20.0 APPENDIX A: SAMPLE INFORMED CONSENT

(Final version to follow institutional standards)

Patient Initials ____ ____ ____

Date ___ / ___ / ___

AUTHORIZATION TO PARTICIPATE IN A RESEARCH PROJECT

TITLE OF STUDY:

A Phase 1/2A Study of the Safety and Efficacy of Modified Stromal Cells (SB623) in Patients with Stable Ischemic Stroke

SPONSOR: SanBio, Inc.
231 S. Whisman Rd.
Mountain View, CA 94041

PROTOCOL NO.: SB-STR01

INVESTIGATOR:

TELEPHONE:

STUDY SITE LOCATION:

INTRODUCTION:

You are being invited to take part in a research study that will last approximately 24 months for you. Approximately 18 patients will participate in this study. It is important that you read and understand several general principles that apply to all study participants:

1. Taking part in the study is entirely voluntary
2. You do not have to be in any research study offered to you by your doctor. When you are deciding if you should join the study, you may want to talk with someone not part of the study about your questions and feelings about joining. This could be a family member, friend, or another health provider
3. Personal benefit to you (improvement in your stroke symptoms) may or may not result from taking part in the study. Knowledge will be gained from your participation that may benefit other patients.
4. You may withdraw from the study at any time without penalty or loss of any benefits to which you are otherwise entitled.

The nature of the study, the benefits, risks, discomforts and other information about the study are discussed below. There may be information in this consent form that you do not understand. Any questions you have should be discussed with the staff members. They will explain it to you.

NOTE: If you are not completely truthful with your study doctor regarding your health history, you may harm yourself by participating in this study.

THE NATURE AND PURPOSE OF THIS STUDY:

You have been diagnosed with stable ischemic stroke, and have had physical therapy for your stroke-related conditions. Your stroke was caused by a blood clot in a blood vessel in your brain and this happened at least 6 months ago, but not more than 60 months ago. This study is being conducted primarily to determine the safety of a cell suspension of SB623 cells administered by injection into your brain around the area of the stroke. In addition, information will be obtained to determine if there might be any improvement in the severity of your stroke. All the usual standard of care procedures and drugs will also be used.

SB623 cells are modified cells derived from bone marrow of other adult humans. From the bone marrow, cells are isolated and then modified using recombinant DNA methods to make cells that have been shown to secrete agents that may be helpful to dying tissue. The product that you will be using is an investigational drug (not approved by any governmental regulatory authorities).

EXPLANATION OF PROCEDURES TO BE FOLLOWED:

After you sign the consent form and before you begin treatment, you will be asked questions about your medical history, medications you are taking, and how you feel. You will also have a complete physical examination. The doctor will check your pulse, blood pressure, respiratory rate and temperature.

Approximately 25 mL (a little less than one ounce or two tablespoons) of blood will be drawn and a urine sample will be requested for monitoring your health status and to confirm that you are eligible to participate in the study. If you are a woman capable of bearing a child, the blood sample will also be used for a pregnancy test.

You will be evaluated for your stroke symptoms by a variety of methods, such as asking you questions and requesting you to make certain movements while you are being videotaped. This will be done twice prior to implantation of the SB623 cells, over a three week period. This is to confirm that your stroke symptoms are stable.

You will also be asked to undergo magnetic resonance imaging (MRI) of your head at your first screening visit. The purpose of the MRI is to determine the precise location and size of your stroke and to ensure there are no other abnormalities. MRI machines only use a magnetic field. In addition, the PET scan will require that you be injected with an agent that contains a radioactive tag so that the wellness of the cells in and around your stroke area can be evaluated.

Surgical Procedure and Administration of the Cells:

The SB623 cells are to be implanted directly into your brain in and around the area of the stroke. To do this, you will have a small hole drilled into your skull. This will be done under local anesthesia. The exact position of the hole to be made will be determined by having you undergo MRI scanning. MRI (Magnetic Resonance Imaging) is a special procedure using an instrument with a very strong magnet. A special apparatus will be used on your head to make sure the hole is positioned such that the implantation of the cells will be precisely into the stroke region, at location also determined by MRI. A needle will be inserted through the hole into your brain extending into and slightly beyond the main stroke region. Cells will be implanted at 5 sites through this one needle injection. Two additional needle insertions with 5 more implantation sites each will also be done at slightly different angles.

There will be 3 groups of patients enrolled in this study. Your assignment to a particular group by the study doctor will depend on when you enter the study. Six patients will be studied in group 1 before proceeding to 6 patients in group 2, who in turn will be studied before proceeding to 6 patients in group 3. The total amount of cells you will receive will depend on which group you are in. Group 1 patients will receive 2.5 million cells; group 2 patients will receive 5 million cells; and group 3 patients will receive 10 million cells. All patients will receive a total of 300 µL of fluid (about $1/3^{rd}$ of mL, or less than $1/10^{th}$ of a teaspoon or about 6 drops from a standard dropper).

Study Procedures:

You will be asked to provide blood samples throughout the study in addition to any samples required for your normal care. Approximately 25 mL (a little less than one ounce or two tablespoons) of blood will be drawn at total of 11 times, including the screening and baseline samples. These will be used to monitor safety and to assess certain markers related to the cells.

After completion of the surgical and cell injection procedures, you will be given CT scan (a type of imaging procedure using a contrast agent and X-rays) to determine that you have no complications, and then will be admitted to a neurosurgical patient ward for 24 hour observation. You will be discharged on the first post-operative day.

Periodically, you will also receive a PET scan. PET stands for Positron Emission Tomography. In this procedure, a marker similar to glucose (a sugar) containing an atom that emits radiation (positron) will be injected into your blood stream. A machine that measures this radiation will determine if your brain cells are behaving in the usual manner in absorbing the glucose marker.

You will be asked to periodically undergo additional MRI scans to assess your progress and to evaluate safety. You will also be asked standardized questions about your stroke symptoms and be asked to make certain movements as you did during your screening.

REQUEST FOR AUTOPSY:

In the event of your death during the study from any cause, the study doctor will ask your family for permission to perform an autopsy. The evaluation of organs and tissues after death is a very valuable method to learn more about any effects of the study agent. You should talk about the possibility of an autopsy with your family and health provider, and advise them of your wishes. The study sponsor will pay all costs of the autopsy.

POSSIBLE RISKS AND DISCOMFORTS:

This is the first time that SB623 cells have been administered to people, so possible side effects are not known, except that mild, post-surgical headache that resolved within 1 week has been reported by all 6 of the first cohort of subjects.. It has been administered to animals (rats and monkeys) with no negative cell-related effects observed. Since the cells did not survive longer than 3 months in rats, possible later cell effects could not be determined.

Studies with SB623 cells to determine its capability to cause harm to an unborn child have not been performed. Therefore, if you are pregnant, or think you might be, you will not be allowed to participate in this study. If you are a woman of childbearing potential, you will be tested for pregnancy at the beginning of the study.

Because you will be receiving a CT scan, you will be exposed to a low level of radiation. The risks of the contrast material used with the CT scan include rare allergic reactions, nausea, flushing, low blood pressure, asthma, stroke and organ damage. The PET scans will also expose you to a low level of radiation from the injected radioactive agent (FDG).

Although animal studies up to 12 months have shown no evidence of any tumor formation, there is the theoretical possibility that SB623 may induce formation of tumors, as has been seen with embryonic stem cells. While this is believed to be very unlikely to occur with SB623, periodic MRI measurements will be carried out to provide an early indication if this should happen.

All of the animal safety studies have used animal models that were highly immunosuppressed to uncover any possible tumor formation. However, you will not be given any immunosuppressant during this study since other studies have suggested that SB623 is itself an immunosuppressant. Nevertheless, there is a possibility that implantation of SB623 could cause local inflammation or a systemic immune response. This will be monitored carefully during the study by making measurements of your blood that include standard laboratory tests and by periodic MRI scans as indicated earlier.

The surgical procedure that you will receive has been associated with a small risk of bleeding and infection. This was documented by studying the records of over 2,650 patients who had undergone this surgical procedure over a period of 28 years. Headaches are a normal and expected symptom following surgery for cell implantation, as is mild pain at the site of the incision. These symptoms may last for several days following your operation. So far, this study has demonstrated a small risk of a special bleeding problem, so-called subacute subdural hematoma, which is a bleed deep in the brain where the needle was inserted. Should this occur, it will be managed by the current standard of care, which may necessitate another surgical procedure to remove the blood. There may also be a small amount of cerebral spinal fluid associated with this, which may also require surgical removal. One subject has also had seizure that was readily treated. This was categorized as possibly related to the surgery, and unrelated to the Study Drug.

Significant new information that becomes known during the course of the research that may affect your willingness to continue participation in the study will be provided to you.

If you experience more than minimal discomfort after completing the implantation procedure, you should:

1. **Call the study doctor at once at telephone number: (xxx) xxx-xxxx**
2. **If necessary, go to the nearest emergency room**

During this study, you will receive the standard care for your condition (including antibiotics, pain medicine, cardiovascular support, ventilator support, and hospitalization) as required.

PREGNANCY/ BIRTH CONTROL:

If you are pregnant or nursing a child, you cannot take part in this study since there is no known information about potential harm to unborn children. If you are a woman who has had a tubal ligation, hysterectomy, or are post-menopausal, you may be eligible to take part in this study. If you are a woman of child-bearing potential you must practice acceptable methods of birth control (oral, implantable, or injectable contraceptives; spermicide in conjunction with a barrier such as a condom or diaphragm; intrauterine device or IUD) for at least the first 6 months of the study.

ALTERNATIVES TO PARTICIPATION:

There are no approved therapies for your stroke-related condition. The study doctor has discussed any other options available to you, including non-participation in this study. If you decide not to take part in this study, it will not affect your future treatment.

POSSIBLE BENEFITS:

Although it is hoped that participation in this trial may lead to some improvement in your condition, the primary goal of this study is to establish safety of the approach rather than to maximize the chance for improvement. Accordingly, you should not expect to receive benefit from participation in this study. However, the knowledge obtained from this research may help the health care professionals caring for you to better treat other patients undergoing treatment for a condition similar to yours.

COMPENSATION FOR PARTICIPATION:

There is **no additional cost** to you for participation in this research study beyond the costs normally associated with your treatment. The SB623 cells will be provided free of charge to you by the Sponsor. The physician visits and associated tests related to the study will also be provided at no cost. You will be reimbursed any out-of-pocket expenses relating to participation in this research study.

MEDICAL CARE FOR INJURY RELATED TO THIS STUDY:

In the event of injury resulting from your participation in this research, medical care will be provided to you by the study doctor. The care will be free of charge to you. The Sponsor of the Study is insured in the event you are injured through participation in the study.

CONFIDENTIALITY AND RELEASE OF MEDICAL RECORDS:

The study doctor will provide information about your treatment to the Sponsor (SanBio Incorporated) and/or its representative. You have the right to privacy, and all information obtained in this study that can identify you individually will remain confidential to the extent possible within the state and federal laws. Only your patient number and initials will be

recorded on study documents and reports. Your name will **not** be revealed in any reports or publications resulting from this study. Other information, including your gender, age, and ethnicity, will be recorded on study documents for the purposes of analyses of the study outcome. Nothing in the study documents will provide any identification of you. Governmental and institutional regulatory authorities and the Sponsor and/or its designee (the site monitor), may inspect and copy your records pertaining to this study. The results of the study will be reported to governmental agencies.

In the rare instances for which regulatory authorities may require patient names, the regulatory authorities will treat such information as confidential, but disclosure to third parties may be required on rare occasions. Therefore, absolute protection of confidentiality by regulatory authorities cannot be promised or implied.

Because this study involves genetically-modified cells, safety information must be reported to the Recombinant DNA Advisory Committee of the National Institutes of Health. This information is available to the public. However, no information by which participants can be identified will be reported with the safety information. We will try to keep your identity and other information collected in this study confidential. There may be some exceptions when the law requires disclosure. Representatives of [study site], and/or the Food and Drug Administration, and/or the National Institutes of Health, or other regulatory agencies outside [study site] may ask to review the data collected from this study. These groups can have access to your name and medical records.

It is possible that the media may want to find out about you because you took part in this study. We will take every precaution to protect your privacy and that of your family. We will also maintain the confidentiality of the research data. To lower the chance that your identity will be made public, all requests for information will be directed to the [study site] Public Relations Office. Despite these efforts, reporters may try to find out who you are without the approval of the [study site]. If the media succeed, they might ask to interview you and your privacy may be invaded. Every effort will be made to protect your privacy but it may not be possible to do so.

VOLUNTARY PARTICIPATION AND WITHDRAWAL:

Your participation in this study is voluntary and you are free to withdraw at anytime. Any new information developed during this research that may be related to your willingness to continue participation will be provided to you. Participation or withdrawal will involve no penalties or loss of benefits to which you are otherwise entitled, and will not affect your future medical care.

Your participation in this study may be discontinued without your consent for the following reasons:

- if treatment appears to be medically harmful to you
- if you fail to follow directions for participation in the study
- if it is discovered you do not meet the eligibility requirements
- if the study is canceled

If you withdraw from, or must be discontinued from the study prior to its completion, you will be asked to have a final close out visit to protect your health status.

POSSIBLE CONFLICTS OF INTEREST:

The study doctor is a researcher in this study. As a researcher, he is interested not only in our health and well being, but also in the results of this study. It is possible that sometimes these two goals may conflict with one another. Researchers protect the rights and interests of participants by carefully following the rules of the study.

This research is sponsored by SanBio, Inc. This means that SanBio is paying the research team for the costs of doing the study. The researchers do not have a financial stake in the results of the study.

OFFER TO ANSWER QUESTIONS ABOUT THIS STUDY:

If you have questions about this study, your condition and/or treatment, or if you experience a research-related injury or illness, you should contact **Insert Name of PI, MD at: (xxx) xxx-xxxx**

If you have questions about your rights as a research patient, you may contact a representative of the **Ethics Committee for this institution at (xxx) xxx-xxxx.**

CONSENT TO PARTICIPATE IN THIS STUDY:

Your consent to participate in research should be voluntary and informed. By signing this form, you acknowledge that you have read this information (or had it read to you), been given an opportunity to ask questions about the information provided in this form, and understand the potential risks and benefits. By signing this form you indicate that you wish to participate in the study at this time.

Having consented, you still have the right to withdraw at any time without jeopardy to your care. If you wish to withdraw, you should notify the study doctor or study coordinator; you do not have to give a reason if you do not wish to. You will not lose any legal rights as a research patient by signing this form.

You will be given a signed copy of this form to keep and refer to as needed.

Signature of Study Patient	Date
Printed Name of Study Patient	
Signature of Person Explaining Informed Consent	Date
Title of Person Explaining Informed Consent	