INFORMATION for POTENTIAL PARTICIPANTS

Name of Study:	A Multicenter, Single-Treatment Study to Assess the Safety and Tolerability of Lyophilized Lucinactant in Adults with COVID-19 Associated Acute Lung Injury
Study Number:	02-CL-2001a
Study Sponsor:	Windtree Therapeutics, Inc. 2600 Kelly Road, Suite 100 Warrington, PA 18976 USA
Study Doctor (Investigator):	[Investigator Name] [Site Address] [Office Hours Tel] [Out of Hours Tel]
Institutional Review Board or Ethics Committee	[IRB/EC Name] [IRB/EC Address] [Office Hours Tel] [Out of Hours Tel]

Why are you receiving this information?

You are being asked to consider whether you (or the person you represent) would like to participate in a clinical research study. The following information describes the study and your role as a possible volunteer. You have the right to know all the details about this research. When you understand these details, including all the possible risks, hazards, or benefits, you may then decide whether you (or the person you represent) would like to participate in this study. Please read this information carefully and do not hesitate to ask the study doctor any questions you may have about the study.

You or the person you represent have been asked to take part because you have been diagnosed with COVID-19 associated acute lung injury and are being cared for in a critical care unit in the hospital.

What is the purpose of this clinical research study?

The coronavirus that was first detected in China in 2019 and which has been detected in over 190 countries on every continent, has infected over 150 million people worldwide (including approximately 3 million deaths), including approximately 35 million in the United States (including

over 600,000 deaths). The virus has been named "SARS-CoV-2" and the disease it causes has been named "coronavirus disease 2019" (abbreviated "COVID-19").

This virus is part of a large family of viruses that are common in people and many different types of animals, including camels, cattle, cats, and bats. Rarely, animal coronaviruses can infect people and then spread between people such as with MERS-CoV or SARS-CoV, and now with this new virus.

While the information we have so far indicates that most COVID-19 illness is mild, early experience suggests serious illness occurs in approximately 16% of people infected with the coronavirus. This study includes patients who are seriously ill with COVID-19.

Surfactant is a naturally occurring substance in the lungs. It works to keep the air sacs in the lung open and to decrease the amount of work required to breathe. Surfactant can be damaged or stop working by infection and inflammation. This can make breathing difficult and decrease the ability of the lungs to get oxygen to the body. In COVID-19, the cells in the lungs that make surfactant are affected by the virus and this may limit their ability to make surfactant.

Lucinactant is a man-made surfactant that has been tested in many studies and is approved by the United States Food and Drug Administration (FDA) for the prevention of respiratory distress syndrome in premature infants at high risk for RDS (NDA 021746). Preliminary data from animal and adult human studies indicate that lucinactant could potentially benefit those with a type of lung injury known as acute respiratory distress syndrome (ARDS). It would do this by improving oxygen levels in the blood and lessening lung damage. Also, lucinactant could possibly lead to less time needed on the breathing machine (mechanical ventilation).

Many studies have found that damage to surfactant and too little surfactant contribute to the development of ARDS. Several studies in adult ARDS have shown that lucinactant can be safely given to critically ill patients and may refill the surfactant pool. A study among patients with ARDS caused by a direct lung injury, such as pneumonia, found that those who received surfactant may have a higher survival rate than those who received standard therapy. In fact, more oxygen in the blood was found across the entire population of patients who received surfactant. Some side effects were observed in these studies, which are described in detail later in this document.

Lucinactant has been safely administered to over 1000 patients for different diseases. In almost all cases, there were no safety signals of concern with rates of side effects being similar to control groups (placebo and active).

The purpose of this study is to evaluate the safety and tolerability of lucinactant in patients with COVID-19 and who are on a breathing machine being treated in a critical care unit in a hospital.

What makes this different from the usual treatment?

Lung surfactant is affected by conditions in the inflamed lung in a way that could lead to the surfactant being inactivated or destroyed. Since some of the major breathing consequences of ARDS may be directly impacted by the lack of surfactant, treatment with lucinactant is potentially effective in treating ARDS. Additionally, lucinactant has been shown to be more resistant to inflammation and to reduce the inflammatory response in lab tests of lung injury when compared to animal-derived surfactants. These lab results indicate that lucinactant treatment may result in reduced inflammation-related lung damage

How long will I be in the trial?

The duration of the study treatment will be approximately 1-2 days. Health information will be collected while in the hospital or until you or the person you represent have been in the study for 30 days (whichever is sooner). If the hospital discharge is before the 30th day of the study, you may be contacted by someone at the hospital to enquire about your health at that time.

What are the treatments and how are they assigned?

If you or the person you represent meet the requirements for the study and you provide consent, you or the person you represent will be enrolled at the site. All patients will be receiving the investigational medicine in this study; there is no control or placebo.

- Up to 30 patients will be administered lyophilized lucinactant (160 ml [~80 mg/kg lean body weight]), reconstituted with sterile water and delivered as a liquid in 4 equal parts into the airways

If you continue to have trouble breathing after receiving lucinactant, you may receive additional doses of lucinactant. You can receive up to 3 additional doses no sooner than 6 hours apart from completion of previous dose.

What if I decide to participate or allow participation?

If you decide to participate or allow participation in this study, you will be required to sign this Informed Consent Form. The medical records and medical history will be reviewed to ensure that you or the person you represent are a good candidate for the study.

A physical exam will be done to see if you qualify to be in the study. In order to be considered for this study, you or the person you represent must be supported by mechanical ventilation for no longer than 7 days.

The following procedures will be conducted for those who qualify:

1) Participants will receive lucinactant, a surfactant, as a liquid into the airways.
2) Before, during, and after each treatment of study drug, vital signs, oxygen and carbon dioxide levels in your blood and breathing machine settings will be checked and documented. These assessments are part of the routine hospital care.
3) Vital signs will be documented every 12 hours for 5 days.
4) The last day of the study is 30 days after study entry . Oxygen and carbon dioxide levels in your blood will be checked at this time.

What will happen at the end of the study?

At the end of the study (30 days after enrollment or sooner if you decide to withdraw from the study), final measurements and information about your health will be collected.

What are the potential risks and discomforts?

People suffering from COVID-19 are at risk of complications, including death. The degree of risk is different for each person and depends on many factors. People who have COVID-19 may require placing a tube in their windpipe and connecting that tube to a breathing machine. These risks are present whether you participate in this study or not. Your doctor or the study doctor can talk to you about these risks.

Lyophilized lucinactant is an investigational drug that is being tested in humans. This means there may be unknown risks to you. It also means it is not known whether this drug will be of any benefit to you or make your problem worse.

In previous studies, lucinactant, given as a liquid into a tube in the windpipe, was found to be generally safe; however, it should be noted that in one study with lucinactant, the rates of dying were 21% and 14% in the lucinactant-treated patients and the untreated group, respectively. The majority of deaths were due to non-respiratory causes and the overall rate of dying for the untreated patients was on the lower end of anticipated number of deaths for ARDS trials at that time.

Previous research has shown that when lucinactant is delivered as a liquid through a tube in the windpipe, side effects may include: a decrease in the oxygen level in the blood for a short period of time, apnea (stopping breathing for a few seconds), a slowing of the heart, and regurgitation, which might occur when the drug first goes into the large airways of the lung. In a study of lucinactant for ARDS in adults, 45% of those who received lucinactant reported a treatment-related adverse event, and 40% of the patients experienced a serious adverse event related to treatment. The most commonly reported side effects were anemia, airway obstruction, pneumothorax (air in the chest cavity), hypotension (low blood pressure), and decreased oxygen saturation. Pneumothorax was identified as a significant side effect and was observed in a total of 22% patients receiving lucinactant and 14% patients receiving standard care. The number of pneumothoraces seen was similar to the number usually seen in ARDS patients.

Overall, side effects for the lucinactant treated patients were not significantly different to the comparison group (standard of care), and, in general, the procedure was considered safe and well tolerated given the severity of illness. Although there were short episodes of low oxygen levels, low blood pressure and a need to adjust breathing machine during the treatment delivery procedure, most subjects completed the procedure. However; if these events or others happen during this study, may require your doctor and/or the study doctor to stop giving the study drug. Treatment may be stopped at any time if it is in your best interest.

One important feature of this study, and a significant difference with the current study, is the dosing procedure. The early lucinactant study used a technique known as bronchopulmonary segmental lavage. This procedure carries some risk in intubated patients. Additionally, the procedure takes time to perform. The degree to which this dosing procedure contributed to the results of the study, if at all, cannot be determined and will be avoided in future investigations. Regardless, the same procedure will not be used in this study and lucinactant will be given as a liquid in the airway.

You will be closely watched by your doctor and health care staff during the study. From the time of starting the study to the end of the study, all of those enrolled will be monitored for all possible side effects, and especially for signs that the breathing problem is getting worse. An independent safety committee (also known as a Data Monitoring Committee or Data Safety Monitoring Board) will also oversee this study safety. This committee, comprised of doctors who are specialists in this field and those experienced in clinical study safety, are not employed by Windtree Therapeutics, Inc. (the Sponsor). This committee will advise the Sponsor about the safety of study subjects and will also evaluate the ongoing scientific strength of the study.

What are the advantages and disadvantages of participation in the study?

As with any investigational product, there is no guarantee this treatment will help anyone participating in the study. New information about the benefits and safety of lucinactant will be obtained from your participation in this study. This new information may benefit others in the future if lucinactant is shown to be safe and effective for those suffering from COVID-19 who require mechanical ventilation.

Are there any alternative treatments?

If you do not wish to take part in this research, you will be provided with the established standard treatment available at this hospital, which may include drugs like remdesivir or steroids. In addition, there are new therapies being studied for those suffering from COVID-19 including antivirals and vaccines.

Will you be informed if new information becomes available during the study?

The study doctor will inform you in a timely manner of any new information learned during the study that may affect your willingness to continue your participation.

Who can you contact with further questions?

You may ask questions about this consent form or the study at any time (before or during the course of the study). If you have additional questions, or if you experience a research-related injury, contact the study doctor using the details provided in the table on the first page of this informed consent.

If you have a complaint or question about your rights as a research subject, you may contact the institutional review board using the details provided in the table on the first page of this informed consent. This is a group of scientific and non-scientific individuals who review research studies with the safety and welfare of research subjects in mind.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by US Law, and the International Clinical Trial Registrations Platform. These websites will not include information that can identify you. At most, the websites will include a summary of the results. You can search these websites at any time. These websites only show data in English, but you can request information from the study staff at any time and have access to data that are publicly available.

What happens if you change your mind?

Participation in this study is voluntary. You or the person you represent do not have to take part, and you may discontinue your participation at any time. There will be no penalty or loss of benefits to which you are otherwise entitled or affect your treatment or your rights at this center in any way. If you enroll in this study and then later withdraw from this study, any information obtained while in the study may be used to evaluate the safety and tolerability of lucinactant.

If you decide to stop study before you have completed the study, tell the study doctor and follow their instructions. It may be helpful if you could explain your reasons. You may also be asked to allow end of study procedures (such as a final medical examination and laboratory tests) to be completed, for safety.

In addition, the study doctor or the Sponsor may withdraw you from the study for his or her own safety, even if you wish to continue to participate. Reasons that the Sponsor may withdraw you from the study include:

- If you need additional medication
- If you experience a study-related injury
- If you or the study site do not follow the study rules

Are there any costs if I decide to participate?

Study drugs will be made available to you at no charge and you will not be required to pay for any study procedures. You or your insurance company may be billed for any standard medical care that is not required for the research study.

Is there a payment if I decide to participate?

You will not receive payment for participating in this study, but the study drugs will be made available to you at no charge and you will not be required to pay for any study procedures.

Will I receive compensation if I become injured because of the study?

If you are injured because of your participation in this study, treatment for the injury will be made available through [name of physician] and [institution]. Windtree Therapeutics, Inc. will pay the costs of this treatment not paid by your medical insurance. No other payment is available from the Sponsor or the study doctor in the event of injury. You are not waiving any legal rights by signing this form, accepting medical care, or accepting payment for medical expenses.

Will the personnel involved in the study receive any payment?

The [institution] receives payment from Windtree Therapeutics, Inc., who is the Sponsor of this study for study-related activities.

What will happen to my data?

- For sites located in California, the HIPAA authorization must be separate from the ICF (at the end of the ICF document) with a separate signature and 14-point font under California's medical privacy laws.

This research study may be performed only by collecting and using your medical information. Your study records will be kept as confidential as possible. Only a number will be used to identify you and you will not be identified in any reports or publications that may result from this research study. Under data protection laws (the Health Insurance Portability and Accountability Act in the US or Law 25326 in Argentina) your study site shall be responsible for ensuring that your personal information is safeguarded.

Because of the research goals of this study, however, your study records cannot be kept completely confidential. The study personnel, the Sponsor, and its agents will need to review the medical information collected from you for use in this study to accurately record information for this study. In addition, to review the study findings, personnel from ethics committees, the US FDA, or ANMAT may review your medical records. The following sections provide a specific description of how your information will be used and disclosed if you consent to participate in this research study. By signing this consent form, you are authorizing such access. If you do not sign this form to authorize access, you will not be able to participate in this study.

The medical information that will be collected from you if you participate in the study includes:

- Information obtained from procedures to determine your eligibility to participate in the study, including a routine medical history, physical exam, and blood and breathing tests.
- Information that is created or collected from you during your participation in the study, including the results of the tests included in the previous bullet point and any other procedures performed during the study.
- Information contained in your medical records about to your medical history and treatment.

The above information may identify you by name, address, telephone number, social security number, health plan number, study number, date of birth, dates relating to various medical procedures, and/or other identifying information.

If you sign this form to participate in the study, the study personnel will be authorized to use the information described above to carry out the purposes of the research study. The study personnel will also be authorized to disclose the relevant information described above to the following parties involved in the research study:

- The Sponsor or other agents designated by the Sponsor to collect or review study data for verification of study procedures and/or adverse event reporting.
- The Institutional Review Board (IRB)/Ethics Committee (EC) that oversees the research study at your site.
- Government regulatory agencies including the FDA.

Once your information is disclosed to the Sponsor, its agents, the IRB/EC, or government agencies as described above, there is a potential that your medical information will be re-disclosed and will no longer be protected by U.S. federal privacy regulations.

The study data may be transferred to other countries for processing, including countries not covered by data protection legislation. The laws of your state may provide further protection.

While the study is in progress, your access to your study records will be temporarily suspended. You will be able to access your information when the research study is completed. You have the right to see and copy the medical information collected from you during the study for as long as that information is maintained by the study personnel and other entities subject to federal privacy regulation.

- Edit the expiration date in the 2nd sentence of this paragraph if a specific date of expiration is required by state law (e.g., CA, MN, IL)

Study data, including your coded medical information, may be used and shared for research purposes related to this study. This consent has no expiration date. In signing this form, you allow the use and disclosure of your information for purposes of the study at any time in the future.

Will I be photographed or filmed?

Your treatment may be filmed for review of treatment procedures (to ensure proper procedures are followed) and possibly for training purposes. Your identity will be obscured by putting a light cloth over a portion of your face while the filming is occurring. If you sign this document, you give permission to [site name] and affiliates to film your treatment and to transmit this video to the

sponsor. Not agreeing to the use of Photography/Videography does not affect your ability to be included in the study.

You have a right to revoke my consent to be photographed, recorded, or to have other images taken in writing at any time.

You may request cessation of photography, video or other imaging during the recording process. If you wish to revoke this consent, it will apply to the use of my images in the future but will not apply to previously made publications or presentations. Photographs, videos, or other images will be maintained in a protected and secure manner as part of your confidential research record.

_____ (***Participant Initials)*** **I will allow photographs, recordings, or other images taken of me.**

_____ (***Participant Initials)*** **I do not want photographs, videotaped images, or other images taken of me.**

Withdrawal of Consent:

You may withdraw your consent at any time by sending a written request to [insert name of responsible study personnel] at [insert address]. If you withdraw your consent, data collected prior to your withdrawal may still be processed along with other data collected as part of the study. Normally, no new information will be collected for the study database unless you specifically authorize that. However, the law does require that any side effects you may have suffered are documented and reported. To complete the study findings, your long-term health status may also be obtained from public sources.

Statement of Consent

- I have read and understand the statements in this informed consent form.
- I have had the opportunity to ask questions and I am satisfied with the explanations provided.
- I voluntarily agree to take part in this study or agree on behalf of the patient as the legally authorized representative.
- I understand that I and/or my legal representative will receive a copy of this signed and dated written consent form.
- I additionally consent, or agree on behalf of the patient, to the use of my coded medical information for future medical or drug company research.

_____	_____	_____
Subject/Legal Representative Name	Signature	Date

_____	_____	_____
Witness (if applicable) Name	Signature	Date

- I have presented the study and answered the subject's questions.
- I will give the subject and/or legal representative a copy of this signed and dated informed consent.

_____	_____	_____
Presenter (Investigator/Delegate)	Signature	Date