#PBRC _____

CONSENT TO PARTICIPATE IN A RESEARCH STUDY FOR AN ADULT
INFORMED CONSENT - PART I

Title of Study: **A Phase 1 Study of Safety and Pharmacokinetics of BKR-017 in Individuals on Statin Therapy *(CL-901)***

Study Sponsor: **BioKier, Inc.**

Key Information

- **Why am I being asked to review this form?**
  - You are being asked to take part in a research study. This form is provided so that you may read and understand the reasons why you might or might not want to participate in the research. Your participation is voluntary.
- **What is the purpose, duration, and procedures of this study?**
  - The purpose of this study is to evaluate the pharmacokinetic profile and systemic exposure of BKR-017 in individuals on statin therapy. This will be done after a single dose and again after seven days of dosing.
  - Your expected time in this study will be up to two weeks consisting of three study visits.
  - The procedures involved in this study include:
    - Vital signs (heart rate and blood pressure) collected two times
    - Blood sample collections
    - Urine sample collections for women who are able to become pregnant
- **What are the possible risks and discomforts?**
  - Blood Draw
    - This is a very common procedure, and the risks are very low but do include the possibility of infection and/or pain and bruising at the vein on your arm where the needle is inserted. Sterile technique and trained personnel minimize these risks.
  - Test Product BRK-017
    - The risks from taking the test product are low. Patients have reported bloating when taking butyrate at much higher doses than what will be used in this study, therefore this risk is not expected.
  - A more comprehensive and detailed description of reasonably foreseeable risks to subjects is included later in Section 6 of the informed consent.
- **What are the possible benefits?**
  - We cannot promise any benefits from your being in the study. Your participation may help us gain knowledge that may help people in the future.
- **If you choose not to participate in the study, are there other choices?**
  - You have the choice at any time not to participate in this research study.

- If you decide not to participate in this study, your other choices may include:
  - Taking part in another study
  - Getting no treatment

Detailed Information

1- Who is doing the study?

Investigator Information:

Principal and Medical Investigator:	Frank L. Greenway, M.D.
	(225) 763-2578 24-hr. Emergency Phone Nos.: (225) 763-2552 (Weekdays 7:30 a.m.-4:30 p.m.) (225) 765-4644 (After 4:30 p.m. and Weekends)
Sub-investigators:	Robert Dubin, M.D.
	Juan Lertora, M.D., PhD

Dr. Greenway will direct and provide medical supervision for this study. We expect 10 people to be enrolled in this study. The study will take place over a period of approximately 3 months. Your expected time in this study will be approximately 2 weeks. This study will take place at Pennington Biomedical Research Center.

2- Where is the study being conducted?

This study will take place in the Clinical Trials in-patient and out-patient Unit at Pennington Biomedical Research Center.

3- What is the purpose of this study?

The purpose of this study is to evaluate the pharmacokinetic profile (the blood levels of the test substance) and systemic exposure (how long the test substance stays in the blood stream) after an oral dose of BKR-017 in individuals on statin therapy.

The active ingredient in BKR-017 is butyrate, which is found in common foods such as milk, cheese, and butter, but as a food source it is digested in the stomach. BKR-017 tablets will pass through the stomach so that butyrate will be released in the lower intestine, where it can act on the cells in the intestine to produce natural substances that control cholesterol levels. The amount of butyrate in your blood will be measured.

You will take 3 tablets of the study product twice daily for seven days. The use of BKR-017 in this study is considered investigational, meaning that BKR-017 is not currently approved treatment of any conditions. We are trying to determine the blood levels of butyrate after one week of dosing.

The use of BKR-017 in this study is investigational. The word “investigational” means that BKR-017 is not approved for marketing by the Food and Drug Administration

(FDA). This study will lead to further studies designed to determine if longer-term dosing with BKR-017 will reduce cholesterol levels.

4- Who is eligible to participate in the study?

- Men and women, ages 18-70 inclusive
- Subjects currently on statin treatments with LDL cholesterol levels more than 100 mg/dL

You may not qualify for this study based on other eligibility criteria not listed. The study coordinator will go over this information in detail.

5- What will happen to you if you take part in the study?

You will have a screening visit to determine your eligibility. If eligible, you will have 2 study visits, both requiring an overnight stay at Pennington in-patient clinic.

You will take 3 tablets of the study product twice daily for 7 days. 3 tablets before your morning meal and 3 tablets before bedtime.

Table 1: Time & Events Schedule Study CL-901	Screening Visit 1	Visit 2	Visit 3
Subject Management	Day -7	Day 0	Day 8
Written informed consent	X		
PK sample collected via IV[1]	X	X	X
Vital Signs	X	X	X
Demographics	X		
Medical history	X		
Medications List	X	X	X
Physical examination	X		X
Blood Draw	X		X
Inpatient Stay		X	X
Urine pregnancy test (females of childbearing potential)	X		X
Weight	X		X
Adverse Event Assessment		X	X
Test product dispensed to Subject		X	
Test product administration (BID during Dosing Period)		X	X
Standard meals supplied in clinic to subjects along with meal diary; three full meals and one snack		X[2]	X[2]
Subject returns unused test product			X

[1] PK blood samples will be collected as follows:

- Visit 2, Day 0: -1 and -0.25, 0.5, 1, 2, 4, 6, 8, 10, 12 and 24 hours post-dose.
- Visit 3, Day 7: -1 and -0.25, 0.5, 1, 2, 4, 6, 8, 10, 12 and 24 hours post-dose.

[2] Day 0 and Day 8 standard meals will be supplied in the clinic immediately after dosing, and after the 4-hour, 8-hour and 12-hour PK sample collections.

At the Screening Visit (Visit 1; 1.5-2hrs): Fasting visit (nothing to eat or drink except water for 10 hours & no alcohol or intense exercise for 24 hours prior to your visit):

- You will be asked to provide consent by signing this Informed Consent Form prior to the start of any study-related procedures.
- You will be asked to provide your medical and medication history.
- Urine will be collected for a pregnancy test for females of who are able to become pregnant (if you are pregnant, you will not be able to take part in the study; if you become pregnant during the study, you will not be able to continue in the study).
- A blood sample (16.5 mL, or a little more than 1 tablespoon) will be collected for routine blood testing.
- Demographic information including age, gender, race, and ethnicity will be recorded.
- A physical examination will be performed, including the assessment of general appearance, skin, neck, heart, lungs, and abdomen.
- Your heart rate, blood pressure, height, and weight will also be measured.
- The results of the routine blood testing will also be used to determine your eligibility for this study. Study personnel will inform you if you are eligible to continue participation and if so, will schedule you for Visit 2. If not, you will be discontinued from the study.

At Visit 2 (overnight): Fasting visit (nothing to eat or drink except water for 10 hours & no alcohol or intense exercise for 24 hours prior to your visit)

- Your weight, heart rate, and blood pressure will be measured.
- You will take three tablets of BKR-017
- There will be an IV line placed for blood draws for the next 24 hours.
- Blood samples (7 mL, or about 0.5 tablespoon) will be collected pre-dose at -1 hour and -15 minutes prior to dosing and after dosing at 0.5, 1, 2, 4, 6, 8, 10, 12, and 24 hours post-dose.
- Standardized meals (moderate calories, carbohydrates, and fat) will be provided immediately after dosing, and after the 4-hour and 8-hour and 12-hour blood sample collection.
- You will stay overnight in the clinic in-patient unit.
- You will be provided with a seven-day supply of BKR-017 and instructed to administer doses of three tablets of BKR-017 before bedtime and before the morning meal, starting immediately after the 24-hour PK sample and to continue this dosing schedule to Visit 3.
- You will be released from the clinic after the 24-hour blood sample.
- You will be instructed to record the time of each administration of test product in a diary, along with any new medications they have taken and any adverse events you may have experienced.

At Visit 3 (overnight); Fasting visit (nothing to eat or drink except water for 10 hours & no alcohol or intense exercise for 24 hours prior to your visit)

- Urine will be collected for a pregnancy test in females of childbearing potential.
- You will be required to bring your diary and any unused test product with you to this visit. Study staff will review the diary with you and discuss any changes to medications or side-effects.
- Your weight, heart rate and blood pressure will be measured.
- There will be an IV line placed for blood draws for the next 24 hours.
- A blood sample (16.5 mL, or a little more than 1 tablespoon) will be collected for routine blood testing. This sample will be collected through the IV line.
- You will take three tablets of BKR-017 and will be given a standard breakfast meal. Blood samples (7 mL, or about 0.5 tablespoon) will be collected pre-dose at -1 hour and -15 minutes prior to dosing and after dosing at 0.5, 1, 2, 4, 6, 8, 10, 12, and 24 hours post-dose.
- Standardized meals (moderate calories, carbohydrates, and fat) will be provided immediately after dosing, and after the 4-hour and 8-hour and 12-hour blood sample collection.
- You will stay overnight in the clinic in-patient unit.
- You will be released from the clinic after the 24-hour blood sample.

The total amount of blood that will be taken during this study (over 2 weeks) is about 150 mL (or about 10 tablespoons). The maximum amount of blood taken on any given day is 75 mL (or a little more than 5 tablespoons).

6- What are the possible risks and discomforts?

Blood Draws

There is the possibility of infection and/or pain and bruising at the vein on your arm where the needle is inserted. Aseptic (sterile) technique and trained personnel minimize these risks.

Test Product BKR-017

The risks from taking the test product are low. People taking large amounts of butyrate, the active ingredient in BRK-017, have reported bloating but BKR-017 is being given in smaller doses in this study and this risk is not expected.

Breach of Confidentiality

Although every precaution will be taken to ensure the confidentiality of sensitive personal information, if confidentiality is breached, you may experience psychological, emotional, financial, social, and/or legal risk or discomfort as a result of this information becoming available.

Unknown Risks

In addition to the risks listed above, you may experience a previously unknown risk or side-effects.

Unforeseeable Risks Involving Pregnant Women

If you are pregnant or become pregnant, BKR-017 may involve risks to the embryo or fetus, which are currently unforeseeable.

Will I be notified if my blood test results in an incidental finding?

During a research study, a researcher may notice something that he or she was not looking for. This is called an “incidental” or “unexpected” finding. These incidental findings are not directly related to the research. However, they may show important information about the health of a research volunteer.

Researchers may share some or all of their findings with you. However, you may not learn about any findings for a very long time. If such findings occur, you will be notified by the medical investigator or trained study personnel and referred to a treatment facility for further testing and/or treatment.

Risks: It can be very upsetting to learn unexpected information about your health. This is especially true if you learn that you have or will develop a condition that has no treatment or cure. There is a chance that unexpected findings could affect your family or social relationships, change your family planning decisions, or affect you financially. You might need more tests and procedures to find out what the information really means. It’s also possible that the information might be incorrect, so you would worry without cause.

Interviews/Questionnaires

You do not have to answer any questions you do not want to answer.

Food Allergies

Because of the way our meals are prepared for research, and the possibility that the ingredients in the foods we get from commercial vendors could change at any time without our knowledge, it cannot be guaranteed that allergens will be identified and removed from the foods used in our research studies. If you have a food allergy, and you are participating in a study where foods are provided, there is a risk that you could have an allergic reaction. All participants with known life-threatening food allergies must inform staff of their allergies.

7- What are the possible benefits?

We cannot promise any benefits from your being in the study.

If you take part in this study, you may help others in the future.

8- If you do not want to take part in the study, are there other choices?

You have the choice at any time not to participate in this research study. If you choose not to participate, any health benefits to which you are entitled will not be affected in any way. You have the right to take part now and change your mind later on.

If you are a Pennington Biomedical Research Center employee and you choose not to participate, there will be no impact on your employment.

9- If you have any questions or problems, whom can you call?

If you have any questions about your rights as a research volunteer, you should call the Institutional Review Board Office at 225-763-2693 or the Executive Director of Pennington Biomedical at 225-763-2513. If you have any questions about the research study, contact Dr. Frank Greenway at (225) 763-2578. If you think you have a research-related injury or medical illness, you should call Dr. Greenway at (225) 763-2578 during regular working hours. After working hours and on weekends you should call the answering service at 225-765-4644. The on-call physician will respond to your call.

10- What information will be kept private?

Every effort will be made to maintain the confidentiality of your study records. However, someone from the Food and Drug Administration, the National Institutes of Health, the Pennington Biomedical Research Center, and BioKier (the sponsor) may inspect and/or copy the medical records related to the study. Results of the study may be published; however, we will keep your name and other identifying information private. Other than as set forth above, your identity will remain confidential unless disclosure is required by law.

Identifiable Private Information or Identifiable Biospecimens

Any identifiers might be removed from your identifiable information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or given to another investigator for future research without additional informed consent from the subject or legally authorized representative.

Medicare/Medicaid Mandatory Reporting

If the study sponsor covers costs associated with a study-related injury or medical illness, they will need to know some information about you like your name, date of birth, and Medicare Health Insurance Claim Number, or, if you do not have one, your Social Security Number. This information will be used to check to see if you receive Medicare, and, if you do, report the payment they make to Medicare. The study sponsor will not use this information for any other purpose.

ClinicalTrials.gov

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov,* as required by U.S. Law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

Biospecimens and Commercial Profit

Information resulting from analysis of your blood samples may be used to develop new drugs or other products that may result in commercial profit that will not be shared with you.

Whole Genomic Sequencing

Your blood samples that are collected for this research study will not include whole genomic, germline, somatic, and/or exome sequencing. This means that the researchers have no plans to look at or try to "read" the protein information that makes up your genes (DNA) from your sample.

11- Can your taking part in the study end early?

Dr. Frank Greenway (Principal and Medical Investigator) or the study sponsor can withdraw you from the study for any reason or for no reason. Possible reasons for withdrawal include the need for you to take a medication that is not allowed, not adhering to the study visit schedule, or an unanticipated side effect. The sponsor of the study may also end the whole study early.

If your participation in the research ends early because of the investigator or by your choice or a reason listed above, termination procedures may need to be completed or follow-up data may need to be obtained to ensure your safety. Termination procedures include returning unused test product and diary cards, obtaining your vital signs, and collecting blood samples for routine testing. If you are a woman able to have children, a urine pregnancy test will be performed. The study staff will go over the details with you.

You may withdraw from the study at any time without penalty; however, information Pennington Biomedical has previously collected cannot be removed from the study. Early withdrawal from the study will not result in any adverse consequences.

If you decide you would like to withdraw your consent, you must provide a written request to the Principal Investigator at:

Frank Greenway, MD
Pennington Biomedical Research Center
6400 Perkins Road
Baton Rouge, LA 70808

12- What if information becomes available that might affect your decision to stay in the study?

Significant New Findings

During the course of this study there may be new findings from this or other research which may affect your willingness to continue participation. Information concerning any such new findings will be provided to you.

Clinically Relevant Research Results

In this study, you will not be informed of any clinically relevant research results, including your individual results that may be discovered.

13- What charges will you have to pay?

None

14- What payment will you receive?

If you agree to take part, we will compensate you up to $850 for completion of the study. If you do not complete the entire study, you will be compensated for each completed visit.

Screening Visit $50 (only if you meet eligibility and are randomized into the study)
V2 (Day 1 and Day 2)- $375.00
V3 (Day 1 and Day 2)- $375.00
V4- $50.00

Your check will be requested from the LSU payroll department when you complete the study or at the appropriate milestone if you are compensated during the course of the study. It usually takes about 3-4 weeks for it to arrive at Pennington Biomedical Research Center.

U.S. citizens, legal resident aliens, and those who have a work eligible visa will need to provide their social security number to receive payment.

All study participant compensation is taxable. Participants receiving collective compensation payments in excess of $600 in a calendar year will be issued a 1099-NEC which will also be reported to the IRS.

Non-US citizens are subject to having taxes withheld from payment and will need a passport, visa and 1-94 for payment to be processed.

I authorize that all information provided on this Informed Consent form and HIPAA Authorization form, including any and all personal and financial data may be shared with the Internal Revenue Service (IRS) for tax reporting. This data will be securely retained indefinitely.

15- Will you be compensated for a study-related injury or medical illness?

The sponsor of the study (BioKier) shall reimburse Study Subjects or treatment facility for reasonable and actual medical expenses resulting from diagnosis and treatment of any injury, illness or adverse reaction, including hospitalization, arising from administration of the test product in accordance with the Protocol, or during the proper performance of procedure required by the Protocol, provided those expenses are not covered by the applicable any third party payor and are in no way attributable to the Principal Investigator's, PBRC's, or any of its employees', investigators' or representatives' negligence, intentional misconduct, breach of this Agreement, failure to follow the Protocol or failure to comply with applicable laws. Notwithstanding the above, Sponsor shall not submit subject injury expenses to Medicare for payment.

No form of compensation for medical treatment or for other damages (i.e., lost wages, time lost from work, etc.) is available from the Pennington Biomedical Research Center. In the event of injury or medical illness resulting from the research procedures in which you participate, you will be referred to a treatment facility. Medical treatment may be provided at your expense or at the expense of your health care insurer (e.g., Medicare, Medicaid, Blue Cross-Blue Shield, Dental Insurer, etc.) which may or may not provide coverage. The Pennington Biomedical Research Center is a research facility and provides medical treatment only as part of research protocols. Should you require ongoing medical treatments, they must be provided by community physicians and hospitals.

16- Signatures

By signing this consent form, I agree to participate in the study as it is described. The study has been discussed with me and all my questions have been answered. I understand that additional questions regarding the study should be directed to the study investigators. I agree with the terms above and acknowledge that I will be given a copy of this signed consent form.

With my signature, I also acknowledge that I have been given either today or in the past a copy of the Notice of Privacy Practices for Protected Health Information.

_____

Printed Name of Volunteer

_____ _____

Signature of Volunteer Date

_____

Printed Name of Person Administering Informed Consent

_____ _____

Signature of Person Administering Informed Consent Date

Frank Greenway, MD

Principal & Medical Investigator