RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: Trial of Roflumilast in Asthma Management (TRIM)

Application No.:

Sponsor: National Institutes of Health (NIH) and
American Lung Association (ALA)

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1. What you should know about this study:

- You are being asked to take part in a research study. This consent form explains the research study and your part in it. Please read it carefully and take as much time as you need.
- Ask your study doctor or the study team to explain any words or information that you do not understand.
- You are a volunteer. If you join the study, you can change your mind later. There will be no penalty or loss of benefits if you decide to quit the study.
- During the study, we will tell you if we learn any new information that might affect whether you wish to continue to participate.
- This study is being conducted by the University of Vermont as part of the American Lung Association's Airways Clinical Research Centers network; participants will also be recruited at six other centers across the United States.
- Biospecimens will be collected in this study if site policies allow it. Biospecimens may include any of the following: blood, tissue, saliva, urine, bone marrow, cells, etc. Most biospecimens contain DNA, which is the genetic code for each person.

- 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.

- If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.

- We encourage you to ask questions and take the opportunity to discuss the study with anybody you think can help you make this decision.

2. Why is this research being done?

- You are being invited to take part in this research study because you have asthma that is not well controlled, and your body mass index (BMI) is greater than 30 kg/m^2 (BMI is a person's weight in kilograms (kg) divided by his or her height in meters squared), which may make your asthma less responsive to asthma medications.

- People who have a BMI greater than 30 tend to have poor asthma control that does not respond well to usual asthma treatments. In fact there are no treatments specifically targeting asthma in patients with a higher BMI. The purpose of this study is to investigate how effective a medication called Roflumilast might work for people with asthma and a BMI greater than 30.

- Roflumilast is available as the medication "Daliresp" in the United States, and has been approved by the FDA to treat COPD. Roflumilast has beneficial metabolic effects that may be useful in the treatment of asthma in patients with a higher BMI. Roflumilast can induce weight loss, which may also lead to improved asthma control.

How Many People Will Take Part In The Study?

- 38 people will participate in the study nationwide

3. What will happen if you join this study?

- If you agree to be in the study, we will ask you to do the following things:

    - This study involves seven study visits over approximately 6 months, and taking study medication and keeping a record of your symptoms every day. Essential clinic visits are visit 2 (week 2) and 7 (week 24). Study visit 2 is when eligibility is established. This visit must be done in the clinic. All other visits maybe done in the clinic or remotely using a secure video conference application. Study medication will be either Roflumilast or a **placebo** (a placebo is a tablet that looks the same as the Roflumilast tablet, but does not actually contain any medication). You will be assigned to either Roflumilast or placebo by **randomization** (a process that assigns people to a specific treatment according to a random process like tossing a coin). You will have an equal chance of being assigned to either group.

- At the first visit you will answer questions to see if you are eligible for the study. We will not be able to determine if you are eligible at the first visit as we reassess at visit 2. We will determine your eligibility at the second, in person, study visit.

- If you are eligible at visit 2, you will be assigned the study drug, Roflumilast or placebo.

- When you receive the study drug, you will be instructed to take 1 capsule Every Other Day Roflumilast (500 mcg) OR placebo for the First Two Weeks.

- After two weeks, if you tolerate the drug well, you will take 1 capsule Every Day (Roflumilast 500 mcg OR placebo), beginning at Visit 3 and continuing for the rest of the study. If you do not tolerate the full dose, you will continue to take one capsule Every Other Day for the duration of the study.

- You will receive study drug at clinic visits starting at the second visit. You will be expected to return all unused study drug at each follow-up in-person visit after that, or at the end of the study if study visits are conducted remotely.

Description of Study Visit Procedures

- Visits 1–7 (each visit estimated time 1-2 hours):

1. Medical History: We will document your medical history by asking you questions about your past and present health status, medical and surgical history, use of medications, and your family history. We will measure your height and weight, and your waist circumference and hip circumference. You will be asked to complete questionnaires about your asthma, gastrointestinal symptoms, and also anxiety and depression symptoms. If you will be followed up remotely, you will complete some questionnaires over the phone and mail back the rest of the questionnaires to the site. We will review medical records of any prior lung function tests and allergy tests. We will show you how to fill out the paper or electronic diary cards so you can record your daily symptoms at home. A scale and tape measure will be given to you during the second study visit so you can record these measurements at home.

2. Urine Pregnancy Test: If you are a female and of childbearing potential, you will be asked to provide a urine specimen to test for pregnancy. If you will be followed up remotely, then an at home pregnancy test will be provided to you and you will be required to send us a picture of the results If you qualify for the study, you will need to use a reliable form of birth control for the duration of the study.

3. Blood Draw at visits 2 and 7: If the clinic policies permit blood draw we will perform a blood draw for analysis of substances in your blood, measuring metabolic and oxidative markers related to your asthma – we will need approximately 15 cc (3 teaspoons) of blood. We will ask you not to eat or drink anything after midnight the night before this morning blood draw. Blood draw is optional.

4. Diary Cards: Complete the provided paper or electronic asthma diary cards daily. On the diary card you will record your peak flow, your asthma symptoms or other symptoms you might experience, and whether you took the study medication or other asthma medication. The diary card will take less than 5 minutes a day to complete. We will ask you to fill out the diary cards on paper, your phone, or your computer. An email or text with a link to the asthma diary card will be sent to you if they will be completed electronically. The purpose of this diary is to see how well your asthma symptoms are being controlled. You will be asked to complete the asthma diary card every day after the first visit until the study is completed. You will be given a peak flow meter at the second study visit. The coordinator will instruct you on how to use it. You will then demonstrate how to use the peak flow meter at home via video conference application. Asthma action plan will be provided for guidance as well.

5. Randomization at visit 2: You will be assigned to study medication (roflumilast or placebo). You will be taking the study medication for 24 weeks, every other day or every day depending on how well you tolerate it.

A schedule of tests and procedures is outlined in the following table.

Outline of Study Visits							
Week	-1	0	2	6	12	18	24
Visit number	V1	V2	V3	V4	V5	V6	V7
Consent	•						
Baseline/interim history	•	•	•	•	•	•	•
Randomization		•					
Pill distribution†		•		•	•		
Pill distribution‡		•			•		
Review of paper/electronic diary cards		•	•	•	•	•	•
Pill Counts			•	•	•	•	•
Asthma Control	•	•	•	•	•	•	•
Anxiety/depression questionnaires	•	•	•	•	•	•	•
GSRS	•	•	•	•	•	•	•
QOL	•	•	•	•	•	•	•
Blood draw¥		•					•
Anthropometrics	•	•	•	•	•	•	•
Pregnancy test*	•	•	•	•	•	•	•
End of study questionnaire							•

† if dose frequency is every day since V3

‡ if dose frequency is every other day since V3

¥ conduct blood draw only if site permits it

*for women of child-bearing potential and participating in remote follow up participants will be mailed testing kit, and asked to send photo of result to coordinator

Request to collect and store blood samples and data for future research

- Your samples and data will be stored for future use with your consent.

- We have several tests planned for the blood samples and information that we collect from you during this study. We are also hoping to store any leftover blood samples and data you provide for future research on obesity and asthma. We will store your samples and data with a code number, not your name, so laboratory personnel will not be able to identify you. The list connecting your name to this code will be stored separately, in a password protected file within the Vermont Lung Center.

  Participation in this long-term storage of samples is voluntary, and if you choose not to allow it or withdraw later, your participation in the main study will not be affected. You will not be able to withdraw specimens already donated.

- Check the box below and place your signature if you give permission for collection of blood samples and related data to be stored/used/disclosed/shared for future research projects.

Yes ☐ _____
Signature of Participant

No ☐ _____
Signature of Participant

How long will you be in the study?

- You will be in this study for six months.

4. What are the risks or discomforts of the study?

- There are risks involved with taking Roflumilast. However Daliresp® (Roflumilast) is a FDA approved drug for COPD in the US. In previous studies the *most common* side effects were:
    - Diarrhea (9.5%),
    - Weight decrease (7% to 20%),
    - Nausea (4.7%),
    - Headache (4.4%),
    - Back pain (3.2%),
    - Influenza (flu) (2.8%),
    - Insomnia (difficulty sleeping) (2.4%),
    - Dizziness (dizzy) (2.1%), and
    - Decreased appetite (2.1%)
- Most side effects generally happened within the first weeks of starting to take study drug and resolved during continued use of roflumilast. As with any drug, you may feel some discomfort or side effects associated with the use of the drug that has not already been reported.
- Use of roflumilast has been shown to be associated with an increase in psychiatric side effects such as insomnia, anxiety, and depression. There have been subject reported cases of suicidal ideation and behavior, including a completed suicide in previous studies. We will ask you to let us know the name of your mental health care provider, if you have one. At each study visit you will complete a questionnaire about anxiety, depression and suicidal thoughts, which we will check before you leave the clinic.
- If you have symptoms of anxiety/depression/suicidal thoughts, we will provide you with information about mental health care resources and/or ask you to schedule an appointment with your mental health care provider. We will check in with you a week later to make sure that you have been able to get follow up care. If we can't reach you, we will discuss this with the study physician (Dr. Dixon, or her designee), who will contact Dr. Desjardins (a psychiatrist at UVM Medical Center) to discuss what follow-up care you might need.
- If you are actively suicidal, we will ask you to contact your primary /mental-health care provider immediately (from our clinic), but if you are unable to reach your primary /mental-health care provider, we will either accompany you to the Emergency Department, or call 911.
- If you have any psychiatric side effects during the study please report the illness to your study doctor immediately.

- Participants and their families/caregivers should be alert for worsening of difficulty sleeping, anxiety, depression, mood changes or suicidal thoughts while on study drug, and should contact the study team immediately to discuss.

- Venipuncture: The main risk of this is bruising and minor discomfort.

5. Are there risks related to pregnancy?

- We will not recruit participants who report that they are pregnant.

6. Are there benefits to being in the study?

- There may be no direct benefit of participation in this study other than the opportunity to learn more about your asthma, and to have your asthma closely monitored. Your asthma control might improve on the study medication. We may learn new information that will help patients in the future who have asthma.

7. What are your options if you do not want to be in the study?

- The only option is to not participate in this study. The decision not to participate will not affect the care you receive. Other potential options to better control your asthma can be discussed with your primary care provider or pulmonologist.

8. Will it cost you anything to be in this study?

- The only cost to you for participating in this study is your time.

9. Will you be paid if you join this study?

- You will receive $50 at visit 2 for a total of $350 for completion of the study. Subjects who must travel 20 miles or more (each way) will be compensated for their mileage at the current University of Vermont rate.

- You may be required to provide your social security number to be paid for taking part in this study. Federal tax law requires that you report your research payments when you file your taxes. If your total payments from Johns Hopkins University exceed $600 per year, Johns Hopkins will report these payments to the Internal Revenue Service and you will receive a 1099-MISC form from us.

10. Can you leave the study early?

- Your participation in this research study is voluntary. You may decline to participate or you may withdraw at any time without prejudice, penalty or loss of benefits to which you are entitled.

- If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Any information collected up to the point you wish to stop your participation will be used for research purposes.

11. Why might we take you out of the study early?

- The investigator may end your participation in this study without your consent for any of the following reasons:
    - it is not in your best medical interests to continue
    - you need treatment not allowed in this study
    - you cancel permission to disclose your health information
    - you fail to follow instructions
    - the study is canceled
    - there may be other reason s to take you out of the study that we do not know about at this time
- If you are taken out of the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

12. How will your privacy be protected?

- We have rules to protect information about you. Federal and state laws and the federal medical Privacy Rule also protect your privacy. By signing this form you provide your permission, called your "authorization," for the use and disclosure of information protected by the Privacy Rule.

- The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records (which may include information about HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

- The research team will know your identity and that you are in the research study. Other people at Johns Hopkins, particularly your doctors, may also see or give out your information. We make this information available to your doctors for your safety.

- People outside of Johns Hopkins may need to see or receive your information for this study. Examples include government agencies (such as the Food and Drug Administration), safety monitors, other sites in the study and companies that sponsor the study.

- We cannot do this study without your authorization to use and give out your information. You do not have to give us this authorization. If you do not, then you may not join this study.

- We will use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside Johns Hopkins who receive your information may not be covered by this promise or by the federal Privacy Rule. We try to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee that your information will not be re-disclosed.

- The use and disclosure of your information has no time limit. You may revoke (cancel) your permission to use and disclose your information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, phone and fax information are on page one of this consent form.

- If you do cancel your authorization to use and disclose your information, your part in this study will end and no further information about you will be collected. Your revocation (cancellation) would not affect information already collected in the study, or information we disclosed before you wrote to the Principal Investigator to cancel your authorization.
- The health information we plan to collect for this study is listed below.
    - Medical history and past pulmonary function tests
    - Information that identifies you, such as your name, address, age, and sex
    - Reports from hospital and clinic visits
    - Laboratory and other test results
    - X-ray and other images and reports
    - Lists of medications you are taking
    - Responses to health surveys and questionnaires

Who is disclosing your health information for this research study?

- The University of Vermont Medical Center
- Other doctors' offices and hospitals where you may receive medical care while this study is active.
- Our research team will use your health information. We may also share it with those who assist with the conduct of the research or oversight of the activities for this study. The representatives from the institutions, organizations, and agencies are listed below.
    - The University of Vermont and its Committees on Human Research
    - The University of Vermont Medical Center
    - Other researchers and centers that are a part of this study, including individuals who oversee research at those sites
    - Officials from agencies and organizations that provide accreditation and oversight of research

- The sponsor of this study, American Lung Association – Airways Clinical Research Center (ALA-ACRC), or others who fund the research, including the government

- Federal and state agencies that oversee or review research information, such as the U.S. Food and Drug Administration (FDA), the Department of Health and Human Services, the National Institutes of Health, and public health and safety authorities

- Your health insurer, for portions of the research and related care that are considered billable

- Your health information is protected by a federal law called the Health Information Portability and Accountability Act (HIPAA). Once your health information is shared outside of the University of Vermont Medical Center, we cannot guarantee that these laws will continue to apply. As a result, your health information could be further disclosed for other purposes. In the absence of a Certificate of Confidentiality, it is also possible for a court or other government official to order the release of study data. The confidentiality of your health information cannot be guaranteed if you agree it may be used in this study.

- Your permission to use your health information will not end until the study is completed. During this study, you will not have access to study data. You may ask for your data once study activities are complete. You have a right to receive a copy of the information in your medical record at any time.

- If you decide not to allow the use and disclosure of your health information, you may not take part in this study. Your decision will have no effect on your current or future medical care.

- If you choose to stop taking part in this study in the future, you may cancel permission for the use of your health information. You should let the research team know that you are cancelling your permission. A member of the research team will assist you in making your decision effective. The study will continue to use your health information already collected for the study before you canceled your permission, and you cannot get back information that was already shared with others.

- If you have questions or concerns about the use and disclosure of your health information, you should ask a member of the study team at (802) 847-2193 or the Privacy Officer at The University of Vermont Medical Center, Inc, at (802) 847-2667.

Safeguarding Your Health Information

- A record of your progress will be kept in a confidential form at the Vermont Lung Center. The security of your record will be maintained by study staff in a locked office. The results of this study may eventually be published and information may be exchanged between medical investigators, but patient confidentiality will be maintained.

- If your record is used or disseminated for government purposes, it will be done under conditions that will protect your privacy to the fullest extent possible consistent with laws relating to public disclosure of information and the law-enforcement responsibilities of the agency.

- You may be requested to provide your name, social security number, and address. This information will be disclosed one time to either the University of Vermont's Procurement Services Department or UVM Medical Center Accounts Payable Department for purposes of reimbursing you for participation in this study. If you are not a US Citizen or Permanent Resident Alien you will be required to complete additional paperwork for payment.

13. What treatment costs will be paid if you are injured in this study?

The UVM Medical Center Policy

- If you are injured or become ill as a result of being in this research, the UVM Medical Center, the hospital partner of the University of Vermont, will provide reasonable and usual medical care for that injury or illness. There will be no cost to you if the conditions listed below apply to your injury or illness. These conditions are:

    1. The investigator, in consultation with the study sponsor, determines that your injury or illness results from the research and not from your underlying condition or its usual treatment.

    2. You let the investigator know about the injury or illness when you first notice it; and

    3. You follow medical advice about proper treatment options for the injury or illness.

- The UVM Medical Center may claim payments for your medical treatment directly from the study sponsor or your insurance company when these payments are allowed.

- For an injury or illness that results from being in this study, the University of Vermont Medical Center will not offer you any other payments, such as lost wages or expenses, except for your medical care. Even though you may receive medical care at no cost to you under certain conditions if you are in this study, the UVM medical center and the University of Vermont do not admit to any responsibility for an injury or illness that results from being in the study. If you agree to take part in this study and you sign this consent form, you are not giving up any of your legal rights.

14. What other things should you know about this research study?

a. What is the Institutional Review Board (IRB) and how does it protect you?

- The Johns Hopkins Medicine IRB is made up of:
    - Doctors
    - Nurses
    - Ethicists
    - Non-scientists
    - and people from the local community.

- The IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies. You may contact the IRB if you have questions about your rights as a participant or if you think you have not been treated fairly. The IRB office number is 410-955-3008. You may also call this number for other questions, concerns or complaints about the research.

- When the Johns Hopkins School of Medicine Institutional Review Board (IRB) reviews a study at another site, that site (institution) is solely responsible for the safe conduct of the study and for following the protocol approved by the Johns Hopkins IRB.

b. What do you do if you have questions about the study?

- You may contact Dr. Dixon, the Investigator in charge of this study, at (802) 847-1158 for more information about this study. If you have any questions about your rights as a participant in a research project or for more information on how to proceed should you believe that you have been injured as a result of your participation in this study you should contact the Director of the Research Protections Office at the University of Vermont at 802-656-5040.

c. What should you do if you are injured or ill as a result of being in this study?

- If you think you are injured or ill because of this study, call Dr. Dixon, at (802) 847-1158.

d. What happens to Data and Biospecimens that are collected in the study?

- Johns Hopkins and our research partners work to understand and cure diseases. The biospecimens and/or data you provide are important to this effort.

- If you join this study, you should understand that you will not own your biospecimens or data, and should researchers use them to create a new product or idea, you will not benefit financially.

- With appropriate protections for privacy, Johns Hopkins may share your biospecimens and information with our research sponsors and partners.

15. What does your signature on this consent form mean?

- Your signature on this form means that: You understand the information given to you in this form, you accept the provisions in the form and you agree to join the study. You will not give up any legal rights by signing this consent form.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

Signature of Participant	(Print Name)	Date/Time
Signature of Person Obtaining Consent	(Print Name)	Date/Time

The rest of this page is intentionally left blank.

Statement of Consent

You have been given and have read or have had read to you a summary of this research study. Should you have any further questions about the research, you may contact the person conducting the study at the address and telephone number given below. Your participation is voluntary and you may refuse to participate or withdraw at any time without penalty or prejudice to your present and/or future care.

You agree to participate in this study and you understand that you will receive a signed copy of this form.

_____ _____

Signature of Subject Date

_____

Name of Subject Printed

This form is valid only if the Committees on Human Research's current stamp of approval is shown below.

_____

Signature of Principal Investigator or Designee Date

_____

Name of Principal Investigator or Designee Printed

Principal Investigator: Anne Dixon
Address: Given D209, 89 Beaumont Avenue, Burlington, VT 05405
Telephone Number: 802-847-1158