RUSH

**CONSENT/AUTHORIZATION FOR PARTICIPATION IN A RESEARCH STUDY**
**For Adult Participants Who Are Able to Provide Informed Consent**
**and**
**Legal Representatives of Participants Who Are Unable to Provide Informed Consent**

**Site Principal Investigator:** John Zajecka, MD

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**Protocol Title:** A Phase II, Multicenter, Randomized, Double-Blind, 12-Week Treatment, 3-Arm, Parallel-Group, Placebo-Controlled Study to Investigate the Efficacy, Safety and Tolerability of Alogabat in Participants Aged 15 to 45 Years with Autism Spectrum Disorder

**Sponsor(s):** F. Hoffman-La Roche Ltd. ("Roche")

**Name of Participant:** _____

**Note:** If you are a parent, guardian or legal representative of a minor or of a person who is not able to consent for themselves, the terms "you" and "your" in this document refer to the research participant.

## Key Information:

You are being invited to participate in a research study of a drug called alogabat (also called RO7017773; hereafter referred to as alogabat), which is being developed for autistic individuals who want help with some of the components of their autism. Research studies answer important questions that might help change or improve the way we do things in the future.

This document explains the purpose of the study, your rights and responsibilities, and what to expect if you participate in the study. This information should help you make an informed decision as to whether or not you want to participate in the study. Please take time to read the following information carefully. Feel free to talk with your personal doctor, nurse, family or friends before deciding.

If you have questions, you may ask your study doctor for more explanation.

Taking part in this research study is voluntary. You do not have to participate in this study and may choose to leave the study at any time. If you decide not to participate in this study or leave the study at a later time, your health care, benefits, or relationship with Rush University Medical Center will not change or be affected.

The purpose of this study is to find out what effects, good or bad, alogabat has on autistic individuals. Alogabat is an investigational drug, which means the U.S. Food and Drug Administration (FDA) has not approved alogabat for the treatment of autism and it must be tested to see if is it a safe and effective treatment method.

If you qualify for study participation, and you and your support person choose to participate, the total length of time in the study will be about 24 weeks (approximately 6 months). You will be asked to complete 9 visits (or 10 visits for adolescent participants) at the study site. For further information about the study visits, see the section, *"How long will you be in the study?"* of this consent form.

During the study visits, you will be asked to complete interviews and questionnaires about your autism, as well as your medical history and medications you are taking (if any). Testing (such as an IQ test) will be conducted, as well as a physical examination, vital signs (heart rate, blood pressure, temperature), electrocardiogram (ECG, a measurement of the electrical activity of your heart), electroencephalography (EEG, a measurement of your brain activity), and blood and urine samples will be collected for laboratory tests. You will be given specific equipment that will be used throughout the study, such as a smartphone, a sleep mat and an optional watch. This equipment is described further in the "Tests and Procedures at Home" section on page 10. All of the study procedures will be described and explained further in the section, "*What are the activities you will be doing if you participate in this study?*" of this consent form.

There may be risks to you for participating in this study. In some cases, side effects can be serious (in very rare cases may be fatal) and may be long-lasting or may never go away. In this study, some of the more common risks include feeling sleepy, headache and fatigue (exhaustion). For a detailed list of risks, see the section, "*What are the risks and discomforts of participating in this study?*" of this consent form.

There is no guarantee that you will receive any benefits from this study, and taking part in this study may or may not cause your health to improve. Information from this study may help doctors learn more about alogabat and the treatment of autism. This information may benefit other autistic individuals in the future.

The sponsor does not intend to provide alogabat or other study interventions to participants after the study is over.

Participants in this study will be randomly assigned (assigned by chance, like tossing a coin) to one of the following three treatment groups: 20 mg of alogabat, 60 mg of alogabat or placebo (a substance that looks like the study drug but contains no active medication). Participants who are assigned to treatment with placebo are not expected to get any health benefits from participating in this study.

Your other choices may include getting treatment or care for the components of your autism that you want treatment for (without being in a study), taking part in another study, or getting no treatment.

Talk to your doctor about your choices, including the risks and benefits of each choice, before you decide if you will take part in this study.

This research study is being sponsored globally by F. Hoffmann-La Roche Ltd (hereafter referred to as Roche) of Basel, Switzerland. However, it may be implemented in individual countries by Roche's local affiliates, including Genentech, Inc. in the United States.

The study is under the direction of Dr. Zajecka and the research staff for Rush University Medical Center. Roche is providing financial support to cover the cost of study-specific procedures performed during this study.

## Detailed Information: Please review the rest of this document for details about the above topics and additional information you should know before making a decision about whether or not you will participate in this study.

### Why are you being invited to participate in this study?

You were selected as a possible participant in this study because you are on the spectrum and you may qualify for this study.

Autism spectrum disorders (ASD) are a group of brain development disorders and are characterized by difficulties in communication, socialization, and repetitive or unusual behavior. In addition to these difficulties, autistic individuals may suffer from a range of other conditions such as irritability, depression or anxiety, attention deficits (i.e., unable to concentrate for periods of time), obsessive compulsive symptoms, seizures, and sleep disruption.

We are not sure what specifically causes autism; however, we do know that there is a link to changes in levels of a natural brain chemical that carries messages in the brain, known as GABA (gamma-aminobutyric acid). Alogabat is thought to increase the activity of GABA in the brain by attaching to specific sites in the brain known as gamma-aminobutyric acid type A ($GABA_A$) alpha (α) 5 receptors. Enhancing the activity of GABA reduces excitatory messaging in the brain, which could be helpful for autistic individuals.

The goals of this study are:

- To collect information on whether alogabat is effective in treating some of the core symptoms of autism. For this purpose, selected tests and activities will be used to measure your social skills and repetitive behaviors. These assessments are described later in this document.
- To learn more about the safety profile of alogabat.
- To learn how alogabat is handled by your body, how long it stays and how your body processes the drug until it is eliminated (this is called pharmacokinetics [PK]).

**How many participants will take part in this study?**

This study is looking for approximately 105 individuals with autism and 15 to 45 years of age. We expect to enroll about 15 participants at Rush University Medical Center.

**What are the activities you will be doing if you participate in this study?**

If you and your support person decide to take part in this study, you will be required to sign this informed consent form and follow the processes listed below:

- Keep your study appointments and complete all study assessments
- If you cannot attend an appointment, please contact the study personnel (i.e., the study doctor or research staff) as soon as possible to schedule a new appointment.
- Please inform study personnel about any symptoms, doctor's or nurse's appointments, or hospital admissions that you may have while participating in the study.
- Agree to remain on stable treatments (both behavioral and medications) throughout the study and not to start or change the doses or treatments you take. Your study doctor may suggest changes of your treatments in case you experience side effects to the study drug.
- Agree not to participate in any other research study
- Inform study personnel if you believe you might be pregnant
- Inform study personnel if you change your mind about participating in the study.
- Inform your primary doctor that you are taking part in this study
- Take the study drug as instructed
- Keep the study drug in a safe place, for your use only, and away from children.
- Return all study-related supplies, including any unused study drug
- Place a sleep sensor under your mattress (a movement sensor that you will receive at the clinic to record sleep behavior)
- Wearing the study smartwatch is optional; if you opt in, ensure you wear the study smartwatch for as long as possible every day (note that the watch displays the time but is otherwise locked and records various signals in the background; see below for more information)
- Complete all the at-home assessments and diaries; these are described in the assessment section
- Agree not to take herbal medicines or nutritional supplements unless they are allowed by the study doctor
- Agree not to drink grapefruit juice
- If you drink alcohol at all, you should avoid drinking alcohol as much as possible and, in any case, not drink more than 1 drink per week (for example, not more than 1 beer (12 ounces/350 mL) that isn't too strong or 1 glass of wine (approximately 3.5 ounces/100 mL) for the duration of the study because alcohol together with alogabat may cause drowsiness and dizziness (see "What are the risks and discomforts of participating in this study?" further below).
- You may start feeling unwell without warning (e.g., feel dizzy or sleepy) especially during the first week of taking the study drug. Therefore you must agree not to engage in any activities requiring complete attention, such as operating machinery, driving a car, or riding a bicycle during this first week of taking the drug and also if you feel unwell later on during the study.

You will also need one person who serves as your support person (for example a family member or a caregiver) and who will be able to accompany you to some clinic visits or possibly perform assessments from their home, answer some questions about you, and who will partner with you during the study.

***How will the study treatment be administered?***
Only you, the actual participant, but not the support person, will receive treatment.

Participants will be divided into 3 groups (to receive either a 20-mg dose of alogabat, a 60-mg dose of alogabat, or placebo). Each group will include about 35 participants. The purpose of these groups is to determine how different doses of alogabat affect individuals with autism, versus not taking alogabat.

You can participate in one group only. Alogabat and placebo will be given as tablets. If you participate in this study, you will take three tablets per day in the morning, preferably with food. You will take the first dose of study drug (three tablets) at the clinic at the Day 1 visit and then three tablets every day in the morning for 12 weeks preferably with food. Tablets can be swallowed whole or dissolved in a small amount of water or juice (except grapefruit juice, which is not allowed in this study). If you choose to dissolve the tablets in water, you will need to make sure you rinse any remaining drug left in the container with liquid and drink it immediately after it dissolves. During the study, your doctor could advise that you change the dosing time to the evening; please do so only if your doctor recommends it.

You will be given a study diary to record the time that you take study drug each day and the method used.

***Are you guaranteed to receive study drug?***
No. You will be assigned by chance to receive either study medication or placebo. This selection is done by a computer program, so it cannot be controlled by the study doctor.

***Will you know what you are receiving?***
No. You will be randomly assigned by a computer program to one of the following treatment groups: 20 mg of alogabat, 60 mg of alogabat, or placebo. When you are "randomized" into the study, this means that you are put into a group by chance (like tossing a coin). You will have a 33% chance of being placed in any one of the treatment groups and thus a 66% chance that you will receive active medication (alogabat) and a 33% chance that you receive placebo. Neither you nor your study doctor may choose the group you will be in or will know which treatment you receive. However, if your safety is at risk, your study doctor can find out which drug you are receiving.

***How long will you be in the study?***
If you qualify for study participation and you and your support person choose to participate, the total length of time in the study will be about 24 weeks (approximately 6 months). You and your support person will have the following visits at the clinic during the study:

- Screening Visit to check if you are suitable for the study. The Screening Visit can be split into 2 visits within 7 days.

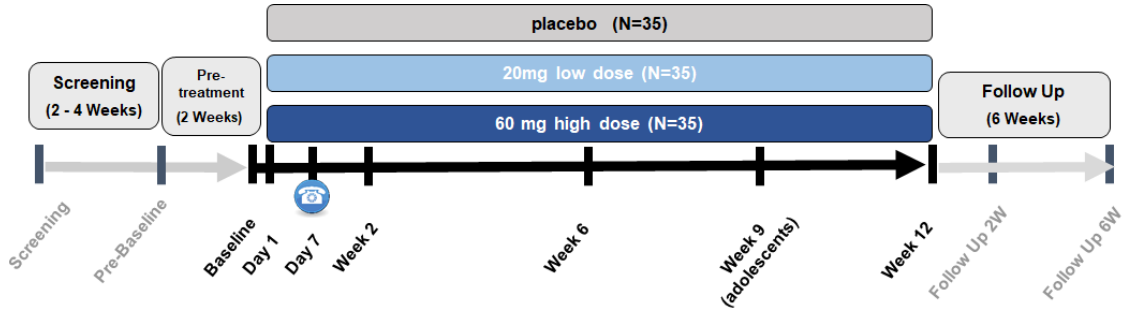
- Pre-baseline Visit (up to 4 weeks after the Screening Visit) for some initial tests and to familiarize yourself with some assessments that will be later part of other visits.
- Baseline Visit (about 2 weeks after the Pre-baseline Visit and up to 3 days before you start your treatment)
- Day 1 (start of your treatment).
- On-treatment visits at Week 2, 6, 9 (adolescent participants only) and 12.
    - At week 9 (adolescent participants only), you will come to the clinic or have a nurse visit you at home.
- After-treatment visits (also called follow-up visits) around 2 weeks and 6 weeks after you took the last tablet.

The pre-baseline, baseline, week 6, week 9 (adolescent participants only), week 12 and after-treatment visits can be split into two visits.

The same support person must attend all study visits where completion of questionnaires is needed so they can be filled out by the same person throughout the study. For the support person of adult participants with an IQ of 70 or higher, it may not be necessary to attend all study visits at the clinic if they opt to perform some assessments at home.

A member of the study team will contact you via phone on Day 7 to check on your health and any changes since the last clinic visit.

***Overview of the Study***




***What will happen if you decide to take part in the study?***

If you agree to take part in this research study, the study doctor will first need to conduct some "screening" tests and/or procedures on you and ask you some questions about your medical history, your history of autism, other psychiatric or nervous system conditions in your family, and what medications you take. Other information, including your age, sex, and race/ethnicity (if permitted) will be recorded.

Some of these tests or procedures may be part of your regular medical care and may be done even if you do not take part in this study.

The results of these screening assessments will determine whether or not you can take part in the study.

***Assessments During Screening Visit:***

- Discussion of the study, review and signing of this Informed Consent Form. No study tests or procedures will be done until you have been able to review and sign this Informed Consent Form and your support person has given their consent on their separate Informed Consent Form.
- A member of the study staff will ask you and your support person some general questions about your health, how you are affected by autism and the medications you are taking, if any.
- You will need to participate in some testing (such as an IQ test).
  One interview (so-called CY-BOCS-ASD) will be conducted with both your support person and you by video conference at the beginning of the study. The Sponsor will not participate in the video conference.
  See table "Summary Table with Types of Questionnaires" for more information about the questionnaires and assessments. Please ask the study doctor for more details about these questionnaires whenever you want.
- Physical examination: The study doctor will conduct a physical examination which will at least include your head, skin, eyes, ears, nose, throat, neck, lymph nodes, heart, lungs, stomach and gut, arms and legs, and nervous system. Your height and weight will also be measured.
- Vital Signs: This includes measurement of your heart rate, blood pressure, and body temperature. The blood pressure will be measured in two positions (supine/resting and standing).
- Electrocardiogram (ECG): An ECG is a measurement of the electrical activity of your heart, a test that tells how the heart is working.
- Blood collection: Approximately 32 mL of blood will be taken for screening tests, which equates to approximately 2.2 tablespoons of blood. Blood samples will be collected for:
  - Standard laboratory tests (includes blood chemistry, hormones, and blood cell counts).
  - Tests to check how quickly your blood clots.
  - Testing for viruses: human immunodeficiency virus (HIV), hepatitis B, and C, coronavirus (COVID-19) may be tested in blood and/or respiratory swab at screening and at any visit where the study doctor decides this is necessary.
- Urine samples will be collected for:
  - Standard laboratory tests
  - Drugs of abuse and alcohol tests.
- Pregnancy Test: A pregnancy test (if you can become pregnant) will also be conducted on your blood sample. If you are pregnant, you cannot participate in this study.
- Columbia Suicide Severity Rating Scale (C-SSRS): You will be interviewed by the physician with regard to suicide-related thoughts, feelings, or behavior. This interview will be conducted as a routine safety measure.

If you are eligible to continue in this study based on the screening tests, you and your support person will be notified by the study doctor that you can continue to participate in the study.

***Assessments at the Pre-baseline Visit***

- Electroencephalography (EEG) and eye-tracking assessments:
  An EEG measures your brain activity with electrodes attached to your head. Measuring your brain activity with electrodes is safe and not dangerous.
  For the EEG assessments, a study technician will attach about 30 electrodes to your head with a conductive gel. The EEG technician will part your hair and lightly scrub away dead skin. The conductive gel can be washed away with water or a special liquid cleaner once the test has been completed. Attaching the electrodes to your head can take between 15 and 45 minutes. The electrodes are connected to wires that run into a small machine.
  An eye-tracker measures the size of your pupils, eye movements, and where you look at in a computer screen, with cameras pointed to your eyes.
  Once set up, the actual EEG and eye-tracking assessment will take about 70 minutes (including breaks). The technician will give you instructions to complete several tasks that involve watching short clips, scenes, or moving objects on a screen in front of you or simply rest with eyes open or eyes closed.
- You and your support person will need to provide feedback and complete some questionnaires and assessments. Some questionnaires will be completed by a member of the study staff and others will need to be completed by you or your support person. The study doctor or study staff will ask you further questions for some questionnaires.
  See table "Summary Table with Types of Questionnaires" for more information about the questionnaires and assessments.
- A sleep mat, a study-specific smartphone and an optional watch will be handed out to you and explained in detail (see "Tests and Procedures at Home" below for more details). You and your support person will run through all smartphone tasks and get trained on how to handle and charge these devices. Additionally, you will receive written instructions for the use of these devices at home.

***Assessments at Baseline and During Study Treatment:***

During the study, you will undergo the following tests and procedures at the following study visits at the clinic (Baseline, Day 1, Week 2, Week 6, Week 9 (adolescent participants only) and Week 12) and on Day 7 the study team will call you by phone. Not all procedures are required at each visit (for details of when each assessment will be performed, see the Study Schedule table):

- Vital Signs: as described for Screening Visit
- ECGs: as described for Screening Visit
- Physical examination: as described for the Screening Visit
- You will be asked about your health and medications you are taking or may have taken at each visit.
- You and your support person will need to provide feedback and complete a few questionnaires and assessments at each study visit. Some questionnaires will be completed by a member of the study staff and others will need to be completed by you or your support person. The study doctor or study staff will ask you further questions for some questionnaires.
  See table "Summary Table with Types of Questionnaires" for more information about the questionnaires and assessments. Please ask the study doctor for more details about these questionnaires whenever you want.

Completing the questionnaires can be time consuming and could take as long as 4 to 5 hours at some visits.

- Blood collection: Approximately 81 (94 for adolescent participants) mL of blood will be taken over the period of study treatment, which equates to approximately 5.5 (6.3 for adolescent participants) tablespoons of blood. These blood samples are for:
    - Standard laboratory tests (include blood chemistry, hormones, and blood cell counts)
    - Coagulation (tests to check how quickly your blood clots)
    - Measuring the amount of study drug present in the blood
    - A blood sample for genotyping will be collected once (this is used to look for genetic factors that may help understand your response to treatment with alogabat or the levels of alogabat in your blood).

  For some of the blood samples, you may have the choice to have a nurse come to your home for taking the blood. If you agree to have a nurse coming to your home to perform the blood draws, please tick the appropriate box on the signature page at the end of this document. If you do not agree for the home visits, you will need to stay in the clinic for all the blood samples required in the study.
- Urine samples will be collected for:
    - Standard laboratory tests
    - Drugs of abuse and alcohol tests
- Hair samples (5 to 10 hairs) will be collected (if you are able to provide) to understand how your body processes chemicals from your own body and from the environment. The hair will be cut from the back of the head using scissors.
- Pregnancy Test: If you can become pregnant, a pregnancy test will be conducted on your urine sample at the baseline visit and during study treatment. If you receive a positive result on a urine pregnancy test, another test on your blood sample will be conducted to confirm the results. If you are pregnant, you cannot participate in this study.
- EEG and eye-tracking assessments: At the Week 12 visit, all but one of the EEG and eye-tracking assessments that were done at the Pre-baseline visit will be performed (see above).

  At the Day 1 and Week 2 visits a much shorter assessment of approximately 15 minutes (plus the time to prepare the EEG of 15 to 45 minutes) will be performed: EEG while resting with eyes open and eyes closed and following a symbol on the screen with the eyes. The Week 2 assessment is optional.

  At the Day 1 visit the short EEG assessment is performed twice, once before the first intake of the medication (this may be shifted to the Baseline visit if needed) and a second time about 3 to 4 hours after the intake of the medication. The EEG electrodes can be left in place between the two recordings.
- Columbia Suicide Severity Rating Scale (C-SSRS): as described for Screening Visit. During the study, if the study doctor is concerned about your safety, he or she will provide medical support and, if necessary, refer you to an emergency room or hospital for a psychiatric evaluation. This assessment is also performed by phone at the Day 7 visit.
- Run all smartphone tests in the clinic (please bring your study phone and study watch if applicable to each visit).
- On days of a study visit, the study drug will be taken at the clinic. On Day 1 and the Week 2 visit, the study drug should be taken with some food. Adolescent participants should take the drug with some food also on the week 6 and week 9 visits.

- For adolescent participants, after the first dose of study drug on Day 1, you will be monitored for a minimum of 7 hours on site and a set of assessments will be performed, including repeated measurement of vital signs. After this 7-hour period, the study doctor will decide whether you can be discharged or whether further on-site monitoring is required. You and your support person will be provided general instructions to follow during the study and in particular during the initial phase of the treatment period. The study doctor will also determine whether you have to stay at home for a 24-hour observation period after the initial study drug administration.

***Tests and Procedures at Home:***

The study-specific smartphone, optional watch and the sleep mat will be used to measure important aspects of your behavior at home, including your activities and some health-related signals:

- The optional smartwatch records your body movement, your pulse, the distance you travel, and how often you go to the same place, but it does not record the actual locations you visit. The smartphone records the volume of noise around the phone and the amount of time that people spend speaking, but it never records the actual words you or other people say except during the active tasks and conversation tasks. You can pause the sound and location recordings whenever you choose.
- Once at home, you should place the sleep mat under your mattress. The mat is very thin, and you will not notice it is there. The mat measures how you sleep (for example, how long it takes for you to fall asleep, how often you wake up during the night, and how much time you sleep in total).
- You should also complete three tasks per week and record a conversation with your support person on the smartphone at least once a week. The tasks take about five minutes in total and the conversation should also last around five minutes. You or your caregiver can choose to delete the conversation recording instead of saving it. There is also a monthly survey to complete. Staff at the study site will show you how to complete the tasks. (There is the option to complete some of the tasks more than once a week.)

When the data are saved, they are encrypted and sent for analysis by secure internet connections. "Encrypted" means that the data are encoded and can only be decoded by someone who has the right key (an encryption key).

Please bring the study smartphone and smartwatch (if applicable) with you to each clinic visit. You must return all equipment at your final visit to the clinic.

***What will happen when you stop taking study drug?***
You will be asked to come to the clinic twice (at approximately 2 and 6 weeks) after you have taken your final dose of study drug.

If your participation in the study is terminated earlier than planned, you will also have a visit at the time of withdrawal. This could be because you have had to stop treatment due to safety concerns, or you or your study doctor determines it is in your best interest to withdraw participation.

The following procedures will be done at the follow-up visits to the clinic after you stop taking study drug (for details of when each assessment will be performed, see the Study Schedule table):

- Physical examination: as described for Screening Visit except for height.
- Vital Signs: as described for Screening Visit.
- ECG: as described for Screening Visit. ECG measurements will be repeated 3 times.
- You will be asked about your health and medications you are taking or may have taken at each visit.
- You and your support person will need to provide feedback and complete a few questionnaires as described above for Assessments during Study Treatment.
  See table "Summary Table with Types of Questionnaires" for more information about the questionnaires and assessments.
- Blood collection: Approximately 17 mL of blood will be taken, which equates to approximately 1.1 tablespoon of blood. These blood samples are for:
    - Standard laboratory tests (include blood chemistry, hormones, and blood cell counts).
    - Coagulation (tests to check how quickly your blood clots).
    - Measuring the amount of drug present in the blood.
- Urine collection: Urine samples will be taken for standard laboratory tests.
- A hair sample will be taken to understand how your body processes chemicals from your own body and from the environment.
- Pregnancy Test: A pregnancy test (if you can become pregnant) will also be conducted on your urine sample. If you receive a positive result on urine test, another test on your blood sample will be conducted.

***Study Schedule***

| | Visits before start of treatment | | | Visits during treatment at Week: | | | | | | Visits during follow-up (after end of treatment) at Week: | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Screening** | **Pre-baseline** | **Baseline** | **1** | **1** | **2** | **6** | **9[a]** | **12** | **2** | **6** |
| | **D-42 to D-15** | **around D -14** | **around D-3 to D-1** | **Day1** | **Day 7** | **Day 14** | **Day 42** | **Day 63 [a]** | **Day 84** | **Week 12 visit + 14 days** | **Week 12 visit + 42 days** |
| **Assessment** | **At site*** ** | **At site*** ** | **At site*** ** | **At site** | **By phone** | **At site** | **At site*** ** | **At site or home** | **At site*** ** | **At site*** ** | **At site*** ** |
| Sign consent form | ✓ | | | | | | | | | | |
| Support person instructions ** | ✓ | | ✓ | | | | | | ✓ | | |
| Questions about medical history and about your life and activities | ✓ | | | | | | | | | | |
| Pregnancy test (person of child bearing potential only) | ✓ | | ✓ | | | | ✓ | ✓ | ✓ | | ✓ |
| Questions about other medicines and changes to health and life | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Physical examination | ✓ | | | | | | | | ✓ | | ✓ |
| Vital signs | ✓ | | | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| ECG (heart beat recording) | ✓ | | | ✓ | | ✓ | | ✓ | ✓ | ✓ | |
| Questionnaires**** | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | | ✓ | ✓ | ✓ |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Hand-out / return of study equipment (sleep mat, study smart phone and watch) | | ✓ | | | | | | | | | ✓ |
| EEG (brain activity recording) and eye-tracking plus associated tests | | ✓ | | ✓ | | ✓**** ** | | | ✓ | | |
| Blood samples* | ✓ | | ✓ | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ | |
| Urine sample | ✓ | | ✓ | | | ✓ | ✓ | ✓ | ✓ | ✓ | |
| Hair sample ***** | | | ✓ | | | | ✓ | | ✓ | | ✓ |
| Dispensing and/or return of study medication | | | | ✓ | | ✓ | ✓ | | ✓ | | |
| Sleep mat, study smart phone and optional watch tasks and monitoring | | ✓ | | | | | | | | | |

* Blood samples will be used for various tests at different visits. See the Study Assessments section for more details.

** The support person instructions will be administered to you by a study team member and may be audio recorded for quality control purposes.

*** These visits may be split into 2 days.

**** Not all questionnaires are done on all days One test belonging to the Neurocognitive battery (see table below) will comprise a follow-up test over the phone approximately 24 h after the on-site test (except if you come to the clinic on 2 consecutive days). Some tests might be done remotely from the study participant's hone if they have a suitable computer.

***** Hair samples are collected from the study participant. In addition, optional hair samples are collected from the caregiver (if consent is given in the applicable Informed Consent Form).

****** This assessment is optional.

[a] Week 9 visit is for adolescents only and can be done at site or at home (see "Consent for Optional Home Visit at Week 9")

| *Summary Table with Types of Questionnaires* | | | | |
|---|---|---|---|---|
| **Scale Group** | **Specific Scale** | **Completed by** | **Time [min]** | **Objective** |
| **Assessments done at Screening only** | | | | |
| **WASI-II** | | Study staff | ~ 30 | An IQ test that measures how you learn. A research team member will conduct the test and ask you to do different activities related to thinking and memory. |
| **ADOS-2** | | Study staff | 35 - 40 | Diagnostic test |
| **SRS-2** | | Support person | 15 - 20 | A questionnaire about your social skills |
| **CY-BOCS-ASD** | | Central rater | ~ 20 | Study partner and participant questionnaire to check repetitive behaviors |
| **Assessments at Pre-baseline and during and after Treatment** | | | | |
| **C-SSRS** | | Study staff | 5-10 | An interview to assess your suicide-related thoughts, feelings or behaviors. |
| **Vineland™-3 (survey)** | | Central rater | 45 – 80 (+20 to 30 min preparation and introduction time) | Interview with your support person about your behaviors and social skills (such as communication, daily living skills, and socialization).<br>The interview will be administered to your support person by a study team member and may be audio-recorded for quality control purposes. |
| **Repetitive Behavior** | RBS-R | Support person | ~ 15 | A questionnaire to check repetitive behaviors |
| | CRRI | Support person | ~ 17 | A questionnaire to check repetitive behaviors |
| **CGI-S Interview** | | Study staff | ~ 30 | Evaluation of the severity of your condition based on an interview done by the study doctor with you and your support person |
| **CGI-S + CGI-I (after initial pre-baseline interview)** | | Study staff | ~15 | Evaluation of the severity of your condition and change during the study based on an interview done by the study doctor with you and your support person |
| **Anxiety** | BAI | Participant | ~ 5 | A questionnaire to assess your levels of anxiety |
| | PRAS-ASD | Support person * | ~ 10 | A questionnaire to assess your levels of anxiety |

| *Summary Table with Types of Questionnaires* | | | | |
|---|---|---|---|---|
| **Scale Group** | **Specific Scale** | **Completed by** | **Time [min]** | **Objective** |
| **Sensory Sensitivities** | Adolescent/Adult Sensory Profile | Participant | 10 - 15 | A questionnaire to measure how sensitive you are to sensory stimuli |
| | SSP-2 | Support person * | ~ 7 | A questionnaire to measure how sensitive you are to sensory stimuli |
| **PedsQL** | Generic Core and Cognitive Functioning Scales | Participant and support person for those with IQ < 70 | ~ 10 | A questionnaire to evaluate your quality of life such as how much of a problem you have had (if any) with your health and activities, your feelings, how you get along with others and your work/studies. There are also some questions about your memory and cognitive functioning. |
| **Neurocognitive battery** | | Participant | ~ 50 | A set of computerized tests the study staff will do with you to assess your memory |
| **Sleep** | PROMIS Sleep Disturbance Questionnaire | Participant and support person for adolescent participants and those with IQ < 70 | ~ 5 | Two questionnaires to evaluate your quality of sleep and to assess how much of a problem you have had (if any) with your attention and activities during the day |
| | PROMIS Sleep-related Impairment Questionnaire | Participant and support person for adolescent participants and those with IQ < 70 | ~ 5 | |
| | Karolinska Sleepiness Scale | Participant and support person for adolescent participants and those with IQ < 70 | ~ 5 | A questionnaire to evaluate if you are feeling sleepy at a particular time during the day. |
| | Epworth Sleepiness Scale (ESS, for adults) or ESS for Children and Adolescents (ESS-CHAD) | Participant and support person for adolescent participants and those with IQ < 70 | ~ 5 | A questionnaire to evaluate if you are feeling sleepy in certain situations over the last month or since the last visit. |
| | Sudden Onset of Sleep Questionnaire | Participant and support person for adolescent participants and those with IQ < 70 | ~ 5 | A questionnaire to evaluate if you are feeling sleepy or have suddenly fallen asleep over the last 6 weeks or since the last visit. |

| *Summary Table with Types of Questionnaires* | | | | |
|---|---|---|---|---|
| **Scale Group** | **Specific Scale** | **Completed by** | **Time [min]** | **Objective** |
| **Entry and exit questions** | | Support person | ~ 5 | Entry questions at the beginning of the study, support persons will be asked about which aspect of autism of the person they support they would want to see improve during the study.<br>Exit questions at the end of the study, support persons will be asked to report if they observed any changes during the study that were important in the your autism and behaviors. |

ADOS-2 = Autism Diagnostic Observation Schedule, Second Edition; BAI = Beck Anxiety Inventory; CGI-I = Clinical Global Impression-Improvement Scale; CGI-S = Clinical Global Impression-Severity Scale, CRRI = Caregiver-Reported Routines Inventory; C-SSRS = Columbia-Suicide Severity Rating Scale; CY-BOCS-ASD = Children's Yale-Brown Obsessive Compulsive Scale Modified for ASD; ESS= Epworth Sleepiness Scale; ESS-CHAD = Epworth Sleepiness Scale for Children and Adolescents; PedsQL = Pediatric Quality of Live Inventory; PRAS-ASD = Parent-rated Anxiety Scale for ASD; PROMIS = Patient-Reported Outcomes Measurements Information System; RBS-R = Repetitive Behavior Scale-Revised; SRS-2 = Social Responsiveness Scale, Second Edition; SSP-2 = Short Sensory Profile, Second Edition; Vineland- 3 = Vineland Adaptive Behavior Scales, Third Edition; WASI-II = Wechsler Abbreviated Scale of Intelligence, Second Edition.

* If you are not able to complete the BAI, adolescent/adult sensory profile, and PROMIS Sleep Disturbance and Sleep-Related Impairment self-reported versions, your support person will complete some forms instead (PRAS-ASD, SSP, PROMIS Sleep Disturbance and Sleep-Related Impairment support person-rated short forms).

**Does this study involve tissue/blood banking?**
Yes. Banking is the long-term storage of tissue and/or blood samples into a repository (or sample bank) for future use and/or research.

Samples collected for study-related analyses will be stored until the study results have been reported, with the following exceptions:

- Blood samples collected to measure the amount of drug present in the blood and hair samples to understand how your body processes chemicals will be stored for up to 2 years after the study results have been reported and, during this time, may be used for additional analyses and/or for improvement of the testing assays and exploratory experiments.
- The blood sample for genetic analysis will be stored for 5 years after the study results have been reported.

In addition, you may also choose to donate your leftover samples for future research, as described in the last section of this Informed Consent Form (see "Consent for Optional Collection of Samples for the Research Biosample Repository").

If you withdraw from the study, any sample collected prior to your withdrawal may still be analyzed as described in the Informed Consent Form, unless you specifically ask for your samples to be destroyed or local laws require destruction of the samples.

**Does this study involve genetic testing?**
Yes, this study involves genetic testing to possibly identify subgroups of individuals with autism in order to tailor future treatments to fit each person's individual characteristics. For example, researchers may check whether participants with certain genes linked to Autism show greater benefit from the drug than other participants.

The use of genetic material in research to study the causes of disease and to help understand how individuals respond to drug treatments is called genetic research. The cells of our body contain a molecule called deoxyribonucleic acid (DNA). DNA is received from our parents and carries a code in the form of genes, which determine our physical characteristics such as the color of our hair and eyes. Ribonucleic acid or RNA for short also acts as a messenger to tell our cells to produce certain features. Just as differences in our genetic codes help explain why we all look different, these differences can also help explain why some people develop certain diseases and others do not. They may also help explain why some drugs are safe and effective for some people but not for others and may provide new avenues for drug development and personalized therapies.

**What do you need to know regarding the collection of biospecimens?**
In this study, when we refer to biospecimens, we are referring to blood and hair samples.

Biomarkers are biological markers in the body that can be measured and used to explain how the body responds to a treatment. By looking at biomarkers in this study, Roche tries to understand if your autism characteristics are different from other people's autism characteristics and if there is

a way to tailor future treatments to fit each person's individual characteristics. Examples of biomarkers are proteins found in blood, or variations in a person's individual genes (DNA).

Your blood sample may be analyzed for your genetic material (DNA and RNA), which serves as an "instruction book" for the cells that make up your body. Data from large numbers of autistic individuals may help researchers to learn how variations in the sequence of genes might affect a disease or a person's response to a treatment, may identify possible links among diseases, and may provide information for drug research and personalized therapies. Toward this goal, a technique called whole genome sequencing (WGS) may be performed on your blood sample at the end of the study to allow for exploration of broad health research questions across disease areas. Information from the WGS analysis will not be made available to you or to the study doctor, unless required by law. Information from the testing will not be part of your medical record and will not be given to your insurance company or employer.

Similarly, your hair samples will be used to understand how your body processes chemicals from your body and from the environment. This information may help researchers better understand which individuals with autism are most likely to benefit from the study drug, and it may support the development of novel therapies in the future. Information from the hair analysis will not be made available to you, your doctor, or your support person, unless required by law. To protect your privacy, information from the testing will not be part of your medical records and will not be given to your insurance company or employer.

You may not benefit from the results of the biomarkers tested in this study since it may take several years for the results to be available. However, it is possible that the treatment of autistic individuals can be improved based on the biomarkers that are evaluated in this study.

**Will your information or biospecimens be used for research in the future?**

You may choose to participate in an additional optional research biosample repository for future research. More information is provided in the "Consent for Optional Collection of Samples for the Research Biosample Repository" at the end of this document.

**Will your cells, tissues, blood or other biological materials (biospecimens) be used to develop commercial products?**

Information from this study, including information from research on your samples, may lead to discoveries and inventions or development of a commercial product. The rights to these will belong to Roche. You and your family will not receive any financial benefits or compensation from, or have rights in, any developments, inventions, or other discoveries that might come from this information.

**What are the risks and discomforts of participating in this study?**

You may have side effects from the medications or procedures used in this study. However, Roche, the study doctor, and other doctors do not know all of the side effects that could occur. Side effects can vary from mild to very serious and may vary from person to person. Many side effects go away soon after you stop what is causing them. In some cases, side effects can be serious (in very rare cases may be fatal) and may be long-lasting or may never go away. You

should talk to your study doctor about any side effects you have while taking part in the study. Everyone taking part in the study will be watched carefully for any side effects, and cared for as appropriate. Your study doctors may give you medications to help lessen side effects.

**Allergic Reactions**
Allergic reactions can occur with any drug and this can be in the form of itching, difficulty breathing, and a skin rash and/or drop in blood pressure. In very rare cases, you could suffer a life-threatening allergic reaction. If you do experience any such reaction, you should tell your study doctor immediately so that you can receive the appropriate treatment.

**Side effects Observed with Alogabat**

In studies in humans, up until now, more than 100 healthy persons have been dosed once or multiple times with alogabat. No serious side effects have been reported in these studies. The most common side effects observed with alogabat, and which you may also expect if you participate in this study, are:

- Somnolence (feeling sleepy)
- Headache
- Fatigue (feeling tired)

Available data from studies in humans do not show is a risk for side effects concerning the gastrointestinal tract (stomach and bowels); however you should inform your study doctor if you experience any gastrointestinal events (e.g., nausea, vomiting, and abdominal pain) during the study.

Other side effects like sudden onset of sleep, dizziness, nausea, memory impairment, disturbance in attention, and muscle pain have also been observed in studies in humans.

The side effects mentioned above were mainly mild in intensity with the exception of four events of moderate intensity (headache and somnolence, each in two participants) and one event of severe intensity (somnolence). The severe event of somnolence happened following a single dose of 375 mg alogabat, a dose 6 times higher than what is tested in this study, along with nausea (moderate) and muscle twitching (moderate). At the high dose of 375 mg, one event of low blood pressure (moderate) was also observed.

Somnolence was reported in all healthy volunteer studies, in 44.7% of participants treated with alogabat receiving either a single or multiple doses of the study drug. The majority of these events were of mild intensity. At the time of writing, two events of somnolence (one of mild intensity and one of moderate intensity) have been reported in this study. Somnolence usually resolved within 48 hours in healthy volunteers, however, a duration of up to 3 months was observed in this study.

In the study with healthy neurotypical participants treated with multiple doses of 20 and 50 mg alogabat, mild increases of liver test values were observed in 2 out of the 8 participants in each

dose group. These elevations of liver tests were not observed in groups at higher doses (100 mg and 200 mg). Participants did not experience any associated signs or symptoms and the liver function was not changed. The affected liver enzymes slowly returned to normal values within 20 days after the study. This means that there is no irreversible damage on the liver. It is unclear whether the increase of the liver enzymes was caused by alogabat. Nonetheless, we will monitor the liver enzymes regularly. If an increase of the liver enzymes is noticed, we will take appropriate actions. For example, you could be referred to the hospital for extra investigations into your liver function.

An ECG change (prolongation of the QT interval) which could cause an abnormal heart rhythm has also been seen in the study with one or multiple doses, at higher concentrations of alogabat than expected in this study. Your ECG recordings will be monitored during the study.

There are other side effects which may occur a few days or weeks after stopping alogabat. These side effects, such as sleeping difficulties, being irritable (touchy, excitable) or trembling have not been observed before but they may occur after the end of alogabat intake. Therefore, please tell the study doctor about all side effects not only during the treatment duration but also those occurring after stopping the medication.

Alogabat, when administered to young rats (corresponding to approximately 1-2 years old in human age), caused a delay in sexual maturation in male rats. However, this finding had no effects on their fertility after dosing was stopped and was not observed in adult animals.

**Risks Associated with Study Procedures**

***Blood Sampling***

During this study, small amounts of blood will be drawn from a vein and used for tests that allow your study doctors to see how you are doing. Drawing blood may cause pain where the needle is inserted, and there is a small risk of bruising or infection at the place where the needle is inserted. Very rarely, a blockage of the vein or a small nerve injury can occur, resulting in numbness and pain. However, this will resolve with time. Some people experience dizziness, upset stomach, or fainting when their blood is drawn.

On days when several blood samples will be taken, we may use a cannula (small plastic tube) inserted in your arm using a small needle, so you only get a needle prick once. This cannula may remain in place for the day and will be taken out before you go to bed at night. There is a small chance of infection by placing the cannula in your arm, but every medical precaution will be taken to avoid an infection.

***Electrocardiogram (ECG)***

You will have small, soft electrodes or pads, placed temporarily on different parts of your body. There is no pain or discomfort during an ECG; however, the area of skin in which the ECG pads will be stuck may need to be shaved, and the pads may cause a skin reaction such as redness or itching. Taking the pads off may cause localized irritation to the skin and/or hair loss, similar to having a bandage taken off.

***Electroencephalography (EEG)***
The procedure of mounting the EEG and wearing the EEG electrodes may sometimes cause side effects including headache, scalp discomfort at the site of stimulation, and tingling. Electrodes will not leave any permanent damage but after the procedure you may see spots on your skin where the electrodes were. After the procedure you may need to wash your hair to remove the gel. The gel is not toxic, but may rarely cause an allergic reaction on the skin in the form of a rash. Recording an EEG does not pose any danger to your brain.

***Devices***
The tests and procedures at home using the study smartphone, optional watch and sleep mat are not expected to cause you harm or major inconvenience.

***Questionnaires***
Filling out the questionnaires or answering the study doctor or study staff's questions could lead you to feel tired, uncomfortable, or upset. Please tell the study doctor or study staff if you feel uncomfortable or upset while filling out a questionnaire or answering questions. You have the right to refuse to answer any questions.

**Reproductive Risks**
***Reproductive Risks for Persons of Child-Bearing Potential (POCBP)***
If you are pregnant or become pregnant, or if you are currently breastfeeding, you cannot take part in this study because you or your child may be exposed to an unknown risk.

If you are able to become pregnant, you must have a blood test that shows you are not pregnant before you can be enrolled in this study. You may also have further pregnancy tests during the course of the study. If the blood test is positive, you will not receive any more study medication.

If you can become pregnant, you must agree to remain abstinent or use birth control methods that are judged to be effective by your study doctor during this study and/or within 28 days after your final dose of study treatment. Check with your study doctor about the methods of birth control to use.

Tell your study doctor right away if you suspect that you have become pregnant during this period. The study doctor will want to follow up with you on the outcome of the pregnancy and collect information on the baby.

***Reproductive Risks for Biological Male Participants***
There are no reproductive risks for biological male participants in this study.

***Possible Risks Associated With Loss Of Privacy***
Although your genetic information will not contain any personal identifying information, there is a very small risk that it could be linked to an outside public database and used to help identify you and your blood relatives. Because some genetic differences can help to predict future health problems experienced by you or your blood relatives, this information might be of interest to health care providers, life insurance companies, and others. It is possible that your genetic

information could be used in ways that would cause you or your family distress, such as by revealing that you or a blood relative carries a genetic disease.

Your privacy is very important, and Roche uses many safeguards to protect your privacy. However, there is no guarantee that your identity will never become known. Refer to the "What are the risks involving genetic information?" below and "What about confidentiality of your medical information?" section for information about laws that protect against certain genetic discrimination.

There may be other risks that may happen that we cannot predict.

**What are the risks involving genetic information?**

While we believe that the risks to you and your family are very low, we are not able to know all of the risks from taking part in genetic research. Your privacy will be protected to the fullest extent possible. Information from the genetic testing being done under this study will not be part of your medical record and will not be given to your insurance company or employer. Certain health concerns that affect you and your blood relatives might be found as inherited traits are studied. Even though your genes are unique, you share some of the same genes with your blood relatives. Genetic information is considered health information and is protected under the Health Insurance Portability and Accountability Act (HIPAA) as is your other health information. While very rare, information could be misused by employers, insurance companies and others. For example, life insurance companies may charge a higher rate based on this information. A federal law called the Genetic Information Non-Discrimination Act (GINA) should help lower the risk from unfair health insurance or employment policies. To learn more about the GINA Law, please go to http://www.ginahelp.org/GINAhelp.pdf or ask the study staff.

**What if there is new information that may affect your decision to participate in this study?**

During the study, you will be told in a timely manner about new information or changes in the study that may affect your health or willingness to continue in the study.

When informed of this new information, if you agree to continue in the study, you may be asked to sign an updated consent form.

**Will you receive your individual results from the study?**

Generally, activities performed are for research purposes. We may learn things about you from this study which could be important to your health or treatment. If this happens, some information may be able to be shared with you, such as results of your laboratory tests.

**Can you leave or be removed from this study?**

Yes. You can decide to stop participating at any time. Tell the study doctor if you are thinking about stopping or decide to stop. The study doctor will tell you how to stop safely. If you leave this study, you will not lose access to any of your regular care.

The study doctor may stop you from taking part in this study at any time, even if you want to continue, for reasons that include but are not limited to the following:

- Your safety would be at risk if you continued in the study.
- You failed to adequately follow instructions or procedures.
- You need a treatment that is not allowed by the study.
- The study has been cancelled.

When your participation ends, no new health information will be collected about you. However, Roche will still be able to use any health information about you that has already been collected during this study.

**What about confidentiality of your medical information?**

This authorization is voluntary. Rush University Medical Center and its affiliates ("Rush") will not withhold or refuse your treatment, payment, enrollment, or eligibility for benefits if you do not sign this authorization. You do not have to sign this authorization, but that means that you cannot be in the study or receive study-related treatment.

By signing this document, you voluntarily authorize (give permission to) Dr. Zajecka, his study team, and other Rush personnel involved with the conduct and review of this study (which may include off-site personnel) to use or disclose (release) health information that identifies you for the study described in this document.

During the study, Dr. Zajecka and his study team will collect Protected Health Information (PHI) about you for the purposes of this research. PHI is your health information that includes your medical history and new information obtained as a result of this study. Some of this information will come from your medical record. The health information that Rush may use or disclose for this research includes:

- Information in your medical record, which is held by the study site.
- Information that is collected or produced during this study, such as results of tests, examinations, study procedures and your response to the study drug ("study data"), which is held by the study site, Roche, Roche affiliates and Roche's representatives (people and companies who work for Roche)
- Other personal information (such as social security number, medical record numbers, date of birth, etc).

Dr. Zajecka and his study team may share your health information and the results of your study-related procedures and tests with people outside of Rush who assist with the conduct and review of this study. The persons who receive your health information may not be required by Federal privacy laws to protect it and may share your information with others without your permission, but only if permitted by the laws governing them. Your health information described above may be used by or disclosed to:

- To the researchers

- The study sponsor (Roche) and its representatives (such as study monitors and auditors), collaborators, licensees and affiliates
- Q2 Solutions (laboratory test vendor)
- ERT (ECG vendor)
- Cogstate (computerized test vendor)
- Clinical Ink (data capture platform)
- Greenphire (provides travel services and reloadable debit card program for reimbursements)
- Biotrial (providing EEG and eye tracking equipment and result analysis)
- Global Care (nursing vendor)
- Endpoint (drug assignment and supply monitoring vendor)
- Monitoring and regulatory agencies such as the FDA and the Rush Institutional Review Board (IRB).

While you participate in the study you will have access to your medical record, but Dr. Zajecka is not required to release to you study information that is not part of your medical record. Rush is required by law to protect your health information, and study records that identify you will be kept confidential. The results of study tests/procedures performed as part of this study may become part of your medical record. Any study information in your medical record will be kept indefinitely. If audio recordings were made as part of this study, they will be destroyed 15 years after study completion on approval by Roche. Your identity will not be revealed on any report or publication, or at scientific meetings.

If you no longer want to be in the study and do not want your future health information to be used, you may change your mind and revoke (take back) this authorization at any time by writing to Dr. Zajecka at Rush University Medical Center, Treatment Research Center, 1645 W. Jackson Blvd., Suite 600, Chicago, IL 60612. If the authorization is revoked, you will no longer be allowed to participate in the study and Roche and previously authorized individuals/entities may still use or disclose health information that they have already obtained about you as necessary to maintain the integrity or reliability of the current study.

This authorization is valid for the entirety of this research study. It will expire upon completion of the study or if you revoke (take back) the authorization.

If you withdraw from this study, the data already collected from you may not be removed from the study records. The study doctor and/or study team may ask you whether they can continue to collect follow-up data on you. If follow-up information will be requested, you will be asked to sign a separate consent form before this information can be collected.

Records of participation in this study will be maintained and kept confidential as required by law. Your study data, including audio recordings and samples, will be labeled with a participant identification (ID) number that is unique to you but is not related to or derived from information that identifies you (such as your name, your picture or any other personally identifying information). Roche and its affiliates and representatives will only have access to study data and samples labeled with a participant ID number, except as described above.

If we discover during the study that you have tested positive for a reportable infectious disease (HIV and/or hepatitis), we will be required to report such findings to the Illinois Department of Public Health, according to applicable Illinois laws. The study doctor will refer you to a doctor for counseling and treatment. The Sponsor, Roche, will not cover the cost of this treatment or further care. This means that along with the test result your personal information (name, birth date, phone number and address) will be released to the public health authorities.

The Rush Institutional Review Board (IRB) will have access to your files as they pertain to this research study. The IRB is a special committee that reviews new and ongoing human research studies to check that the rules and regulations are followed regarding the protection of the rights and welfare of human participants.

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. This research study can be found by searching for the following Clinical Trial Registry Number (NCT#): NCT04299464.

**What are the costs to participate in this study?**

You will not be charged for the study drug (alogabat or placebo) while you are participating in this study.

Also, all procedures that are required only for this study (such as study visits, questionnaires and assessments, laboratory tests, ECGs, etc.), and that are not part of your regular medical care, will be provided to you at no charge.

You or your health plan will need to pay for medicines and clinic, hospital, and doctors' services that are part of your regular medical care, as well as any emergency room visits if the study staff refers you at the screening visit for psychiatric evaluation or treatment. Some health plans will not pay these costs when an individual is taking part in a research study. You should contact your insurance provider to verify coverage. If you have health insurance, the insurance may or may not pay for the costs associated with your participation in this study. You will have to pay for any co-payments, deductibles or co-insurance amounts that your insurance coverage requires.

After your participation in the study ends, you or your health plan will continue needing to pay for medicines and clinic, hospital, and doctors' services that are part of your regular medical care.

**Will you be paid for your participation in this study?**

Information from this study, including information from research on your samples, may lead to discoveries and inventions or development of a commercial product. The rights to these will belong to Roche. You and your family will not receive any financial benefits or compensation from or have rights in any developments, inventions, or other discoveries that might come from this information.

You will be reimbursed up to $150.00 for each on-site study visit that you complete in the main study (including the screening visit), up to a maximum of $1350.00 (USD) if you are an adult participant and $1500 (USD) if you are an adolescent participant. Your support person will be reimbursed $125.00 for each on-site study visit they attend with you (including the screening visit) up to a maximum of $1125.00 (USD) for supporting an adult participant and $1250.00 (USD) for supporting an adolescent participant.

These stipend amounts are reimbursement for study-related expenses incurred by you as the study participant and your support person. This includes expenses such as:

- Meals for you and your support person
- Public/personal transportation services, such as: bus, train, taxi, car services
- Tolls (if applicable) and mileage if you or your study partner drive.

The sponsor for this clinical research study has contracted with a third-party company to provide reimbursement via a reloadable debit card, which can be used anywhere major credit cards are accepted. Amounts are based on regulatory guidelines and approved by the study staff at the study site.

Parking at the study site location will be provided at no cost to you or your study support person.

You, as the study participant, will also be reimbursed for activities on the Wavelength app. This will be a one-time payment of up to $60 USD. At every study visit you will get feedback on your adherence with your tasks. After completing the study and based on your overall adherence during the whole study, the total amount due will be issued to the reloadable debit card that has been provided to you.

No additional reimbursement will be provided.

You do not need to submit any documents in order to get reimbursed as described above. We are, however, required to collect your social security number in order to make payments to you for study participation and for potential tax reporting purposes to the United State Internal Revenue Service (IRS).

Travel Assistance and Participation Support Services may be able to arrange lodging and transportation services in certain circumstances. Please talk to the study staff to learn more.

**Additional Program Information**

Should you decide to utilize Travel Assistance and Participation Support Services at any point during your participation in the clinical research study, you are agreeing to share the relevant contact/personal information needed to provide these services. Your data will only be used for program purposes and will be protected in accordance with international data privacy standards. Your data may be transferred out of the country that you reside in and/or the country where your

study site is located. Please be assured that all organizations involved in the debit card programs are committed to protecting your data privacy. At any time, should you wish to review information you have provided and/or request a change or deletion, or object to the processing of your information, please speak with your study site staff to coordinate this.

**What if you are injured as a result of your participation in this study?**

It is important that you tell your study doctor, Dr. Zajecka, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him at 312-942-5592 or 312-980-0585 (24-hour answering service).

You will get medical treatment if you are injured as a result of taking part in this study. Your study doctor will explain the treatment options to you and tell you where you can get treatment.

Roche will pay for the reasonable costs of immediate care for any physical injury to you that specifically results from the study medication, but only if:

- Roche and the study doctor agree that your injury resulted from the study drug medication and not from a preexisting medical condition.
- Your injury did not result from a failure to follow study protocol or instructions, or from the negligence, mistakes, or misconduct of the study personnel.

If you seek treatment on your own and your insurance is billed and pays for any of that treatment, Roche will cover costs not paid for by your insurance.

You will not receive any other kind of payment.

If you get injured in this study, you will not lose any of your legal rights to seek payment by signing this form.

Rush University Medical Center has no program for financial compensation or other forms of compensation for injuries which you may incur as a result of participation in this study.

**What other information should you know about?**

***Investigator Dual-Role***

If your health care provider is an investigator on this research study, he or she is interested in both your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may ask for a second opinion about your care from a clinician who is not associated with this study. You are not obligated to participate in any research study offered by your clinician. The decision to not participate will not affect your clinical care now or in the future.

***Additional Information About Your Study Data***

Your privacy is very important, and Roche uses many safeguards to protect your privacy, in accordance with applicable data privacy laws and laws related to the conduct of clinical trials.

Roche, Roche affiliates, and Roche's collaborators and licensees may use study data labeled with your participant ID number. Your study data may also be shared with independent researchers or government agencies, but only after personal information that can identify you has been removed. Your study data may be combined with other people's data and/or linked to other data collected from you. Your study data may be used to help better understand why people get diseases and how to best prevent, diagnose, and treat diseases, and to develop and provide access to new medicines, medical devices, and health care solutions.

Your permission for the study sponsor to use and share your health information does not have an expiration date. Study data will be retained by Roche for a period of 25 years after the final study results have been reported or for the length of time required by relevant national or local health authorities, whichever is longer. No records may be destroyed during the retention period without the written approval of Roche. Rush will retain your study data for a period of at least 15 years after completion or discontinuation of the study, or for the length of time required by relevant national or local authorities, whichever is longer.

You have a right to inspect and copy the information to be disclosed with this authorization and you may obtain a copy of the information by contacting the office listed on page 1 of this consent. You have the right to see and get a copy of your medical records kept by the study site that are related to the study. However, by signing this consent form, you agree that you generally will not be able to review or receive some of your records related to the study until after the entire study has been completed. This is to protect the scientific integrity of the study.

Your information will not be given to your insurance company or employer, unless required by law. If the results from this study are published in a medical journal or presented at a scientific meeting, you will not be identified.

***Study Results***

A clinical study report containing the results of this trial will be made available to anyone who requests a copy. Before this report is provided, additional steps will be taken to protect your information from being linked to you.

***Medicare***

If you are eligible for Medicare, federal law requires Roche to inform the Centers for Medicare & Medicaid Services (CMS, the agency responsible for administration of the Medicare program) if Roche is going to reimburse you for patient injury expenses. To comply with a Medicare reporting obligation, Roche or its representative may need to collect and share certain personal information about you, such as your name, date of birth, sex, social security number, and Medicare ID number (if you have one) with CMS.

**Who can you contact for more information about this study?**

Questions are encouraged. If you have further questions about this study, you may call Dr Zajecka at 312-942-5592 or email him at john_zajecka@rush.edu.

**Who can you contact if you have concerns about your rights as a study participant?**
Questions about the rights of research participants may be addressed to the Rush University Medical Center Office of Research Affairs at 1-800-876-0772.

**What are your rights as a study participant?**
Taking part in this study is voluntary. If you decide to take part in this study, you may leave the study at any time. If you choose not to participate in this study or to leave the study at any time, your health care, benefits or relationship at Rush University Medical Center will not change or be affected. No matter what decision you make, there will be no penalty to you. You will not lose any of your regular benefits, and your standard medical care will not be affected.

If you choose to leave this study and you do not want any of your information to be used, you must inform Dr. Zajecka in writing at the address on the first page. Dr. Zajecka may still use your information that was collected prior to your written notice.

I agree to home visits for blood sampling (if I do not agree, then all samples that are needed will be taken at the clinic): ☐ Yes ☐ No

**SIGNATURE BY THE PARTICIPANT OR THE PARTICIPANT'S LEGAL REPRESENTATIVE:**
By signing below, you are consenting to participate in this research study. You have read the information given or someone has read it to you. You have had the opportunity to ask questions, which have been answered satisfactorily to you by the study staff. You do not waive any of your legal rights by signing this consent/authorization form. You will be given a signed copy of this document.

_____
Name of Participant

_____ _____
Signature of Participant Date of Signature

_____ _____
Signature of Parent, Guardian or Legal Representative (if applicable) Date of Signature

_____ _____
Minor Assent (if applicable) Date of Signature

**SIGNATURE BY THE INVESTIGATOR/INDIVIDUAL OBTAINING CONSENT:**
I attest that all the elements of informed consent described in this consent document have been discussed fully in non-technical terms with the participant or the participant's legally authorized representative. I further attest that all questions asked by the participant or the participant's legal representative were answered to the best of my knowledge.

_____ _____
Signature of Individual Obtaining Consent Date of Signature

**SIGNATURE BY WITNESS:**
I observed the signing of this consent document and attest that, to the best of my knowledge, the person signing the consent form is the participant or the participant's legally authorized representative, and the person signing the form has done so voluntarily.

☐ Check here if a separate witness signature is not necessary.

_____
Name of Witness

_____ _____
Signature of Witness Date of Signature

## CONSENT FOR OPTIONAL COLLECTION OF SMARTWATCH DATA

**Why are these procedures being performed?**
You are being asked to optionally use a study smartwatch in Study BP41316. The smartwatch records your body movement, pulse, distance you travel, and how often you go to the same place, but it does not record the actual locations you visit.

Taking part in optional procedures is entirely voluntary. No matter what you decide, it will not affect your participation in the main study or your medical care.

**What will happen if you take part?**
If you agree to take part, you will be asked to wear the smartwatch daily and charge it overnight as described earlier in this consent form (see "What will happen if I decide to take part in the study?").

**What are the possible side effects or risks?**
Wearing the smartwatch is not expected to cause you harm or major inconvenience.

**Are there benefits to taking part?**
You will not receive any direct benefit from using the smartwatch. However, information from these additional procedures may benefit other people with autism or a similar condition in the future.

**Will you be paid if you take part?**
If you opt in, you, as the study participant, will also be reimbursed for wearing the smartwatch. This will be a one-time payment of up to $25 USD. Reimbursement will be provided via a reloadable debit card, which can be used anywhere major credit cards are accepted. At every study visit you will get feedback on your adherence with the watch data collection. After completing the study, the total amount due will be issued to the provided reloadable debit card based on the overall adherence during the whole study.

**How will your privacy be protected?**
Your information related to use of the smartwatch will be kept under the same level of privacy used for the main study. Samples will be stored for up to 5 years after the final study results have been reported.

**Can you change your mind about taking part?**
Yes. You can change your mind at any time. If you want to withdraw your consent for using the smartwatch, tell your study doctor that you no longer want to participate.

**Signature**
I willingly consent to use the smartwatch.

_____
Name of Participant

_____ _____
Signature of Participant Date of Signature

_____ _____
Signature of Parent, Guardian or Legal Representative (if applicable) Date of Signature

_____ _____
Minor Assent (if applicable) Date of Signature

**SIGNATURE BY THE INVESTIGATOR/INDIVIDUAL OBTAINING CONSENT:**
I attest that all the elements of informed consent described in this consent document have been discussed fully in non-technical terms with the participant or the participant's legally authorized representative. I further attest that all questions asked by the participant or the participant's legal representative were answered to the best of my knowledge.

_____ _____
Signature of Individual Obtaining Consent Date of Signature

**SIGNATURE BY WITNESS:**
I observed the signing of this consent document and attest that, to the best of my knowledge, the person signing the consent form is the participant or the participant's legally authorized representative, and the person signing the form has done so voluntarily.

☐ Check here if a separate witness signature is not necessary.

_____
Name of Witness

_____ _____
Signature of Witness Date of Signature

## CONSENT FOR OPTIONAL COLLECTION OF SAMPLES FOR THE RESEARCH BIOSAMPLE REPOSITORY

### Introduction

Roche wants to better understand why certain patients are more likely to respond to treatment than others, to facilitate the development of personalized medicines—to get the right medicine to the right patient. To achieve this goal, Roche would like to collect samples of your blood, for future research. Roche would also like to use any leftover (unused) blood and hair samples that were collected during the study.

If you agree to donate samples for research, they will be stored in the Research Biosample Repository (RBR), a place where human samples are securely stored. Your samples will be stored in the RBR for up to 15 years after the final study results have been reported.

Donating your samples to the RBR is entirely voluntary. No matter what you decide, it will not affect your participation in the main study or your medical care.

### Why are these samples being collected and stored?

The samples in the RBR may be used to help researchers to:

- Better understand why certain people are more likely to respond to medicines than others.
- Better understand how and why diseases act differently in different people.
- Develop new treatments for diseases or medical conditions.
- Find reasons why certain people are more likely to have side effects to medicines than others.
- Find out how medicines are processed by people's bodies and how such treatment may affect people's bodies.
- Develop better ways for preventing diseases or treating diseases earlier.
- Develop or improve tests or tools that help with detection or understanding of diseases, and identifying the right medicine for the right patient.
- Analyze your genomic material and hair samples to allow for exploration of broad health research questions across disease areas.

  Your genomic material (DNA and RNA) serves as an "instruction book" for the cells that make up your body. Your samples may be used for analysis of all of your DNA through whole genome sequencing (WGS), analysis of portions of your DNA that code for proteins, or research on gene interactions. Analyses of samples collected from a large number of autistic and typically developing participants may help researchers identify possible links among diseases, learn how variations in the sequence of genes might affect a disease or a person's response to treatment, and discover new avenues for drug development and personalized therapies.

**What will happen if I agree to participate?**

If you agree to participate in the RBR, your leftover blood and hair samples will be transferred to the RBR and additional blood samples will be collected for the RBR as described below:

- Every effort will be made to collect a blood sample at the same time as one of your scheduled blood draws. If an additional sample has to be collected, a needle will be inserted into your vein so that a small amount of blood (about 12 mL or 0.8 tablespoon) can be withdrawn.

**What are the possible side effects or risks?**

***POSSIBLE RISKS ASSOCIATED WITH SAMPLE COLLECTION***

Risks associated with participating in the RBR are described below:

- Drawing blood may cause pain where the needle is inserted, and there is a small risk of bruising or infection at the place where the needle is inserted. Some people experience dizziness, upset stomach, or fainting when their blood is drawn.

***POSSIBLE RISKS ASSOCIATED WITH LOSS OF PRIVACY***

Although your genetic information will not contain any personal identifying information, there is a very small risk that it could be linked to an outside public database and used to help identify you and your blood relatives. Because some genetic differences can help to predict future health problems experienced by you or your blood relatives, this information might be of interest to health care providers, life insurance companies, and others. It is possible that your genetic information could be used in ways that would cause you or your family distress, such as by revealing that you or a blood relative carries a genetic disease. Your privacy is very important, and Roche uses many safeguards to protect your privacy. However, there is no guarantee that your identity will never become known.

**Are there benefits to donating samples?**

You will not receive any direct benefit from donating your samples. However, research performed on these samples may benefit autistic individuals or those with a similar condition in the future.

**Will I be paid if I donate samples?**

You will not be paid for donating samples to the RBR.

Information from this research may lead to discoveries and inventions or development of a commercial product. The rights to these will belong to Roche. You and your family will not

receive any financial benefits or compensation from, nor have rights in any developments, inventions, or other discoveries that might come from, this information.

**How will my privacy be protected?**

To ensure that your health information is kept confidential, the forms, records, and samples that are maintained by Roche for the RBR will be labeled with your participant identification number; they will not be labeled with your name, picture, or any other personally identifying information. The samples and your information will be kept under the same level of privacy as described above for the main study. Roche, people and companies who partner with Roche, and others acting on behalf of Roche may study the RBR samples and associated research data in any country worldwide. Roche may then send the research results to health authorities worldwide. Information from this research may be published in a medical journal or presented at scientific meetings, so that other doctors can find out about the results. Your identity will not be disclosed.

Information from the sample analyses will not be shared with you or your doctor, unless required by law. Information from the analyses will not be part of your medical record and will not be given to your insurance company or employer. The results are for research only.

Data from analysis of RBR samples may be shared with researchers or government agencies, but only after personal information that can identify you has been removed. These data may be combined with or linked to other data and used for research purposes, to advance science and public health, or for analysis, development, testing, and commercialization of products that treat or diagnose disease, or improve care. These data will not include information that identifies you.

**Can I change my mind about storing my samples in the RBR?**

Yes. You can change your mind at any time. If you want to withdraw your consent for the use of your samples during the study, tell your study doctor that you no longer want your samples stored or used for research. If you want to withdraw your consent after the close of the study, follow the instructions provided to you by the study doctor. After you withdraw consent, any samples that still remain will be destroyed or, if this is not technically possible (e.g., when tissue microarray samples are collected), will no longer be linked to you. If you change your mind and your samples have already been tested, those results will still remain as part of the overall research data. In the event of your death or loss of competence, your specimens and data will continue to be used as part of the RBR. If you withdraw or discontinue from the main study, your RBR samples will continue to be stored and used for research unless you specifically ask that they be destroyed.

**Signature**

I willingly consent to allow my samples to be stored in the RBR and used for the types of research outlined above.

_____
Name of Participant

_____ _____
Signature of Participant Date of Signature

_____ _____
Signature of Parent, Guardian or Legal Representative (if applicable) Date of Signature

_____ _____
Minor Assent (if applicable) Date of Signature

**SIGNATURE BY THE INVESTIGATOR/INDIVIDUAL OBTAINING CONSENT:**
I attest that the individual providing consent had enough time to consider participation in the Research Biosample Repository, had opportunity to ask questions, and voluntarily agreed to allow this optional sample collection, storage in the repository, and research outlined above.

_____ _____
Signature of Individual Obtaining Consent Date of Signature

## CONSENT FOR OPTIONAL HOME VISIT AT WEEK 9

(for adolescent participants only)

**Why is a home visit being performed?**

If you are an adolescent or a caregiver for an adolescent participant, you and the participant are being given the option to have a home visit at Week 9. Instead of coming to the study site, this visit can be performed by a nurse who can visit the participant at their home or at another suitable location to make it easier for the participant in this study. This service is optional, and you are free to decide whether or not to have a home visit. This document tells you what will happen if you have a home visit, to allow you to make an informed decision. No matter what you decide, it will not affect your or the participant's participation in the main study or other medical care.

**How will the home visit be planned and organized?**

If you agree to have the home visit at Week 9, a nurse will contact you to arrange a study-compliant visit schedule that is convenient for you based on instructions from the participant's study doctor. If for any reason you or the participant cannot make this visit, please contact the study doctor immediately, and the study doctor will make other arrangements for the visit.

**What will happen if I take part?**

If you agree to have the home visit, a nurse will perform the following tests or procedures during the visit:

- Measurement of the participant's vital signs (breathing rate, heart rate, blood pressure, and body temperature)
- A pregnancy test (if the participant can become pregnant)
- Collection of blood samples
- ECG (heartbeat recording)
- Assessment of any side effects or changes in the participant's health
- Review of any changes in the participant's medications
- Questionnaires

The average duration of a mobile nursing visit is 4 to 4.5 hours.

**What are the possible side effects or risks?**

The risks associated with tests or procedures performed at the home visit are described in the main consent form (see "What are the possible risks or side effects or being in the study?").

Home visit is not equipped to handle serious health emergencies at the same level as a hospital or clinic. However, the nurse will be properly trained to manage in the best possible way health concerns that might occur to participants during the visit.

**Are there benefits to taking part?**

There is no guarantee that you or the participant will receive any benefit from the home visit. Taking part in the home visit may be more convenient for you and the participant, and may decrease the amount of travel needed for you to take part in this study.

**What other choices do I have if I do not take part in the home visit?**

You do not have to agree to the home visit to participate in the study. You may choose to undergo all tests and procedures at the study site, according to the study visit schedule.

**Will I be paid if I take part in the home visit?**

You and the participant will still be paid the standard "on-site" study visit reimbursement for your participation in the home visit.

**Will it cost me anything to take part in the home visit?**

There are no costs to the study participant or to the participant's health plan or to the caregiver for the home visit.

**How will my privacy be protected?**

The nurse who visits your home will collect and record information about the participant during the visit. This information will include medical and personal information about the participant, such as information about their general health, how they have responded to study drug, any side effects they may have experienced, and results of any testing performed during the visit. The health information collected about the participant will be held by the study site and Roche.

The participant's health information related to the home visit will be kept under the same level of privacy used for the main study.

**Signature**

I willingly consent to a home visit at Week 9.

_____

Name of Participant

_____ _____

Signature of Participant Date of Signature

| | |
|---|---|
| Signature of Parent, Guardian or Legal Representative (if applicable) | Date of Signature |
| Minor Assent (if applicable) | Date of Signature |

**SIGNATURE BY THE INVESTIGATOR/INDIVIDUAL OBTAINING CONSENT:**
I attest that the individual providing consent had opportunity to consider this optional home visit and ask questions and voluntarily agreed to allow this optional home visit as outlined above.

| | |
|---|---|
| Signature of Individual Obtaining Consent | Date of Signature |