

Consent

Date of Issue 6/5/2018

Alzheimer's Prevention Through Exercise (APEX)

ClinicalTrials.gov: NCT02000583

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## CONSENT FORM

Alzheimer's Prevention through Exercise (the APEx study)

Funded by: National Institutes of Health (NIH) and Avid Radiopharmaceuticals

### **Why am I being invited to take part in a research study?**

You are being asked to join a research study examining the role of aerobic exercise in brain health, metabolism and aging. You are being asked to take part in this study because you have enrolled in the Alzheimer's Disease Center (ADC) Registry, where a Florbetapir PET Scan was performed and showed amyloid deposits in your brain. This study involves a one year exercise program. No medication or treatment will be administered. This research study will take place at the University of Kansas Medical Center (KUMC).

### **What should I know about a research study?**

You do not have to participate in this research study, and you may change your mind at any time. Participating in research is different from getting standard medical care. The main purpose of research is to create new knowledge for the benefit of future patients and society in general. Research studies may or may not benefit the people who participate.

This consent form explains what you have to do if you are in the study. It also describes the possible risks and benefits. Please read the form carefully and ask as many questions as you need to, before deciding about this research.

You can ask questions now or anytime during the study. The researchers will tell you if they receive any new information that might cause you to change your mind about participating. You may be asked to sign a new consent form if this occurs.

If you have participated in studies with the ADC previously, we may use information from those studies to determine your eligibility for this study. When appropriate, we may also use data previously collected by the KU ADC as data for this study. Furthermore, data collected by this study may be shared with the KU ADC for future research.

### **Why is this research being done?**

Alzheimer's disease (AD) is a progressive brain disorder which causes memory and thinking problems. In most people with symptoms of Alzheimer's disease, a protein called amyloid beta collects and forms deposits in the brain. The precise role of these deposits in causing Alzheimer's disease continues to be debated but many scientists believe that over time amyloid deposits may cause the death of nerve cells that result in memory and thinking problems. The brain deposits of amyloid appear to occur years, perhaps decades, prior to the first symptoms of memory loss become apparent. Studies are ongoing to define more precisely what it means to have amyloid in the brain but early evidence suggests having amyloid in the brain may increase the risk of developing Alzheimer's disease. On the other hand, it is clear that many individuals with amyloid in the brain never develop memory and thinking problems and other factors such as your genes and lifestyle influence whether you develop the disease.

By doing this study, researchers hope to learn about the possible benefits of exercise in controlling or reducing the amount of amyloid present in the brain, reducing changes in

the brain structure that may lead to AD, and increasing the cognitive ability in individuals that have amyloid deposits and are at risk to develop AD. By using this information, researchers hope to create a possible prevention strategy for individuals who may be at risk to develop AD in the future.

**How long will the research last?**

We expect that you will be in this research study for about 13 months.

**How many people will be studied?**

About 100 people will be in the study.

**What will I be asked to do?**

If you are found to be eligible and decide to participate, your participation will involve clinical evaluations to assess your memory and thinking skills, quality of life, laboratory blood testing, MRI and PET scans of the brain, and physical fitness testing. These evaluations may take up to 30 days to complete. You may be asked to repeat your PET scan if your prior scan was not done in the last 90 days. After you successfully complete these evaluations, you will be randomly assigned (like a flip of a coin) to either an aerobic exercise intervention group or a control group. You will have a 70% chance of being placed in the Aerobic Exercise Group and a 30% chance of being placed in the Control Group.

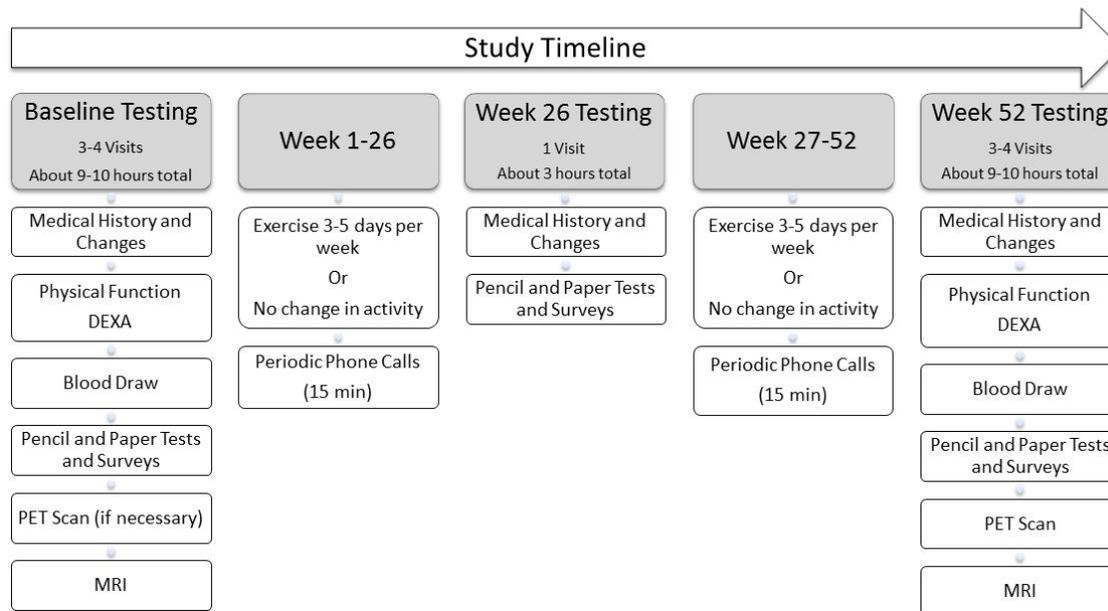
If you are assigned to the exercise group, you will be provided a membership to the local YMCA or another exercise facility that has been approved by the KUMC Institutional Review Board. You will exercise at your exercise facility 3-5 days per week for 52 weeks under the supervision of a certified personal trainer.

If you are assigned to the control group, you will be provided materials on exercise and healthy lifestyle, but you will not be provided support or guidance with an exercise program. At the end of the study, you will be provided with a one-year membership to the YMCA.

Regardless of group assignment, you will be asked to repeat the memory and thinking skills assessment during week 26 of the study and all of the clinical assessments at Week 52 of the study. If you decide to participate you will be asked to sign this consent form and a signed copy will be given to you for your records.

**Evaluations**

Below is a table, followed by a description, of each evaluation and procedure you will be required to complete during the study. All evaluations will be completed on the University of Kansas Medical Center campus. You will be asked to complete evaluations at the beginning, middle and end of the study.



**The following is a description of each test and procedure listed above:**

Medical History and Current Medications: You will be asked about your medical history, such as surgeries, medical illnesses or reactions, or medications and supplements you are taking. Every time you are contacted by study staff you may be asked about changes in your health or the medicines and supplements you take.

Cognitive and Health Assessments: These tests will take approximately 3 hours to complete. You will be asked to perform paper and pencil memory and thinking skills assessments. During these tests you will be asked to remember and repeat things, to answer questions about your daily life and to write down words or draw specific figures.

Fasting Blood Test: This will take about 20 minutes to complete. Approximately 4 tablespoons of blood will be drawn from a vein in your arm for routine laboratory tests. You will be asked to not eat or drink, except water for 8 hours before coming to the clinic for these tests.

Magnetic Resonance Imaging (MRI) of the Brain: The entire MRI will last about 1 hour, and the visit may last up to 2 hours.

During this procedure, you will be asked to lie still in a magnetic resonance imaging machine (MRI) while a picture of your brain is taken. A special ring will be placed around your head to provide better images and your head and shoulders will be placed in a tunnel. The researchers will make you as comfortable as possible with padding and

blankets. As the MRI examination is performed, you will hear loud knocking noises coming from the MRI scanner and you may feel warm. This is all normal for an MRI examination. You will be provided ear protection including earplugs and/or earmuffs.

After pictures of your brain are taken, you may be asked to perform tasks while an MRI scan is performed. The tasks are simple and require watching or responding to images you see on a screen in front of you.

Physical Function and Fitness Level Assessments: These following 3 assessments will be completed in one visit, which will take approximately 2 hours to complete

- Physical Function Tests: You will have several standardized tests to measure your ability to perform physical activities such as rising from a chair, walking, lifting a book, measuring your hand grip strength and climbing up and down stairs. You will be asked questions about your independence in performing activities of daily living such as dressing, washing, feeding and questions about your physical activities.
- Aerobic Fitness Level Assessment: You will also be asked to walk on a treadmill to assess your body's response to exercise. This is similar to a stress test, except you will breathe through a mouthpiece. The mouthpiece is connected by a tube to a computer to measure the air you breathe in and out. Your heart rhythm will be monitored by sensors attached to your chest. Your blood pressure will be assessed every 2 minutes during the test. The tester will start the treadmill slowly and gradually increase the walking speed and slope at two-minute intervals. The test will assess your maximum effort, but you can stop the test at any time. However, minimum criteria must be met to qualify for the study and you may have to repeat the test if you do not meet the minimum criteria.
- Body Composition Assessment: Your body composition will be assessed using a DEXA scan. This scan will determine your current levels of body fat, lean tissue and bone density. You will be asked to lie very still during the scan.

PET Scan: The entire procedure will take approximately 1 ½ to 2 hours to complete.

A PET scan is an imaging technique that produces a three-dimensional image or picture of the body. You had a PET scan as part of the screening for this study. If your PET scan occurred more than 90 days prior to deciding to participate in this study, we will ask you to complete another one as part of your baseline evaluations. During this scan your vitals will be monitored. You will be asked to sit or lie down while a small catheter (plastic tubing with a needle on the end) is inserted into a vein in your arm. Florbetapir, a dye that will attach to amyloid in the brain, will be injected through this catheter.

About 50 minutes after the Florbetapir injection, you will be placed comfortably in the PET scanner. You will stay in the PET scanner for about 20 minutes while pictures are being taken. During this time you will be asked to hold your head as still as possible.

Phone Checks: Periodically, you will be asked in person or by phone whether you have had any changes in your health such as illnesses, injuries or medication changes. You will receive calls from the study staff at week approximately 6, 12, 18, 32, 39, and 46 weeks during your participation in the study. We will also ask you about how well you are keeping with the group you were assigned to: exercise or control.

### **Exercise Group Assignment**

Upon successful completion of baseline evaluations, you will be randomly assigned (like a flip of a coin) to either an aerobic exercise group or a control group. You will have a 70% chance of being placed in the Aerobic Exercise Group and a 30% chance of being placed in the Control Group.

Control Group: If you are assigned to the control group you will be provided educational materials on exercise and healthy lifestyle, but you will not be provided support or guidance with an exercise program.

Exercise Program: If you are assigned to the exercise group you will be asked to exercise 3-5 days per week for 52 weeks at a facility approved by KUMC. You will receive a membership and be supervised by a certified personal trainer. Prior to starting your program, you will be asked to attend an orientation session at your facility which will be conducted by one of the study staff. You will be required to follow the study's exercise program and not do other types of exercise while you are in the study.

Exercise will consist of walking on a treadmill or using other aerobic exercise equipment. During week 1 of the exercise program, you will start performing 60 minutes of exercise per week spread over 3 days. Each exercise session will also include about a 5 minute warm up and a 5 minute cool down. Each week you will gradually increase the duration of each exercise session. By week 6, you will be exercising 150 minutes per week over 4-5 days. How hard you exercise will be increased every 3 months based on your heart rate. You will be issued a heart monitor to wear during your exercise sessions to help you gauge your intensity. You may slow down and stop to rest at any time during your sessions.

A certified personal trainer will directly supervise each of your sessions for the first 6 weeks of the program. During weeks 7 – 52, you will only be required to have direct supervision by the certified personal trainer one time per week, as long as you are tolerating the program without difficulty, and there are no safety concerns. You will make appointments for the supervised sessions directly with the personal trainer assigned to you.

You will have your own exercise log or chart that will stay at your approved exercise facility. You will record your exercise in the log. Your trainer will assist you with this task until you can do it on your own.

In the event that you will not be able to exercise at your facility due to travel plans, family obligations, etc, you will need to continue your exercise regimen on your own. We will

issue you a heart rate monitor that you will wear to monitor and record details of your exercise. These accommodations for exercise outside of the exercise facility should not be made for more than two weeks at a time and for more than 6 weeks total during the study.

### **Testing Results**

It is important you know that all data collected in this study are intended for research and do not necessarily provide the same information that a physician would use for a clinical evaluation. For example, the research MRI scans are generally not adequate for detecting abnormalities and your scan will not be reviewed by the research team or a physician for the presence of clinically relevant abnormalities. In fact, these scans are often not viewed and analyzed by the research team until after your participation is complete.

At the end of the study you will be given copies of your pre and post-exercise physical function and body composition tests. We will give you feedback on these measures because typical performance is well known. We will also give you information on maintaining a healthy diet and regular exercise. Eating right and being physically active over your lifetime are two ways to modify risk factors for developing AD.

### **Is there any way being in this study could be bad for me?**

You may experience one or more of the following risks by being in this study. In addition, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

#### Cognitive and Quality of Life Assessment Risks:

There is a risk of feeling uncomfortable or embarrassed by some of the questions the researchers ask you. If you feel uncomfortable you may skip a question or stop participating all together.

#### Fasting Laboratory Blood Test Risks:

The risks of drawing blood from a vein may include discomfort, bruising, swelling of the vein, soreness, pain, and, rarely, infection, fainting or bleeding. This will be minimized by careful and clean techniques.

#### Magnetic Resonance Imaging (MRI) Risks:

MRI scanning is not generally associated with any health risks. However the MRI uses a magnet to create an image and we are using a closed MRI unit. If you have metal or any foreign object in your body, the MRI magnet may cause it to displace, which can cause bodily injury. To minimize this risk, you will be prescreened by the study team before scheduling the MRI. This is further minimized by careful and thorough screening by the MRI technician.

You may find the narrow space in the closed MRI frightening or uncomfortable, especially if you have known anxiety or claustrophobia (fear of tight spaces). To help lessen this, the MRI unit has a mirror so that you can see outside of the scanner. Also, the MRI unit

makes loud noises during the examination. To minimize any possible discomfort, you will be given earplugs and ear phones to block the noise. You may choose to end the MRI at any time.

If you are anxious about the MRI, claustrophobic, or if you have trouble laying still in the MRI machine, a doctor might prescribe some anti-anxiety medication. This medication might make you drowsy and you may fall asleep during the scan. This will change the types of scans that will be performed. If you receive sedation, blood oxygen will be monitored during the MRI scan for your safety. If you receive sedation, you will need someone to drive you to and home from appointment. You may be drowsy from the anti-anxiety medication for less than 24 hours and you should not perform any duties requiring mental acuity as related to driving, operating machinery or executing any type of legal or binding documents for at least 24 hours.

Physical Function, Fitness Level Assessment and Exercise Program Risks:

Exercise testing is commonly performed on individuals with heart disease and these studies can be used to provide an estimate of the test's risk in healthy older adults. The risk of exercise testing in healthy older adults appears to be low. If you have a recent history (in the past two years) of heart disease (for example, heart attack, arrhythmia, congestive heart failure) you may be excluded from the study. The fitness level assessment is intended to evaluate your maximal exercise ability, so you will be asked to exercise to the point of fatigue. You may experience shortness of breath, dizziness, muscle fatigue, sweating, fatigue, muscle soreness, injury to tendons, ligaments, joints, bone or muscle during the testing. You may experience muscle soreness for up to 3 days after testing. Although rare, with any form of exercise, potential risks of the exercise test include unpredictable changes in blood pressure or heart rhythm, heart attack and death. To minimize potential risks during the exercise assessment, the researchers and a clinician will review your medical history and a resting electrocardiograph (ECG). If you experience heart rhythm or ECG changes during exercise testing, we may ask you to be evaluated by a cardiologist to obtain clearance for exercise. The adhesive patches on your chest, arms, and legs used for ECG monitoring may cause redness, rash, itching, or blisters.

If you have had a stress test in the past, we will ask you to sign a medical release of information form so that we can obtain those records, for our review, prior to testing. If you experience chest discomfort, dizziness or any other problems, the test will be discontinued immediately.

Body Composition (DEXA) Assessment Risks:

You will be exposed to a low level of radiation during the DEXA scan. This radiation exposure is not needed for your medical care. You are exposed to background radiation every day from the sun and the earth. The amount of radiation you receive during a DEXA scan is less than the amount you receive in 2 months from the earth and sun. The risk from this radiation exposure is very low. The DEXA scan machine uses a laser to align to your body. Although the laser is not normally hazardous to eyesight, you will be asked to close your eyes.

PET/CT Scan:

You will be exposed to radiation from a PET/CT scan. This radiation exposure is not needed for your medical care. The amount of radiation you receive during the PET/CT scan is about the same amount that you receive in about 5-6 years from the earth and sun. The risk from this radiation exposure is very low.

Florbetapir will be used during the PET scan and is FDA approved as an imaging agent. The most common side effects seen with the use of Florbetapir are headache, injection site reactions, musculoskeletal pain, nausea, fatigue, back pain, anxiety/claustrophobia, insomnia, hypertension, and neck pain.

Possibility of Unknown Risks

There may be other side effects or risks that are not yet known.

**NEW INFORMATION**

You will be told about anything new that might change your decision to be in this study. You may be asked to sign a new consent form if this occurs.

**Will being in this study help me in any way?**

You may or may not benefit from this study. Researchers hope that the information from this research study may be useful in the prevention and deterrence of AD in the future.

**What other choices to do I have?**

This research project is voluntary. The alternative to this study is to receive your usual care from your clinician.

**Will it cost anything to be in the study?**

Other than the gas, to get to and from your clinical assessments and to your exercise facility, there should be no cost to you for participating in this study. You and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay.

Any other medical visits and procedures you have outside of the study due to other standard of care treatments or other health issues are billable to you or your insurance through normal hospital billing practices. Standard of care means necessary for the care of a medical issue as determined by your doctor and not necessary for this study.

Your insurance may not cover some or all of the standard care services if you are part of a research study. You may want to talk to your insurance company and review your specific benefits and coverage before deciding to participate. You will be responsible for normal co-pays, deductibles and non-covered services that are not the responsibility of the study. Some procedures require Pre-Certification from your insurance company. Pre-Certification is not a guarantee of payment.

You can still be in the study even if your insurance denies coverage for your standard of

care treatment or if you are uninsured. The hospital has a financial assistance program which it makes available to all patients who qualify. If your insurance denies coverage and you do not qualify for the financial assistance, you will be charged for all bills that are not the responsibility of the study. The study staff will be able to provide more information to you.

**Will I get paid to participate in the study?**

If you live more than 10 miles from the exercise facility where you will be going, we will compensate you \$10 for gas expenses per round trip you make to the facility.

You will be given a ClinCard, which works like a debit card. Every 3 months, payment will added onto your card by computer. The money will be available within 1 business day. You can use the ClinCard at an ATM (ATM fees may apply) or at a store. No one at KUMC will know where you spent the money.

You will be given one card during the study. If your card is lost or stolen, please call (866) 952-3795. The KUMC Research Institute will be given your name, address, social security number, and the title of this study to allow them to set you up in the ClinCard system. Study payments are taxable income. A Form 1099 will be sent to you and the Internal Revenue Service if your payments are \$600 or more in a calendar year.

Your personal information will be kept on a secure computer. It will be removed from the computer after the study is over and the money on the card has been used. Your information will not be shared with other businesses. It will be kept completely confidential.

**What happens if I am hurt by the study?**

If you have any problem during the study, you should immediately contact Dr. Burns at 913-588-0555. If the problem is a medical emergency, call 911.

If you think you have been harmed as a result of participating in research at the University of Kansas Medical Center (KUMC), you should contact the Director, Human Research Protection Program, Mail Stop #1032, University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160. Under certain conditions, Kansas state law or the Kansas Tort Claims Act may allow payment to persons who are injured in research at KUMC.

**INSTITUTIONAL DISCLAIMER**

If you think you have been harmed as a result of participating in research at the University of Kansas Medical Center (KUMC), you should contact the Director, Human Research Protection Program, Mail Stop #1032, University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160. Under certain conditions, Kansas state law or the Kansas Tort Claims Act may allow for payment to persons who are injured in research at KUMC.

### **Financial Disclosure**

The investigator and the KUMC Research Institute, Inc. will receive Florbetapir from Avid Radiopharmaceuticals, and will be used for research purposes only.

Dr. Jeffrey Burns (principal investigator) serves as a speaker for Eli Lilly, the company that makes, Florbetapir F18, the imaging agent that detects the amount of amyloid in the brain. Dr. Burns received payment from the company for these activities. Two committees at the University of Kansas Medical Center have independently reviewed this project and they will continue to monitor it. Their goal is to minimize any influence that the financial interests may have on the conduct of the study. However, you should make your own decision about whether these financial interests affect your decision to participate. If you would like more information, please ask the person discussing informed consent with you. If you have additional questions, you may also contact the Office of Compliance at (913) 588-1288 or toll-free 1-877-588-5757 and TDD (913) 588-7963.

### **CONFIDENTIALITY AND PRIVACY AUTHORIZATION**

Study records that identify research participants will be kept confidential as required by law. Researchers cannot guarantee absolute confidentiality. Efforts will be made to keep your personal information confidential. If the results of this study are published or presented in public, information that identifies participants will be removed.

The privacy of health information is protected by a federal law known as the Health Insurance Portability and Accountability Act (HIPAA). By signing this consent form, you are giving permission (“authorization”) for KUMC to use and share health information about you for purposes of this research study. If you decide not to sign the form, you cannot be in this study.

To do this research, the research team needs to collect health information that identifies participants. The information may include items such as name, address, phone, date of birth, or other identifiers. The research team will collect information from study activities described in the Procedures section of this form and information that relate to study participation. By signing this form, you are giving Dr. Burns and the research team permission to share information about you with persons or groups both inside and outside KUMC.

The health information and data collected in this study will be used inside KUMC by Dr. Burns, members of the APEX research team, members of the KU Alzheimer’s Disease Center (KU ADC) research team, collaborating investigators on the KUMC campus who are doing similar work, the KUMC Research Institute and officials at KUMC who oversee research, including members of the KUMC Human Subjects Committee and other committees and offices that review and monitor research studies.

All health information and data collected for this study may be shared with groups outside of KUMC by collaborating investigators doing similar work, the YMCA or your KUMC approved exercise facility, Avid Radiopharmaceuticals, representatives of The National Institutes of Health (the sponsor of the study), and U.S. agencies that oversee human research (if a study audit is performed). These groups or entities may make copies of

study records for audit purposes. The purpose for using and sharing the information is to minimize participant and study staff burden when possible, to make sure the study is done properly, to collaborate with other investigators doing similar work, and to evaluate the safety and effectiveness of this new intervention.

Some of the persons or groups who receive the health information, including the sponsor, may not be required by law to protect it. Once the information has been shared outside of KUMC, it might be disclosed by others and no longer protected by the federal privacy laws or this authorization.

Your permission to use and share your health information will not expire unless you or cancel it. Any research information that is placed in the medical record will be kept indefinitely. However, some research-specific information is kept only by the researcher. Access to all of the research-specific information may not be available until the end of the study.

**Who can I talk to about the study?**

Before you sign this form, Dr. Burns or other members of the study team should answer all your questions. You can talk to the researchers if you have any more questions, suggestions, concerns or complaints after signing this form. If you have any questions about your rights as a research subject, or if you want to talk with someone who is not involved in the study, you may call the Human Subjects Committee at (913) 588-1240. You may also write the Human Subjects Committee at Mail Stop #1032, University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160.

**What happens if I say yes, but I change my mind later?**

You can leave the research study at any time. Your decision to stop will not prevent you from getting treatment or services at KUMC. You will be told about anything new that might change your decision to be in this study. You may be asked to sign a new consent form if this occurs.

You have the right to cancel your permission for researchers to use your health information. If you want to cancel your permission, please write to Dr. Jeffrey Burns. The mailing address is Dr. Jeffrey Burns, University of Kansas Medical Center, 4350 Shawnee Mission Parkway, Fairway, KS 66205. If you cancel permission to use your health information, you will be withdrawn from the study. The researchers will stop collecting any additional information about you unless they need information about a side effect of the intervention. They may use and share information that was gathered before they received your cancellation.

**Can my participation be stopped early?**

This study might be stopped, without your consent, by the investigator or the sponsor. Possible reasons for removal include failure to comply with study procedures, inappropriate behavior towards study staff or the end of funding for the study.

Neither the sponsor, nor the investigator, nor the University of Kansas Medical Center will

be obligated to provide you with the study treatment if the study is stopped early. Your physician will decide about future treatment, if it is needed.

**CONSENT**

Dr. Burns or the research team has given you information about this research study. They have explained what will be done and how long it will take. They explained any inconvenience, discomfort or risks that may be experienced during this study.

By signing this form, you say that you freely and voluntarily consent to participate in this research study. You have read the information and had your questions answered.

***You will be given a signed copy of the consent form to keep for your records.***

\_\_\_\_\_  
Print Participant's Name

\_\_\_\_\_  
Signature of Participant

\_\_\_\_\_  
Time

\_\_\_\_\_  
Date

\_\_\_\_\_  
Print Name of Person Obtaining Consent

\_\_\_\_\_  
Signature of Person Obtaining Consent

\_\_\_\_\_  
Date