the Study Doctor will review the results of these tests to see whether you are eligible to take part in the Study. If you are eligible, we will ask you to return to the Clinic within 4 days from your screening visit.

Visit 2	**In-Clinic Study Visit(s) (Baseline visit)**
Details	You will check in to the Clinical Research Unit on Day 1 (the day you first receive the Study Drug). If you are randomised to receive the study drug you will remain on the Unit for approximately 6 hours. If you are randomised to the standard of care, you will not receive the study drug and will remain on the Unit for approximately 2 hours.
Procedures Performed	• Review of Study eligibility criteria • Review of medical history since Screening visit and any medications you may have taken • Targeted physical examination if it was not performed at Screening or if you're having any symptoms

Visit 2	In-Clinic Study Visit(s) (Baseline visit)
	• Vital signs • ECG (electrocardiogram) recording of the electrical activity of your heart. If you are male, your chest hair may need to be shaved so the ECG patches will stick to your skin. If you are female, you may need to remove your bra. (This is part of the screening assessment). • Randomisation to determine if you will receive study drug • Blood and urine samples will be collected: o for routine lab tests o urine pregnancy test (women of child bearing potential only) o to measure the level of the Study Drug and its breakdown product • blood sample for storage for future scientific research • Single throat and nose swab • 10 nose swabs across 6 hour period (not required if randomised to no extra treatment) • 5 saliva samples across 6 hour period (this involves chewing an absorbent pad) • 10 tear test strips across 6 hour period (this involves placing a small strip of paper under your lower eyelid and blinking) • Receive Study Drug or standard of care (no extra treatment) • Questions about how you're feeling • Dispense medication to be taken at home (treatment group)
Additional Information	All meals, snacks and drinks will be provided for you during your stay at the Unit. Dosing will start on Day 1, and will continue for a maximum of 5.5 days. The frequency of dosing will be 2 times daily. Before receiving the Study Drug, you will be informed of the dose level, dosing duration, and dosing frequency for your assigned group. Telephone calls: Any day that you are not attending clinic (up to day 15) you will receive daily telephone calls from the research team to check on your health and well-being, review any medications you may have taken and to confirm that you have taken your study medication (treatment group). Hospitalisation:

Visit 2	**In-Clinic Study Visit(s) (Baseline visit)**
	If you are admitted to hospital we will collect some general information about your health.

Day 3 (and day 8)	**Clinic Visit**
Details	Each visit will last approximately 2 hours.
Procedures Performed	• Shortened physical examination if you're having any symptoms • Vital signs • Throat and nose swab • Review of any medications you may have taken • Questions about how you're feeling • Confirm that you've been taking the medication and dispense further study drug if required (treatment group only)
Additional Information	If any of your lab test results are abnormal, we may ask you to return to the Unit for additional blood tests until they return to normal. If you withdraw from the Study, follow-up assessments may be performed at the time you withdraw.

Day 5	**Follow-up Visit**
Details	If you were randomised to receive the study drug you will remain on the Unit for approximately 6 hours. If you were randomised to the standard of care, you will not receive the study drug and will remain on the Unit for approximately 2 hours.
Procedures Performed	• Targeted physical examination if you're having any symptoms • Vital signs • Blood and urine samples will be collected: o for routine lab tests o to measure the level of the Study Drug and its breakdown product

	• blood sample for storage for future scientific research • Single throat and nose swab • 10 nose swabs across 6 hour period (not required if randomised to no extra treatment) • 5 saliva samples across 6 hour period (this involves chewing an absorbent pad) • 10 tear test strips across 6 hour period (this involves placing a small strip of paper under your lower eyelid and blinking) • Receive Study Drug or standard of care (no extra treatment) • Questions about how you're feeling • Dispense medication to be taken at home (treatment group)
Additional Information	If any of your lab test results are abnormal, we may ask you to return to the Unit for additional blood or urine tests until they return to normal. If you withdraw from the Study, follow-up assessments may be performed at the time you withdraw.

Day 11 (and day 15)	**Clinic Visit**
Details	Each visit will last approximately 2 hours.

Procedures Performed	• Shortened physical examination if you're having any symptoms
	• Vital signs
	• Throat and nose swab
	• Blood and urine samples will be collected:
	  o for routine lab tests
	  o to measure the level of the Study Drug and its breakdown product
	• blood sample for storage for future scientific research
	• Review of any medications you may have taken

	• Questions about how you're feeling
Additional Information	If any of your lab test results are abnormal, we may ask you to return to the Unit for additional blood tests until they return to normal. If you withdraw from the Study, follow-up assessments may be performed at the time you withdraw.

Day 22	**Clinic Visit**
Details	Each visit will last approximately 2 hours.
Procedures Performed	• Shortened physical examination if you're having any symptoms • Vital signs • Throat and nose swab • Blood and urine samples will be collected: o for routine lab tests o to measure the level of the Study Drug and its breakdown product • Review of any medications you may have taken • Questions about how you're feeling
Additional Information	If any of your lab test results are abnormal, we may ask you to return to the Unit for additional blood tests until they return to normal. If you withdraw from the Study, follow-up assessments may be performed at the time you withdraw.

Day 29	**Clinic Visit**
Details	Each visit will last approximately 2 hours.
Procedures Performed	• Shortened physical examination if you're having any symptoms • Vital signs • Throat and nose swab • Blood and urine samples will be collected:

	○ for routine lab tests ○ urine pregnancy test (women of childbearing potential only) ○ to measure the level of the Study Drug and its breakdown product • blood sample for storage for future scientific research • Review of any medications you may have taken • Questions about how you're feeling
Additional Information	If any of your lab test results are abnormal, we may ask you to return to the Unit for additional blood tests until they return to normal. If you withdraw from the Study, follow-up assessments may be performed at the time you withdraw.

During the Study, blood will be taken from you (approximately 15 blood samples over approximately 40 days. The total volume of blood taken during the Study, including the Screening visit, will be no more than 400 mL (a standard blood donation is 450 mL). A cannula (small plastic tube inserted into a vein in your forearm using a needle) may be used on the days when multiple blood samples need to be taken. A cannula allows blood to be taken without the need for a needle to be used each time.

10) What are the possible benefits of being in the study?
We do not know if the treatment being tested will be therapeutic (have a beneficial effect) or help you with your symptoms, but this study should help inform how we treat future patients.

11) What are the possible risks of receiving study drug?
The Study Drug (EIDD-2801) is an antiviral drug that is being studied for the treatment of several different viruses, including the COVID-19-causing coronavirus. The drug works by interfering with the virus's ability to reproduce itself, by causing changes to the reproduction process resulting in mutations in the virus. With enough mutations, the virus is no longer able to quickly multiply. In animal models (studies in animals used to predict what might happen in humans), EIDD-2801 was shown to treat influenza, SARS, and MERS.

EIDD-2801 has been given to healthy volunteers but this will be the first study of EIDD-2801 in people with coronavirus. Therefore, there is limited information about the effects and side effects that may be seen in humans. The type of side effects that will occur are not well known and how severe they could be is not well known. There is a risk of side effects that could be mild, severe, or life-threatening.

EIDD-2801 has been studied in animals to see what kind of side effects happen so that some information is available about what might happen in humans. Although we know what happens in animals, it does not mean that these effects will be seen in humans. The effects

in humans could be the same or different, and more or less serious. In animals treated with high and repeated doses of EIDD-2801, there were side effects involving the bone marrow. Cells that make blood were affected and blood counts of platelets (blood cells that help form clots to stop bleeding) were reduced. There were also effects on red blood cells and white blood cells. These effects went away after stopping drug treatment. Subjects will be monitored for these effects with regular blood tests. If these effects occurred in humans, there are treatments available that could be used in serious cases.

Other effects of EIDD-2801 when administered to animals at high doses (more than 50 times higher than the highest dose planned for this Study, in dogs) were vomiting and diarrhoea, and evidence of bleeding in the lining of the gastrointestinal tract. Some sores in the mouth were seen; weight loss associated with decreased eating was seen. At even higher doses (more than 100 times higher than the highest dose planned for this Study, in rats) changes were seen in blood tests that measure the function of the liver. Single doses of drug given to animals at high doses were associated with vomiting, soft faeces, and weight loss. Based on all of the animal studies, the lowest dose tested that was not considered to cause adverse events in dogs was 6 mg/kg/day for 28 days of dosing. When converted to a human dose based on size differences, the dose would be more than 200 mg. The starting dose in the single dose part of the study is 50 mg and the highest dose to be tested is 200 mg. Doses administered in the multiple dose portion of the study will not exceed those that were tested in the single dose portion of the study. It is not known whether humans will absorb EIDD-2801 better or less well than was seen in dogs.

EIDD-2801 was found to be positive in a bacterial reverse mutation assay (also called an Ames test). This is a genetic toxicology screening study that shows that EIDD-2801 can cause mutations in bacteria, and therefore might act to cause cancer. This is because many compounds that are positive in the Ames test can be shown to cause cancer in rats. The rate at which compounds cause cancer in humans compared to rats depends on many factors. In different tests to look at genetic toxicity, the in vitro and in vivo micronucleus tests, EIDD-2801 did not show positive results. More testing needs to be done to best predict whether there is a risk that EIDD-2801 will cause cancer. It is not possible at present to determine how much risk there is, if any, that EIDD-2801 can cause cancer. Although certain chemicals can cause cancer with limited exposure, it is thought that limiting the number of doses may reduce any risk of cancer.

The Study Drug may have side effects that are currently unknown. There is a remote chance that the Study Drug (and indeed any drug product) may cause an allergic reaction, which in some cases may be severe. This is known as an anaphylactic reaction. Symptoms of an anaphylactic reaction include sudden shortness of breath, decreased consciousness and rash. An anaphylactic reaction may require emergency treatment. Report any unusual signs or symptoms you notice to the Unit medical staff straight away.

If there are any changes to the potential risks associated with the study drug during the study, you will be informed by the Study Doctor.

12) What are the possible risks of being in the study?

You may also experience other unwanted effects or discomforts with the study procedures such as:

- **Blood Sample:** Collecting blood may cause bruising at the place where the needle or a catheter is inserted. Fainting, and in rare cases infection, may occur. In hospital an indwelling catheter is often routinely inserted and may stay in place for a few days or a longer period. Using a catheter helps in two ways, first it prevents scars or blemishes at the sites of repeat blood samples; and helps in proper administration of medications, fluids, nutrition given via saline, and for collecting a blood sample. If a needle is used, a new needle will be used for each blood sample.
- **Blood Pressure:** The blood pressure cuff used to take your blood pressure may cause discomfort or bruising to your upper arm.
- **Nose and Throat Swabs:** During collection of swabs, you may experience sneezing, retching and eye tearing. There is also the potential for those people that are susceptible to nose bleeds to experience one.
- **Electrocardiogram (ECG):** The ECG procedure may cause discomfort and/or bruising during the attachment and removal of the leads (sticky pads) to and from the skin as well as irritation at the site of the lead application. Skin irritation is rare but could occur during an ECG from the electrodes or gel that is used. The sticky pads may be cold upon contact to the skin. In some cases, we may have to shave the area of the body where the sticky pads are attached to ensure that the pads stick to your body.
- **Tear Sample:** You will need to remove your contact lenses or glasses before the test. The strip may be mildly irritating or feel uncomfortable. You will not be able to wear contact lenses for about 2 hours after the last sample. You should avoid rubbing your eyes for about 30 minutes after removal of each strip.

13) Pregnancy and Contraception

For women

We have not tested the study treatment in pregnant women. You will not be able to take part in the trial if you are pregnant or breastfeeding. We will ask you to have a pregnancy test during the screening phase and also on the last day of the study.

Female patients, who have not passed the menopause or been surgically sterilised, must agree to use at least 2 forms of contraception, one of which must be highly effective (outlined below) during treatment and for a minimum of 50 days after the day 29 follow up visit.

Suitable methods of contraception:

- Hormonal contraception:
    - Oral combined or progesterone pill
    - Injection

  - Implant
  - Intrauterine device (Mirena coil)
- Intrauterine device (IUD)
- Sex with a vasectomised partner (confirmed by 2 negative semen analyses)
- Absolute and complete sexual abstinence

In the event that you become pregnant while you are taking part in the study you should consult your doctor immediately and inform your research nurse. Your research nurse will then report the pregnancy to the Southampton Clinical Trials Unit who are running the study. Should you become pregnant during the study you will be provided with additional information and your partner may be asked to consent to health information during the pregnancy and the birth being provided to the research team.

For men

It is not known what effect EIDD-2801 will have on the testes, it is possible that the EIDD-2801 will affect sperm or semen.

If there is a possibility your partner could become pregnant, you must use condoms and you or your partner must use at least one other form of highly effective contraception (outlined above) during treatment and for a minimum of 100 days after the day 29 follow up visit.

In the event that your partner becomes pregnant while you are taking part in the study, you should consult your doctor immediately and inform your research nurse. Your research nurse will then report the pregnancy to the Southampton Clinical Trials Unit who are running the study.

If you or your partner becomes pregnant while in this study, you must tell your trial doctor immediately. The doctor will advise you of the possible risks to your unborn baby and discuss the options for managing the pregnancy with you.

14) Can I stop the study treatment or my participation early?

If you or your doctor want to stop the study treatment before the course has been completed, then you are free to do so. If you decide that you do not wish any more information to be collected about you, you are free to say so (although de-identified information that has been collected up to that point will continue to be analysed by the research team).

15) What if new information becomes available?

Sometimes during the course of a clinical trial, new information becomes available about the drugs that are being studied. If this happens, your doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw, your

doctor will make arrangements for your care to continue. If you decide to continue you will be asked to sign an updated consent form.

Also, on receiving new information your doctor might consider it to be in your best interests to withdraw you from the study. He/she will explain the reasons and arrange for your care to continue.

16) What if something goes wrong?

If you have a concern about any aspect of this study, you should ask to speak with the research doctor/nurse who will do their best to answer your questions.

If taking part in this research study harms you, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay your legal costs. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanism will be available to you.

If you have private medical insurance, you may wish to check with your company before agreeing to take part in the study to ensure that participation in the study will not affect your insurance cover.

If you would like independent advice, further information or want to make a complaint you may find it useful to contact The Patient Advice and Liaison Service (PALS) which offers confidential advice, support and information on health-related matters. They provide a point of contact for patients, their families and their carers. Their contact details can be found in section 23 of this information sheet or you can find officers from PALS in your local hospital or you can find your nearest PALS office on the NHS website.

17) What will happen to any samples I give?

The following samples will be collected regardless of which treatment group you are randomised to.

Swabs: During the study additional swabs will be taken from the nose and throat to assess whether the virus is still present. The extra swab samples to be taken are detailed below.

Screening (at any time in the 4 days before treatment) and baseline (the 1st day of treatment before your first dose of study drug) and then on days 3, 5, 8, 11, 15, 22 and 29.

Blood samples: Blood samples will also be taken to monitor your progress and to check for any side effects.

- **Treatment group only (PK):** If you have been randomised to the treatment group you will be giving some additional samples so that we can assess the level of the drug in your body over time. This is called pharmacokinetics (PK).

  At day 1 and day 5, collected pre-dose, 0.5hours, 1hour, 2hours, 4 hours post dose. (5 samples per day)

Each blood sample at these time points will be 2ml which is approximately less than 1 teaspoon.

Two additional swabs will also be taken from your nose at these time points. We will also collect saliva samples and tear samples.

All PK samples (blood, saliva, tears and swabs) will be labelled using a patient Identifier, not your name. The samples will be processed and stored securely before sending onto the central laboratories.

- **Treatment and control group:** In addition to the routine and safety blood samples (listed above) there will also be additional blood samples taken to assess how well the drug is working to stop the virus. We would also like to look at the virus. This is called pharmacodynamics. At clinic visits when we are taking the safety blood sample we will take and additional blood sample which will be 5 mL and is approximately 1 teaspoon.

  All pharmacodynamic blood samples will be labelled using a patient Identifier, not your name. The samples will be processed and stored securely before sending onto the central laboratories.

You will be asked to give your consent to the storage of your samples (blood, saliva, tears and swabs) for use in future ethically approved research studies. Neither you nor your relatives will be contacted about them once they have been taken. Some of your samples may be sent for testing outside of the UK and the European Economic Area.

18) Will my taking part in the study be kept confidential?

Yes. If you decide to take part in the AGILE trial, any data collected and any results produced will not identify you personally. Your medical records will only be available to the research doctors, your hospital consultant, individuals from the Study Sponsor organisation, Southampton Clinical Trials Unit, regulatory authorities, authorised individuals from Ridgeback Biotherapeutics (the USA based company who manufacture and supply EIDD-2801) and NHS Trust.

The electronic copy of your consent form will be held on servers located in the USA. Access to this data will be strictly controlled by Southampton Clinical Trials Unit (SCTU) and applicable Data Protection Legislation will be abided by.

When you join the study you will be assigned a study number by Southampton Clinical Trials Unit, which will be used instead of your name and will be linked to all of your study data. This is called 'pseudonymised data' and you cannot be directly identified from this. Pseudo-anonymised data will be held on servers located in the EU and USA but access to this data will be strictly controlled by Southampton Clinical Trials Unit and all applicable current data protection regulations will be abided by.

University of Liverpool is the sponsor for this study based in the United Kingdom. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. University of Liverpool will keep identifiable information about you for 30 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information at
https://www.southampton.ac.uk/ctu/about/index.page

Liverpool University Hospitals NHS Foundation Trust will collect information from you and your medical records for this research study in accordance with our instructions.

Liverpool University Hospitals NHS Foundation Trust will use your name, NHS number and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from University of Liverpool, Southampton Clinical Trials Unit (SCTU) and regulatory organisations may look at your medical and research records to check the accuracy of the research study. Liverpool University Hospitals NHS Foundation Trust will pass these details to UHS and SCTU along with the information collected from you and your medical records. The only people in UHS and SCTU who will have access to information that identifies you will be people who need to audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

Liverpool University Hospitals NHS Foundation Trust will keep identifiable information about you from this study for 30 years after the study has finished.

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

Your information could be used for research in any aspect of health or care, and could be combined with information about you from other sources held by researchers, the NHS or government.

Where this information could identify you, the information will be held securely with strict arrangements about who can access the information. The information will only be used for the purpose of health and care research, or to contact you about future opportunities to

participate in research. It will not be used to make decisions about future services available to you, such as insurance.

Where there is a risk that you can be identified your data will only be used in research that has been independently reviewed by an ethics committee.

Anonymised information collected during the study may be transferred within or outside of the European Economic Area and Southampton Clinical Trials Unit is responsible for ensuring compliance with current Data Protection Regulations and protection of your privacy. At any time in the future, authorised people may look at the data which will be anonymised so your identity will not be known to them.

With your permission, we will tell your General Practitioner (GP) that you are taking part in the AGILE trial.

In the long term we would like to access your follow up details through information managed by NHS Digital (formerly known as the Health and Social Care Information Centre), so that we can obtain information on your clinical outcome in the event that you lose touch with your hospital trial doctor. With your consent, we will collect and share your name (and previous names), postcode, NHS number and date of birth with NHS Digital. The information we share will be used by NHS Digital and other central UK NHS bodies in order to provide us with information about your health status. We will keep it separately from the other information/data we collect as a result of this trial. Southampton Clinical Trials Unit complies with current Data Protection Regulations to hold such information on a confidential basis. Your data will be sent outside the UK where the data protection is different and may vary to the UK.

19) Are there any financial costs or payments?

You will be reimbursed £30.00 per visit for your time. Please discuss any necessary travel arrangements with the study team prior to the visit.

20) What will happen to the results of the research study?

When the study ends, the results will be analysed and presented at national/international meetings before being published in a medical journal. The confidentiality of all patients will be maintained. You will not be personally identified in any reports or publications resulting from the study. If you would like to obtain a copy of the published results, please ask your doctor.

21) Who is organising and funding this research?

This study is being coordinated by Southampton Clinical Trials Unit.

The study is funded by the Department of Health, the National Institute for Health Research and Ridgeback Biotherapeutics (the USA based company who manufacture and supply EIDD-2801).

None of the doctors or other staff conducting the research are being paid directly for recruiting patients into the study.

22) Who has reviewed this study?

This study has been reviewed by number of medical specialists during its development and approved by the Research and Development Department and the West Midlands - Edgbaston Research Ethics Committee to confirm that this study considered the patients' rights and protection of patients' health.

23) Contact for further information

If you have further questions about your illness or clinical studies, please discuss them with your doctor.

If during the course of the study you have any questions regarding your participation or would like further study specific information before making your decision please contact:

Doctor:
Name: Dr Richard Fitzgerald
Telephone Number: 0151 706 4860 or 0755455648

Research Nurse:
Name: Becky Lyon
Telephone number: 0151 706 4860

Patients Advisory Liaison Service (PALS) contact details: 0151 706 4903/4908/4909

If you find the wording difficult to understand or would like us to explain things to you once more, please feel free to ask your doctor or nurse.

Thank you for taking the time to read this information sheet. If you wish to take part you will be given a copy of this information sheet and a signed consent form to keep.

	Screening (up to 4 days prior to randomisation)	**Treatment** (to commence on day of randomisation)	**Baseline (Day of randomisation) Day 1**	**Day 3**	**Day 5**	**Day 8 (±1 days)**	**Day 11 (±1 days)**	**Day 15 (±1 days)**	**Day 22 (±1 days)**	**Day 29 (±2 days)**	**Daily if in hospital**
Informed consent	X	Initial dose to be given in clinic. Treatment for dose 2 onwards to be provided for patient to take home. Dose on day 5 to be given in clinic.									
Telephone Contact				Daily apart from in clinic days							X[1]
Nose and Throat swabs	X		X	X	X	X	X	X	X	X	
ECG	X										
Blood tests (Routine)	X		X		X		X	X	X	X	If required for normal standard of care
Urine sample			x								
Pregnancy test (if required)	X									X	
Questionnaire to ask about symptoms			X	X	X	X	X	X	X	X	
Physical examination	X			X	X	X	X	X	X	X	
Randomisation			X								
Assessment of side effects	X (from consent)		X	X	X	X	X	X	X	X	
Chest X-ray/other imaging	If required for normal standard of care			If required for normal standard of care							
Additional PK samples (blood, swabs, tears, saliva) [2]			X		X						
PD samples (blood)	X		X		X		X	X		X	
Drug dispensed[3]			X		X						
Drug returns to clinic[3]				X	X	X					

1 If hospitalised, a daily call wherever possible to the hospital to obtain data.
2 PK sampling time points for Day 1 and 5: Predose (0), 0.5 h, 1 h, 2 h, 4 h post dose
3 Not applicable to patients allocated Standard of care arm in phase I trial.