Title: Evaluating the Safety, Tolerability, Pharmacokinetics and Receptor Occupancy of BMS-984923

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COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH STUDY

YALE UNIVERSITY SCHOOL OF MEDICINE

Study Title: An Open-Label, Single-Ascending Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Receptor Occupancy of BMS-984923
Principal Investigator: Adam Mecca, MD, PhD, 1 Church Street, Suite 800, New Haven, CT 06510
Phone Number: 203-764-8100

Invitation to Participate

We are asking you to join a research study. You have been invited to take part in this study because you do not have memory problems and you are between 50 and 80 years old. 24 subjects will take part in this study at Yale University.

To help you decide, you should understand the study and what it will involve for you. To make an informed decision to take part – you should know the purpose of the study, the procedures, the benefits and risks of the study, the discomforts and the precautions taken. This process is called 'informed consent'. Please take the time to read the following information carefully and discuss it with others. Please ask your study doctor if there is anything that is not clear or if you would like more information.

Once you have decided that you want to take part, you will be asked to sign the informed consent form. You will be given a copy of the signed form to keep, and the original will stay at the study center.

This study is funded by the National Institute on Health (NIH).

What is the purpose of this study?

The purpose of this research study is to find out whether the study drug, BMS-984923, is safe and well-tolerated in humans. The study also aims to find out what dose of BMS-984923 is needed to reach a target level of drug in the blood stream. This drug has never been given to humans before.

What will happen during the study?

If you agree to take part, after signing this Informed Consent Form, you will undergo a series of screening tests to confirm if you are eligible for the study and to establish your health status at the beginning of the study before receiving treatment. The screening period could take up to 90 days. The screening visit may take up to 5 hours and require multiple visits to the Yale Alzheimer's Disease Research Unit (ADRU).

If you are eligible, you will enter the in-clinic phase of the study. During this phase, you will check-in to the Yale Hospital Research Unit (HRU). The study staff will run a series of tests to make sure that you are still eligible to receive the study drug. If you are, the study staff will administer the study drug to you. The study drug is taken by mouth. Then, the study staff will monitor you and collect blood samples for 48 hours. At the end of the 48 hours, you will undergo

additional safety assessments. Once you have completed all the study procedures, you will be discharged to go home.

The study will have six cohorts of six participants each for a total of 36 participants. Each cohort will be given a different dose of the study drug. The dose you receive will depend on when you enroll in the study. Subjects who enroll in the study later will receive higher doses of the study drug.

Study staff will continue to follow up with you for seven days after you receive the study drug. On Day 5 after the in-clinic phase, the study staff will call you to ask about your general health. On Days 4 & 7 after the in-clinic phase, you will be required to return to the ADRU for additional study assessments. Each of these in-person visits will take up to 2 hours.

The following tests/assessments will be done at some or all of the study visits:

- Informed Consent: You will need to read, confirm understanding, and sign this informed consent.
- Medical History: A complete medical history will be taken, including any medications you have used or are currently using and any other therapies you have had.
- Physical Exam & Vital Signs: Your blood pressure, temperature, heart rate, height, and weight will be measured. Additionally, your study doctor will examine you physically. Some of these exams will include a complete physical while others will be based on the symptoms you are having.
- Safety Assessments. Tests will be done to assess how well you are thinking, how well you are performing your daily activities, and how well you are feeling. They take the form of interviews and questionnaires.
    - Some of the questions will ask about your mood. If there are concerns about your mood, you will be referred to appropriate care that may include the emergency department.
- Monitoring of any adverse effects (side effects) you are experiencing on the treatment.
- Electrocardiogram (ECG): ECGs measure electrical activity of your heart by putting small sticky patches on certain areas of your body.
- Concomitant medication monitoring: The study doctor will record all the medications you take while on the study.
- You will have the following blood and urine tests:
    - Blood tests related to how BSM-984923 works, including measuring the levels of BSM-984923 in your blood
    - Blood and urine tests for standard safety and health assessments
    - If you are a woman, you will have a blood test to show that you are not of child-bearing potential unless you have a documented bilateral tubal ligation or hysterectomy. You cannot participate if you are pregnant.

Schedule of Study Procedures

Study Phase	Screening	In-Clinic				Follow-up		
Study Day	-90 to -1	Day 1		Day 2	Day 3	Day 4-7		
		Admission	6 hours post-dose	24 hours post-dose	48 hours post-dose	Day 4 (Phone Call)	Day 5 (Visit)	Day 7 (Visit)
Informed Consent	x							
Medical History Questions	x	x						
Memory and Thinking Tests	x	x	x	x				x
Blood Tests	x	x	x	x	x		x	x
Urine Tests	x	x		x				x
ECG	x	x	x	x	x			
Physical Exam	x	x		x				
Vital Signs	x	x	x	x	x		x	x
Demographic Questions	x							
In-Clinic Admission		X (Admit)			Discharge			
Study Drug Administration		x						
Review of Medications	x	x	x	x	x	x	x	x
General Health Questions	x	x	x	x	x	x	x	x

What will I have to do?

- You will have to go to the study visits and follow the instructions the doctors give you.
- You must not take part in any other studies while you are taking part in this study.
- Some of the assessments regarding how well you are thinking will require you to have a study partner. The study partner should be someone who knows you well, for example, a spouse, sibling, or close friend. Your study partner is important to this study and by signing the statement in this form must agree and be able to:
    - Accompany you to some of the study visits or be available over the phone.
    - Provide information about you to the study doctor and staff. Your study partner will be asked about how well you are thinking, performing your daily activities, and feeling.
- You should tell the study staff immediately if you get any new symptoms of any kind, worsening of already existing symptoms, or any unwanted effects.
- You should tell the study staff about any procedures you have had (for example, a dental visit).
- If you are female and able to have children or male and able to get a woman pregnant, you must practice effective contraception during the entire study.
    - If you or your partner become pregnant during the study after receiving a dose of study medication, we will follow you to learn the outcome of the pregnancy.
- If you are male, you must practice effective contraception during the study and for three months after receiving the study drug. You must agree to use condoms during the trial and for 3 months after the last dose unless the woman is using an acceptable means of birth control. Acceptable forms of birth control include abstinence, birth control pills, or any double combination of: intrauterine device (IUD), male or female condom, diaphragm, sponge, and cervical cap.
- Inform your study doctor about any medication you are taking or changes to your medications (including herbal or alternative remedies and health supplements or medicines you buy over the counter) and avoid taking prohibited medications during the study. Your study doctor will discuss allowed and disallowed medications in more detail with you.

What are the risks associated with participating in this study?

Risks Associated with the Study Drug, BMS-984923

BMS-984923 has not previously been studied in humans. Studies have been completed in rats and non-human primates, with no adverse effects at the doses comparable to the dose you will receive in this study. There may be side effects that are currently unknown or that are unpredictable.

Side effects can go away shortly after you stop taking the study medicine, but some side effects could be long lasting, permanent, serious, life threatening, or even cause death. Everyone in the study will be watched carefully for any side effects. You should talk to your study doctor about any side effects you have while in the study.

Should information become available that could change your decision to be in this study, you will be told immediately. You can always decide whether or not to continue being in this study. As new risks are identified, you will also be told of these risks. At times you may be asked to sign a new consent form that shows that you have been made aware of the new risks and agree to continue taking part in this study.

Exposure to the sun can cause unexpected or exaggerated sunburn, or a rash on sun-exposed skin, minutes to hours after exposure to both a drug and ultraviolet light. We will minimize your exposure to sunlight during the treatment phase.

In animal studies, rats experienced serious side effects including lethargy, stress responses, and death. However, this was with repeated exposure to the drug at doses higher than will be used in this study.

Risks Associated with Blood Draws
Drawing blood and inserting an intravenous (IV) line into an arm vein are safe and standard medical procedures. Sometimes a bruise will occur at the puncture site and rarely a blood clot or infection will occur in the vein. Some people may feel light-headed, or experience upset stomach or fainting when their blood is drawn. The total volume of blood collected during this study will be up to approximately 9.5 tablespoons (2/3 cup). This amount of blood loss is safe for study participants.

Risks Associated with Electrocardiograms (ECGs)
There is no pain or discomfort during an ECG; however, removing the pads may cause some irritation to your skin.

Risks Associated with Psychological Stress
You might find some of the test questions boring, frustrating, or embarrassing. You can ask to skip a question or stop answering questions at any time.

What are the benefits of participating in this study?
This study does not directly benefit you. What we learn from your participation may provide information to help develop treatments to help others with memory loss and Alzheimer disorder.

Will I be paid for participating in this study?
You will be paid for participating in this study. You will receive $75 for the screening visit ($25 for a second screening visit, if needed), $200 for the study drug administration, and $250 for each overnight night stay during the in-clinic period. If you complete all study procedures, you will receive an additional $300. If you do not complete all study procedures, you will be paid for the visits you complete.

The total amount of compensation is $1075 for completion of all parts of the study. This amount may increase if you need to repeat study visits or if you need to an additional overnight stay during the in-clinic study period. These payments include a stipend to cover your travel and parking costs related to the study visits.

Your study partner will not be paid for participation in the study or reimbursed for parking and transportation costs.

You will receive payment(s) via a Bank of America pre-paid debit card. Please note that your name, address, and telephone number will be shared with Bank of America for ePayments. After your first payment (screening visit), you will receive a card in the mail which you will need to activate over the phone. Any subsequent payments will automatically add additional funds to your card.

Payment received as a research subject may be taxable income to you. If payment is more than $600.00 in a calendar year, the study clinic is required to report this to the Internal Revenue Service (IRS). An IRS Form 1099 (Miscellaneous Income) will be issued to you and a copy sent to the IRS.

What are the costs associated with participating in this study?

You will not have to pay for taking part in this study. The only costs include transportation and your time coming to the study visits.

What are my choices if I decide not to take part in this study?
You do not have to participate in this study. Because this is a study of healthy individuals, there are no alternative treatments to participating in this study.

Investigator Interest
A co-investigator in this study, Dr. Strittmatter, has a financial interest in this this study and the company Allyx Therapeutics' intent to license the drug.

Yale University has an institutional conflict of interest related to this study. The University may receive financial benefits related to use of the study drug used in this study. Yale has taken actions to protect participants in this research from any risks that may result from these financial interests. If you have questions, you may contact the Yale Human Research Protection Program at 203-785-3488 or icoi.committee@yale.edu.

Confidentiality and Privacy

Any identifiable information that is obtained in connection with this study will remain confidential and will be disclosed only with your permission or as permitted by U.S. or State Law. Examples of information that we are legally required to disclose include abuse of a child or elderly person, or certain reportable diseases. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity unless your specific consent for this activity is obtained.

We understand that information about you obtained in connection with your health is personal, and we are committed to protecting the privacy of that information. If you decide to be in this study, the researcher will get information that identifies you and your personal health information. This may include information that might directly identify you, such as your name, date of birth, address, or telephone number. This information will be de-identified at the earliest reasonable time after we receive it, meaning we will replace your identifying information with a code that does not directly identify you. The principal investigator will keep a link that identifies you to your coded information, and this link will be kept secure and available only to the PI or selected members of the research team. Any information that can identify you will remain confidential. The research team will only give this coded information to others to carry out this research study. Files are kept in an area protected by a security system, in a locked room and file cabinet. All desktop computers contain encryption software and are password protected. The link to your personal information will be kept indefinitely. Information or specimens collected in the course of this research study may be used for future research studies or distributed to another investigator for future research studies without additional informed consent, but only after all identifying information is removed.

The information about your health that will be collected in this study includes:

- *Demographic (personal information) and geographic information which may include name, date of birth, gender, race, address, e-mail, and telephone number;*
- *Research study records, including phone calls made as part of this research, records about study visits, and records about any study drug that you received;*
- *Medical and medication history;*
- *Medical and laboratory records of services provided in connection with this study, including physical and neurological exams, questionnaires, laboratory results, brain*

imaging, ECG, and other test results.

Information about you and your health that might identify you may be used by or given to:

- *Representatives from Yale University, the Yale Human Research Protection Program, and the Yale Human Investigation Committee (the committee that reviews, approves, and monitors research on human subjects), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential;*
- *Those individuals at Yale who are responsible for the financial oversight of research including billings and payments;*
- *The Principal Investigator Dr. Mecca, co-investigators, and members of the research team;*
- *The U.S. Department of Health and Human Services (DHHS) agencies;*
- *The U.S. Food and Drug Administration (FDA). This is done so that the FDA can review information about the new drug product involved in this research. The information may also be used to meet the reporting requirements of drug regulatory agencies;*
- *Governmental agencies to whom certain diseases (reportable diseases) must be reported;*
- *Health care providers who provide services to you in connection with this study;*
- *Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan;*
- *Data and Safety Monitoring Boards and others authorized to monitor the conduct of the study;*

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Institute of Health (NIH) which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

By signing this form, you authorize the use and/or disclosure of the information described in this form for this research study. The purpose for the uses and disclosures you are authorizing is to ensure that the information relating to this research is available to all parties who may need it for research purposes. You do not have to give this authorization. However, if you do not, you will not be able to take part in the study.

All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at Yale University School of Medicine and Yale-New Haven Hospital are required to comply with HIPAA and to ensure the confidentiality of your information. Some of the individuals or agencies listed above may not be subject to HIPAA and therefore may not be required to provide the same type of confidentiality protection. They could use or disclose your information in ways not mentioned in this form. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

You have the right to review and copy your health information in your research record in accordance with institutional medical record policies. However, by deciding to take part in this study and signing this form, you will not be allowed to look at or copy your study related information until after the research is completed.

This authorization to use and disclose your health information collected during your participation in this study will never expire.

What happens to the blood samples collected from me?

Your blood samples will be used for scientific research. These samples may be used to help scientists understand how the study drug might work. The results of tests done on these samples are only for scientific research. They will not be used for your medical care. They will not be used to make a diagnosis about your health. Therefore, results from any of the blood tests s will not be reported to you or your doctor or put in your medical record.

Your samples will be sent to Aptuit (Verona) Center for Drug Discovery and Development, a privately owned pharmaceutical services provider, for testing. Your samples may also be shared with other investigators studies to learn more about how study drugs work, without additional informed consent. If your sample is shared with other studies, it will be pooled with other samples.

To protect your privacy, your samples will be labeled with your study number and participant number. No personal identifiers are used (such as name, initials, social security number). The scientists analyzing the samples will not know your identity.

You blood samples will not be used for genetic testing.

You will not be paid for any use of your samples, results, or inventions made from research on them.

In Case of Injury

It is important that you tell your study doctor if you feel that you have been injured because of taking part in this study. If you have any injury, bad effects, or any other unusual health experience during this study, make sure that you immediately contact Dr. Adam Mecca or study staff at 203-764-8100. You can call at any time, day, or night, to report such health experiences. If this is not practical because of emergency, travel, or any other reason, you

should obtain treatment through an appropriate health care provider and notify your study doctor as soon as possible

If you are injured as a result of your participation in this study, treatment will be provided. You or your insurance carrier will be expected to pay the costs of this treatment. Yale School of Medicine and Yale-New Haven Hospital do not provide funds for the treatment of research-related injury. No additional financial compensation for injury or lost wages is available.

You do not give up any of your legal rights by signing this consent form.

Voluntary Participation and Withdrawal

Participating in this study is voluntary. You are free to choose not to take part in this study. Declining to participate will involve no penalty or loss of benefits to which you are otherwise entitled (such as your health care outside the study, the payment for your health care, and your health care benefits). However, you will not be able to enroll in this research study and will not receive study procedures as a study participant if you do not allow use of your information as part of this study.

Withdrawing From the Study

If you do agree to participate, you are free to stop and withdraw from this study at any time during its course. There will be no penalty to you. If you begin thinking about withdrawing from the study, you should inform the study personnel so that they may advise you on what follow-up care can be most helpful to you.

To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part. This will cancel any future appointments.

The researchers may withdraw you from participating in the research if necessary. The researchers may withdraw you from participating if they believe it is in your best interest, if you do not follow the study rules, or if the study is stopped, even if you want to continue.

Withdrawing from the study will involve no penalty or loss of benefits to which you are otherwise entitled. It will not harm your relationship with your own doctors, Yale-New Haven Hospital, or with Yale University.

Withdrawing Your Authorization to Use and Disclose Your Health Information

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by telling the study staff or by sending written notice to Dr. Adam Mecca, One Church Street, 8th floor, New Haven, CT 06510. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others until the end of the research study, as necessary to insure the integrity of the study and/or study oversight.

Questions

We have used some technical terms in this form. Please feel free to ask about anything you don't understand and to consider this research and the consent form carefully – as long as you feel is necessary – before you make a decision.

If you have questions about the study, please ask us before signing this form. If you or your family has any additional questions later, or during the study, you may contact Dr. Adam Mecca or study staff at 203-764-8100.

If you have any questions regarding your rights as a research subject, you may contact the Yale Human Investigation Committee at (203) 785-4688. If after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at (203) 432-5919. A signed and dated copy of this form will be given to you as a subject in this study if you agree to participate.

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.

Subject Consent

I have read (or someone has read to me) this form and have decided to participate in the project described above. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a copy of this consent form.

By signing this form, I give permission to the researchers to use and give out information about me for the purposes described in this form. By refusing to give permission, I understand that I will not be able to be in this research.

_____	_____	_____
Name of Participant (Print)	Signature of Participant	Date
_____	_____	_____
Name of Person Obtaining Consent (Print)	Signature of Person Obtaining Consent	Date

Study Partner Consent

I have read (or someone has read to me) this form and have decided to participate in the project described above as the study partner of _____(name of participant). My responsibilities have been explained to me to my satisfaction. My signature also indicates that I have received a copy of this consent form.

_____	_____	_____
Name of Study Partner (Print)	Signature of Study Partner	Date
_____	_____	_____
Name of Person Obtaining Consent (Print)	Signature of Person Obtaining Consent	Date