PARTICIPANT'S PARENT/GUARDIAN INFORMATION SHEET AND CONSENT FORM

Study Title:	An Exploratory, Multicenter, Randomized, double-blind, placebo-controlled study evaluating the effect and safety of pitolisant in children and adolescents with autism spectrum disorders.
Protocol/Study Number	P21-01
IRAS ID:	1007904
Study Sponsor:	Bioprojet Pharma, 9, rue Rameau, 75002 Paris, France
Study Doctor & Research Site Address:	*[Principal Investigator First and Last Name]* *[Site Name and Address]* *[Office Hours Tel]* *[Out of Hours Tel]* *to be added by the site*
Telephone:	*Insert Site (study team) Contact Number/s including 24hr Emergency Contact Phone Number and any relevant Instructions for emergency e.g., ask for registrar on call explaining that your child is participating in a clinical trial etc.* *to be added by the site*
Participant Number:	*to be added by the site*

We would like to invite your child take part in a medical research study. **Your child's participation is completely voluntary. You are free to say yes or no.**

This document is called a "Parental Information Sheet and Consent Form". It explains the purpose of the study, what you can expect if you decide to have your child take part, including the risks and possible benefits, and how your child's medical information will be used. Before you decide if you want your child to take part in this study, you can have a copy of this parental information sheet and consent form to take home and review. If you wish, you may ask advice from others, such as your child's general practitioner (GP) or family before you decide.

Please read this parental information sheet and consent form carefully. Take time to ask the study doctor or study team as many questions about the study as you would like. You may ask questions before you decide to start the study and at any time during the study. The study doctor or study team can explain any words or information that you do not understand. Reading this parental information sheet and informed consent form and talking to the study doctor, or study team may help you decide whether or not you want your child to take part.

If you decide to have your child, take part in this study, you must write and sign your name, and put the date, at the end of the parental information sheet and consent form. You must sign the parental information sheet and consent form before any study-related tests and procedures can be performed. Only sign the parental information sheet and consent form when you fully understand

the details about the study and agree to your and your child's commitment. For a child to take part in this study, his parents or legal guardian(s) must sign the parental information sheet and consent form. If one parent cannot attend the Screening Visit, he/she must be informed remotely by site team and sign the parental information sheet and consent form prior to any study-related procedure.

After signing the parental information sheet and consent form, **you are free to change your mind** at any time and take your child out of the research study; without giving a reason. If you decide not to have your child take part, or if you decide to take your child out of the research study, this will not affect the healthcare he receives, there will be no penalty, and your child will not lose any health benefits he would otherwise have received. You will not give up any legal rights by signing the parental information sheet and consent form. You will be given a copy of the signed parental information sheet and consent form.

You and your child will be told about any new information found during the study that may affect whether you want your child to continue to take part. You and your child will receive this information verbally and in writing. You and your child may be asked to sign a new informed consent form during the course of the study if there is new information available.

1 INTRODUCTION

Your child is being asked to take part in this research study because he has been diagnosed with an autism spectrum disorder (also referred to as ASD throughout this document). Children and adolescents with ASD may have varying degrees of difficulty in social communication and interaction, repetitive behaviours, and restricted interests that can be difficult for the child and their family. The causes of ASD are not well understood, and research shows that some brain neurotransmitters (little molecules, for example histamine) that are important for the communication between brain cells do not function well and could play a part in the type of difficulties that people with ASD experience.

The company sponsoring this study, Bioprojet Pharma (referred to as the Sponsor in this parental information sheet and consent form), has developed a study drug called BF2.649 (also referred to as pitolisant throughout this document) for the treatment of problems with social interactions in people with ASD. Pitolisant increases the activity of histamine in the brain by connecting to histamine receptors. Receptors are like small locks on the surface of cells. The activity of the cell can change depending on which type of key is available to open the lock. Pitolisant acts as a key for histamine receptors, which increases histamine in the brain helping to improve attention, learning, and memory. Studies in animals have shown that pitolisant helped to improve social interaction behaviour. It is therefore thought that pitolisant will be beneficial in people with ASD.

Pitolisant's safety, effectiveness, and how it works in people with ASD is still being studied. Pitolisant has not been approved for use by government agencies in any country as a treatment for ASD. Pitolisant has been authorised for treatment of narcolepsy, a sleep disorder, in adults for use in Europe, USA, and other non-European countries and in children above 6 years old for use in Europe. Pitolisant has been also approved in Europe for the treatment of sleepiness in adult patients with obstructive sleep apnoea (a problem in which the breathing pauses during sleep).

This research has been reviewed and approved by the responsible Research Ethics Committee (REC). A REC is a group of scientific/medical experts and regular people who review any research conducted in humans to protect the welfare, rights, and privacy of the participants in the study.

2. WHAT IS THE PURPOSE OF THE RESEARCH STUDY?

The main purpose of this study is to investigate the effect, safety, tolerability (whether side effects can be handled by participants), and pharmacokinetics (PK) of pitolisant in male children and adolescents affected by ASD. PK relates to how long the body takes to absorb the drug, metabolise it (so it can work in the body) and excrete it (get rid of it from the body).

3. INFORMATION ABOUT THE STUDY

About 62 male participants with ASD, from 6 to 17 years of age, will take part in this study in approximately 20 clinical research sites in Europe and UK.

This is a placebo-controlled, double-blind, randomised research study. Placebo-controlled means that your child may receive a placebo (which looks like pitolisant, but it has no active ingredients); this provides a way to measure the actual effect of pitolisant. Double-blinded means that neither your child, you, the Sponsor, nor the study doctor and study team will know whether your child is receiving pitolisant or placebo. However, your child's study doctor can always find out this information if it is needed urgently for your child's medical treatment. Randomised means that a computer will decide if your child will receive either pitolisant or placebo completely by chance (like flipping a coin).

Your child will take the Investigational Medicinal Product or medication, which refers to pitolisant or placebo, by mouth every morning when he wakes up in the form of 1 or 2 tablets.

Your child's participation in the study will last up to 15 weeks and includes 3 periods:

1. The screening period (2 to 3 weeks prior to treatment start) to confirm that your child meets all of the study requirements and is eligible to take part in this study.

2. The treatment period (up to 12 weeks).

3. The follow-up period (1 week after end of treatment) to confirm your child tolerability of the medication.

4. WHAT WILL HAPPEN TO YOUR CHILD DURING THE STUDY?

If you allow your child to take part in this research study, you and your child will need to visit the study clinic about 5 times over the 15 weeks of the study (this does not include any unscheduled visits that may be needed). Additionally, 2 phone calls (or more if necessary) are planned at Visit 3 and during Follow-up for each participant during the study. The on-site visits will be scheduled by the clinical site depending on site organisation and participants/parents or legal guardian availability in accordance with the figure of procedures at the end of this section. If you sign the

parental information sheet and consent form, you are agreeing for you and your child to follow the instructions given by the study team during the study. During all parts of the study, your child will be assessed to see if he is able to continue taking part and to monitor his health and the effects of the medication. It is important that the same parent/legal guardian accompanies the participant to complete the study assessments at all on-site visits (except Visit 2) and that your child comes to all study visits at the scheduled time. If you or your child cannot attend at the scheduled time, please set up a new time as soon as possible by using the contact details on the first page.

Each study visit will include some or all of the following tests/procedures. Please refer to the picture below:

- **Informed Consent:** You will review the parental information sheet and consent form with study team, ask questions, and sign the consent form.

- **Demographic Questions:** The study team will record your child's month and year of birth, sex, and school level.

- **Qualifying Questions:** The study team will ask questions to determine whether your child is able to be in this study, based on specific study requirements.

- **Medical History Review:** You and your child will be asked about any significant illnesses/conditions he has experienced in the past and any illnesses/conditions he currently has. This will include a confirmation of his diagnosis of ASD. If your child's ASD diagnosis has been confirmed within 3 years before the Screening Visit and if the results are available, then there be no need to confirm your child's ASD diagnosis at the Screening Visit. The study team will ask questions to measure your child's intellectual ability. If an intelligence test was done less than 3 years prior to screening, the study team will accept those results.

- **Physical Exam:** Your child will undergo an overall examination of his body according to common medical practice (head, neck, ears, eyes, nose, throat, lungs, heart, chest, lymph nodes, abdomen, skin, muscles, and skeletal, and nervous system). Your child's height and weight will also be measured.

- **Vital Signs:** Your child's pulse (the number of heart beats per minute) and blood pressure (how much pressure it takes to move blood through the body) will be measured. Your child will be asked to lie on his back or sit while his blood pressure is measured.

- **Electrocardiogram (ECG):** This is a test that measures the electrical activity of the heart. Your child will be asked to lie down, and small sticky pads will be placed on his arms, legs, and across his chest.

- **Blood Sampling for Safety Testing:** Blood samples will be collected to assess whether your child is able to take part in the study and to assess your child's general health throughout the study. Your child may receive a medication with numbing cream (e.g., special cream or patch) and may inhale (breathe in) a special gas before any safety tests are done to help with distress during procedures that may cause discomfort.

  - **Blood Sampling for medication Measurement (PK-** analysis of the level of medication in the blood**):** A blood sample will be collected at Visit 5 before your child takes his dose of the medication. This blood sample will be used to measure how much of the medication is present in the blood at that time. The samples remaining after analysis may be stored for future research in a serum bank under the responsibility of Bioprojet Biotech for a maximum duration of 10 years after finalisation of study analysis. These samples may be used for research purposes to better understand autism and pitolisant. You will be asked in the statement of consent if you agree or refuse the storage of your child's samples after the end of the study.

- **Urine Drug Screen:** Urine samples will be collected to test if your child has taken any street drugs (including cannabis, opioids, cocaine, amphetamine). Your child will not be able to take part in the study if the tests are positive.

- **Questionnaires:** You will be asked to complete questionnaires that will assess the following:

  - Communication, emotional, and social behaviour of your child

  - Your child's daily life and activities

  - How often certain types of behaviours occurred

  - Sleep habits and difficulties

  - Your child's study doctor will also complete some questionnaires about your child's health and behaviour

- **Digit-tracking**: This test consists of presenting a set of blurred images to your child. Your child will be asked to place his finger on the screen with the image, which will unblur a part of the image. Your child will then be asked to move his finger around the screen, "exploring" the image either freely or following precise instructions during a limited time and/or distance. The images will be presented one after another.

- **Side Effect Review:** Your child will be asked how he is feeling and to report any side effects or symptoms he may experience while in the study. The study team will monitor any changes in your child's health throughout the study.

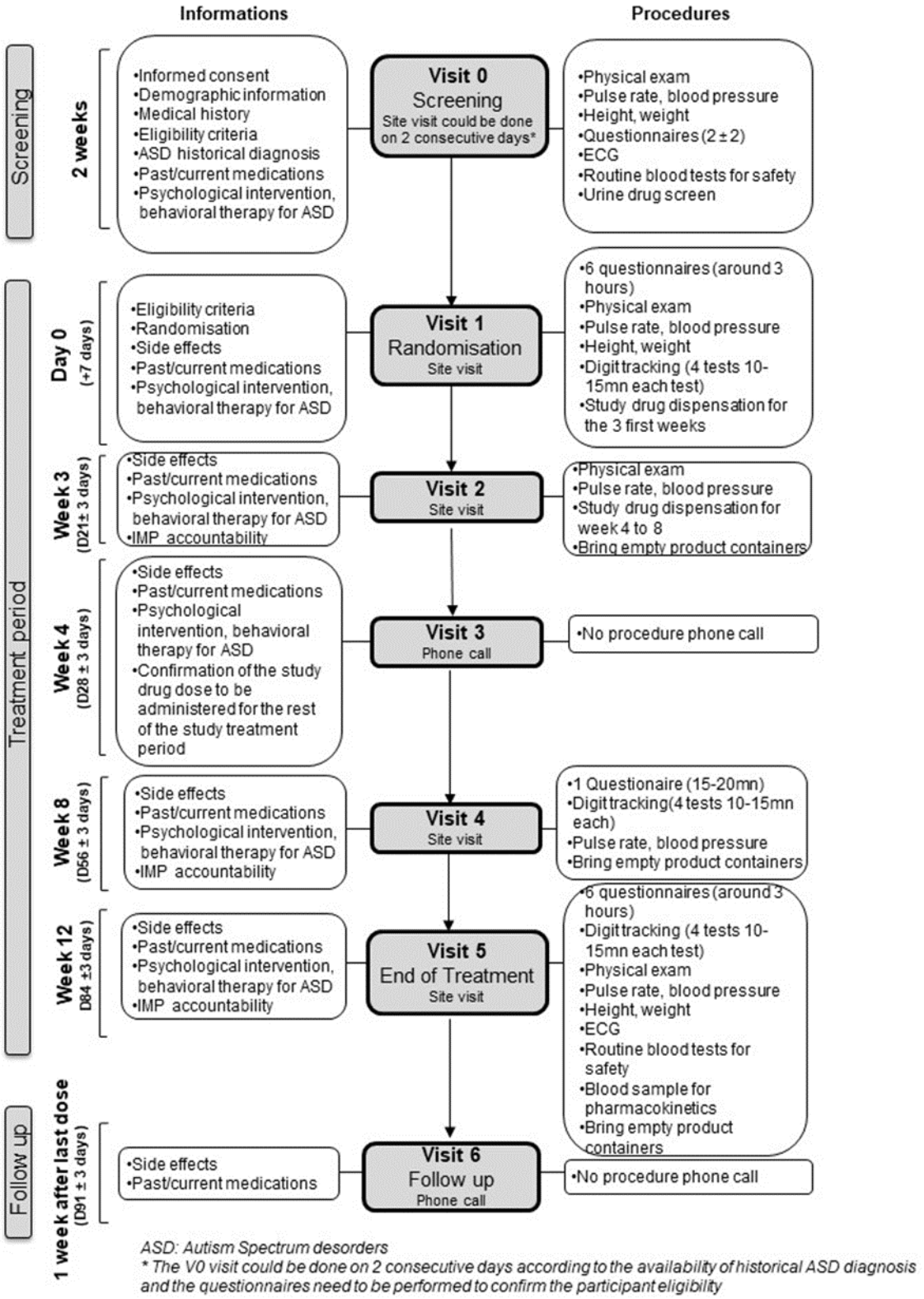
- **Medication and Treatment Review:** You will be asked about your child's medication history. You should try to be as honest and accurate with the study team about your child's medication history as possible, or it may not be safe for him to be in this study. You will be asked, and it is very important that you tell the study team, if he takes any over-the-counter or prescription medicines. Throughout the study, you will be asked to report any changes in your child's medications or treatments. Certain medications are not allowed during the 4 weeks before the Screening visit and during the total period of study participation. For certain medications, your child must have taken the same dose for 4 weeks before the Screening Visit and he must keep taking the same dose throughout the study. The study doctor will discuss any of these restrictions with you.

- **Psychological Intervention and Behavioural Therapy**: The study team will ask about any psychological intervention and/or behavioural therapy that your child may be receiving during the past 4 weeks from the Screening Visit and during the study. If your child is receiving psychological intervention and/or behavioural therapy, their frequency should be kept stable during the study.

- **IMP (Investigational medicinal product) Medication (**which refers to pitolisant or placebo)**:** The appropriate dose and amount of medication will be given to you and your child for you to take at home. You will receive more medication than needed to be sure your child has enough (in case you are not able to attend the scheduled study visit). Information on how to take the tablets and store them will be given to you by the study doctor.

- **Medication Accountability**: You must bring all of your child's unused medication and empty product containers to each study visit. This is to check if your child has taken each of his doses of medication.

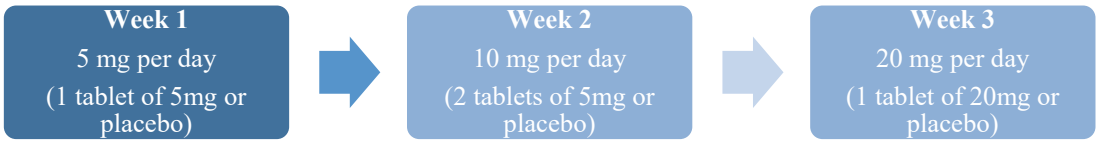
The following figure shows how many times and when these procedures will be performed throughout the 15 weeks of study duration and the approximate duration of each questionnaire:



ASD: Autism Spectrum desorders
** The V0 visit could be done on 2 consecutive days according to the availability of historical ASD diagnosis and the questionnaires need to be performed to confirm the participant eligibility*

Pitolisant or placebo will be provided as tablets. During the treatment period you should make sure that your child swallows his tablets as instructed, once every day in the morning when he wakes up, with food and/or a drink.

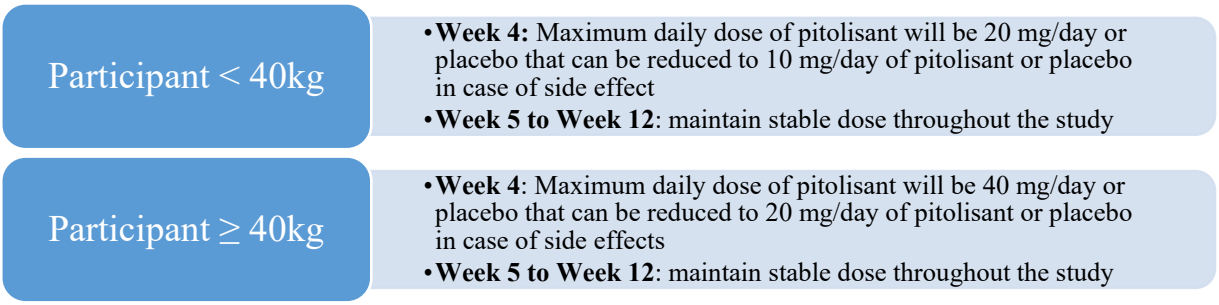
Over the first 3 weeks, the dose will be adjusted as follows:



If necessary, during this 3-week dose adjustment period you will be able to call the study doctor and discuss any symptoms and difficulties your child may have.

After the first 3 weeks, if your child is tolerating the medication, and depending on his weight, the dose may increase again or stay the same for another 7 days (through Week 4). After that (at Week 5), the dose will stay the same for the rest of the study (through Week 12) unless it is not tolerated. If needed, the dose can be reduced after a discussion with the study doctor. You will receive clear instructions on how your child should take the medicationbased on your child's body weight and tolerance.

The diagram below shows details about dosing, depending on your child's weight:



5. WHAT WILL MY CHILD AND I BE EXPECTED TO DO WHILE IN THE STUDY?

Having your child take part in a research study can impact your and your child's daily life. Please consider the study time commitments and responsibilities you and your child will have before you decide to have your child take part. Your responsibilities as a parent/legal guardian of a study participant include the following:

- Provide information about your child's medical history, medications received, psychological intervention and behavioural therapy received, current condition, and if necessary, this includes the time after the study ends/is halted, and until any side effects disappear.
- Agreeing to be contacted by the study team as necessary, by telephone or in writing.

- Telling the study doctor whether your child has previously participated in a clinical trial.
- Making sure your child and you or his guardian come to all study visits on time or to reschedule the study visit if unable to attend. The parent or guardian completing questionnaires at the first visit should remain the same throughout the duration of the study.
- Making sure your child's guardian brings all unused medication and empty containers with them to Visits 2, 4 and 5.
- Making sure your child takes the medication as directed by the study doctor and study team. This includes making sure that your child does **NOT take the** medication **before Visit 5** (as blood sampling will be done before the medication is given).
- Telling the study doctor about any new medications your child receives during the study.
- Making sure your child follows any rules about any medicines that he should not take while in this study. The study doctor or study team will talk to you and your child about these. You will receive a participant card to document that your child participates in the study, and you need to present this card each time your child visits a physician outside the clinical team.

  The following medications are explicitly prohibited for your child during the study and for at least 4 weeks prior to screening:
  - anti-depressant medications (bupropion, fluoxetine, paroxetine, etc.)
  - antiarrhythmic medications (quinidine, etc.)
  - anti-epileptic medications (carbamazepine, phenytoin, etc.)
  - some antibiotics (rifampicin, etc.)
  - anti-psychotic medications (aripiprazole, risperidone, clozapine)
  - anti-histamine H1 medications (pheniramine maleate, chlorpheniramine, diphenhydramine, promethazine, mepyramine, milnacipran)
  - tricyclic and tetracyclic antidepressants medications (amitriptyline, clomipramine, imipramine, maprotiline, nortriptyline, trimipramine, mirtazapine, etc.)
- Telling the study doctor about any problems your child has during the study.
- Ensuring the medicationis not shared with anyone else and is stored in a secured place out of reach of children while at home.
- Making sure that your child's dose(s) of any other allowed medication (melatonin; medications for the treatment of other diseases or ASD related symptoms, other than those listed above), psychological intervention and behavioural therapy he may be taking/receiving is kept stable.
- Keeping your child's social environment as stable as possible during his participation in the study.
- Telling the study doctor if you (parents/legal guardian) or your child wish to withdraw from the study before its planned completion and coming to the study clinic for a withdrawal visit. You and your child should follow any instructions given during this visit. Your child's participation in the research study may also end at any time for any reason, even if your child does not want to stop participating.

6. RISKS AND DISCOMFORTS OF THE STUDY

Pitolisant is already approved by regulatory health agencies and has been on the market in some countries since 2016 for treatment of diseases other than ASD.

Your child may not directly benefit from his participation in this research study. Although pitolisant has been tested in humans for safety, the effect of pitolisant has not yet been tested in people with ASD.

Your child may receive placebo instead of pitolisant. Placebo will not treat ASD.

Some treatments, in combination with pitolisant which could lead to a worsening of your child's condition, are prohibited during the study participation. These treatments must not have been taken at least 4 weeks before the first study visit, for your child to be able to participate in the study.

Placebo Risks

Regarding placebo, there are no anticipated side effects. Your child's symptoms of ASD may not improve or may even worsen. This will not have an impact on your child's future treatment.

Side Effects of Pitolisant

The clinical program supporting pitolisant development includes data from over 3000 people to date (healthy volunteers and patients), among which over 2000 were exposed to pitolisant during double-blind studies and 97 of them were children. Please be aware that, like any other medicine, pitolisant may cause side effects and may have side effects that are not known at this time.

In previous research studies with pitolisant in humans, participants received pitolisant at doses of up to 240 mg. In these studies, pitolisant was well tolerated and considered safe.
However, the possible mild-to-moderate side effects your child may experience when taking pitolisant at the maximal therapeutic dose of 40 mg may include:

- Headache (11%)
- Insomnia (being unable to sleep, 5.5%)
- Hypertension (high blood pressure, 2.7%)

All these effects went away on their own or when the dose of pitolisant was reduced and there have been no lasting serious side effects associated with pitolisant.

It is possible that after your child stops taking pitolisant, he could experience symptoms related to pitolisant withdrawal which may include fatigue, insomnia, increased appetite, dysphoria (feeling unhappy or dissatisfied), vivid or unpleasant dreams, and movement and thinking difficulties.

Your child may also experience some symptoms of an allergic reaction which are shortness of breath, itchy rash (hives) or swelling, flushing (feeling warm), low blood pressure, and slow heart rate. However, if your child experiences side effects (any unwanted symptoms or health problems) during this study, you should contact the study doctor and the study doctor will provide adequate treatment/care for these side effects.

Blood Sampling

All blood tests will be done by a qualified nurse or doctor to ensure that the risks of drawing blood are minimal. To take blood from your child, a needle will be inserted into his vein. The risks of taking blood include fainting and pain, bruising, swelling, or rarely, infection where the needle was inserted. The total amount of blood to be collected during your child's participation in this research study will be approximately 15 mL (approximately 1 tablespoon). This does not include

additional blood samples that may be collected during unscheduled visits, if necessary. This amount of blood taken will not have any impact on your child's health and will not exceed 20 mL (approximately 1 and 1/3 of a tablespoon).

Electrocardiogram (ECG)
The sticky pads placed on your child's skin for the ECG may sometimes cause some skin irritation, such as redness or itching.

Risks to an Unborn Child:

Studies in animals have shown effects on semen parameters (morphology abnormalities and decreased motility) without a significant impact on reproductive performance in males. Pitolisant does not appear to cause changes to genetic material or development of cancer.

If your child thinks that his sexual partner has become pregnant, he should tell the study doctor at once. The study doctor may request permission from your child's partner and her parent(s) to collect additional information regarding the pregnancy and the child, as this is a requirement of regulatory agencies.

Unknown Risks

There may be risks to your child that are currently not known or cannot be predicted from taking the medication alone or with other drugs your child may be taking. Your child's condition may worsen, remain the same, or improve as a result of participating in this research study. Please seek treatment immediately and tell the study doctor and study team if your child has any of the symptoms mentioned in this section, or any other side effects, during the study (even if you think they are not related to his participation in this study). You child might have side effects or discomforts that are not listed in this section. Some side effects may not be known yet. New ones could happen to your child.

New Findings:
In the case of incidental findings (e.g., from clinical tests) that could contribute towards preventing, confirming, and treating an illness, or one that could be expected in the future, you may choose, (a) to be directly informed of these findings; (b) to not be informed of the findings, if that is your wish; or (c) to leave the decision with your study doctor (see statement of consent).

7. WHAT OTHER TREATMENTS ARE AVAILABLE FOR MY CHILD?

Your child does not need to take part in this research study to receive treatment for ASD. Treatments for your child's ASD include psychological intervention and behavioural therapy for ASD, melatonin, and medications for treatment of concomitant diseases or symptoms related to ASD.

If you decide for your child not to participate in the study or at the end of his participation, your study doctor can discuss the alternative treatments or therapies available. Please note that pitolisant

will not be available to your child after the study is over, as it is an medication and as such, it is not available outside of the clinical trial for treatment of ASD.

8. ARE THERE ANY BENEFITS TO BEING IN THE STUDY?

Your child may or may not receive any benefit from being in this study. It is possible that he may get better, stay the same, or get worse. If your child takes part in this study, other people with ASD may be helped by the research.

9. WILL IT COST ANYTHING FOR MY CHILD TO BE IN THIS STUDY AND WILL MY CHILD BE PAID TO BE IN THE STUDY?

The medication and all tests, procedures, and visits required by the study are provided at no cost to you. The Sponsor will pay for them. The costs of other medications and treatments that your child takes or uses independently of the study are not covered by the Sponsor of this study.

You and your child will not be paid for being in this study. It is not expected that it will cost you anything to participate in this study. Reasonable expenses (e.g., travel, meals, insurance during on-site visits) will be reimbursed, after receipts for the payments are provided, and in agreement with the study doctor. You will receive some additional materials from a company called VOUTE SAS, which will explain the process of the reimbursement and what information will be collected for this purpose.

10. DOES THE DOCTOR GET PAID FOR CONDUCTING THE STUDY?

Bioprojet Pharma, the Sponsor of the study, is paying the study doctor and study team for their work in this study.

11. WHAT IF MY CHILD IS INJURED DURING THE STUDY?

If your child health is impaired or your child suffers any injury or side effects during or after the research study, please contact the study doctor responsible for this study (contact details are on the first page). The study doctor will begin the necessary steps for your child. If your child is harmed or become sick as a direct result of taking the study medication or the study procedures, medical treatment will be offered to your child by the Sponsor. The Sponsor will compensate your child for any injury caused by taking part in this study in accordance with the guidelines of the Association of the British Pharmaceutical Industry (ABPI).

The Sponsor will pay compensation where the injury probably resulted from:

• A drug being tested or administered as part of the trial protocol.

• Any test or procedure you received as part of the trial.

Any payment would be without legal commitment. (Please ask if you wish more information on this). The Sponsor would not be bound by these guidelines to pay compensation where the injury resulted from a drug or procedure outside the trial protocol or where the protocol wasn't followed. For this purpose, the Sponsor has taken out an appropriate insurance in your favour with the policy number ML6BBA3849AX with CNA Hardy international Services Limited for and on behalf of Hardy (underwriting agency) Limited, Floor 13, 20 Fenchurch Street, London, EC3M 3BY.

By signing this form, you do not waive any rights to pursue personal injury claims.

12. WILL MY CHILD'S PERSONAL DATA BE KEPT PRIVATE?

COLLECTION AND PROCESSING OF PERSONAL DATA FOR THE RESEARCH STUDY

Your child's personal data will be processed and shared during the study by your child's GP, study team, and representatives/designees of the Sponsor for the following purposes:

1. Reliability and Safety Purposes: Your child's personal data will be processed in order to ensure that study data is reliable and that safety requirements have been met for your child's participation in the study.

2. Research Activity Purposes: Your child's personal data will be processed for scientific research purposes related to P21-01 study.

The legal bases for processing and sharing your child's personal data for the purposes mentioned above are:

1. Reliability and Safety Purposes: For personal data, the legal basis is the Sponsor's compliance with a legal obligation under the national law implementing ICH-GCP (GDPR Article 6(1)(c)). For sensitive personal data, the legal basis is 'public task' as processing is necessary for the performance of a task carried out in the public interest (GDPR Article 9(2)(i)).

2. Research Activity Purposes: For personal data, the legal basis is the Sponsor's legitimate interests (GDPR Article 6(1)(c)). For sensitive personal data, the legal basis is that processing is necessary for scientific research purposes (GDPR Article 9(2)(j) and Article 89(1)).

For the purposes mentioned above, the Sponsor and the study doctor may use the following personal data:

- Identification data: your and your child's name, sex, address, date of birth, study identification, contact number, and email address
- Unique participant identification number

The Sponsor and study doctor will also use the following sensitive personal data:

• General information relating to your health condition

Who are the authorised recipients of your child's personal data?

- Sponsor or persons working on behalf of the Sponsor (e.g., representatives of Sponsor, monitors and auditors of the Sponsor, or representatives of Worldwide, the contract research organisation working with the Sponsor on this study)
- The study doctor and study team
- Research Ethics Committees
- Competent Authorities
- Regulatory authorities, such as the Medicines Health Research Agency (MHRA), Food and Medication Administration (FDA), other US governmental agencies, or the European Medicines Agency
- Other Government Agencies (including those outside of your country of residence)
- Laboratories working with the Sponsor on this study
- Vendors working on this study
- Individuals involved in obtaining marketing authorisation for the study medication.
- Service providers who assist in managing, administering, or delivering reimbursement services
- Your child's regular health care provider (for safety)

How will my child's personal data be processed?

The study doctor and team, and representatives/designees of the Sponsor will process and use your child's personal data collected during the research study and during the Screening Period. Your child's personal data will be collected via study forms that will include additional information relating to his health and medication history, and the results of examinations and tests completed during the research study.

At the Screening visit, your child will be assigned a unique participant identification number. This unique participant identification number will be used to identify him on study forms, and he will not be identified on any study form by name or other personal information. Any personal data processed outside of the study clinic will only refer to your child by his unique participant identification number. Decoding will only take place as required by law.

While at the study clinic, the study doctor and team, and designees/representatives of the Sponsor will have direct access to the directly identifiable personal data collected to ensure they are correct and that the study was conducted properly (monitoring and auditing purposes). The study team will use your name and contact details to contact you about the research study (e.g., visit reminders or follow-up purposes), make sure that relevant information about the study is recorded for your child's care, and to oversee the quality of the study. You may also be contacted after the study has ended to inform you of the study outcome. The study team may also need to correct or provide missing information about your child even after your child's

study participation is over and review of your child's medical records may also take place after the study is over.

Bioprojet Pharma is the Sponsor of the study and as such, will act as data controller with respect to the research data/records (except for your child's medical data used for standard care purposes) and the conduct of the study. The Sponsor's data protection representative in the United Kingdom can be contacted by sending a request by email (dpo@bioprojet.com) or mail at Bioprojet Pharma's address, "to the attention of Bioprojet Pharma's DPO".

The Sponsor will keep your child's study records for up to 25 years after the end of the study/2 years after the date a marketing application is approved, or longer if required by applicable law and/or clinical guidelines.

Specific data uses:

Biological Samples: Blood samples for analysis of the level of medication in the blood and urine samples taken during the study will be labelled with the study number, information related to the sample, the sample date, and a code. The 'key' that links this code with your child's identification number will be kept at the study clinic. Access rights to this key are only granted to authorised personnel. It is not possible to trace any personal data back to your child without this key. Decoding will only take place as required by law. No directly personal identifiers (such as your child's name or date of birth) will be recorded on the sample labels. The Sponsor must follow applicable laws and regulations and that all collected information will be coded so that no individual persons can be identified during analysis of data. Your child's pharmacokinetic samples will be stored and analysed at Bioprojet Biotech (4 Rue du Chesnay Beauregard, 35760 Saint-Grégoire – France), until the end of the study, and then destroyed.

Urine samples will be analysed at Eurofins Central Laboratory B.V. (Bergschot 71, 4817 PA Breda – The Netherlands) and destroyed after analysis.

However, the pharmacokinetic samples remaining after analysis could be stored for future research in a serum bank under the responsibility of Bioprojet Biotech for a maximum duration of 10 years after finalisation of study analysis and used for research purposes to better understand autism and pitolisant if you consent to it. The samples cannot be passed on or transferred without your prior approval. You will be asked in the statement of consent if you agree or refuse the storage of your child's samples after the end of the study. If you also agree to it in the statement of consent, your child pseudonymised data (coded data that do not identify you) could be reused after the end of the study for research purposes to better understand autism.

Registries and Publications:

A description of this clinical study will be available on the European Union Medication Regulating Authorities Clinical Trials Database as required by European laws. This website will not include information that can identify you and your child. The website will include a summary of the results. You can search this website at any time.

The results of the study will be submitted to one or more Sponsor offices, health/regulatory authorities, qualified third-party researchers, and other approving bodies. The results may also be presented at meetings or published in medical journals. You will not be identified in any presentation or publication resulting from the study.

Regulatory Authorities: The regulatory authorities will be granted direct access to your original study records in order to audit, monitor, and verify the proper conduct of the study, evaluate study results and adverse events, and provide approval/marketing authorisation.

Will your child's personal data be shared?

Your child's personal data will only be shared with and disclosed to authorised third parties and recipients, if instructed and allowed by the Sponsor. Some of those third parties and recipients might be located outside the United Kingdom (UK) and/or the European Union (EU) where the level of protection for coded data might not be as strict and advanced as in your country and may not stop coded study data from being shared with others. A transfer of personal data outside the UK may pose a security risk, as well as the risk that you may not be able to exercise certain rights, or may have more difficulty exercising such rights, in respect to these recipients. In those cases, your child's personal data will only be transferred where appropriate safeguards are in place to protect them (such as Standard Contractual Clauses). You can find more information on these safeguards by contacting the study doctor (using the contact details on the first page), who will contact the Sponsor's data protection officer as needed.

All third parties and recipients are obligated to observe the rules of professional confidentiality and will only use your personal data for the purpose of the study and as described in this section.

What are my child's rights?

You and your child have the right to access personal data and correct inaccurate personal data processed in the study. You and your child may also have the right to erase, limit, or object to the processing of yours and your child's personal data (including your child's biological samples), where such processing is a) no longer necessary for the purposes described in this section, or, b) is processed only for scientific research purposes and the Sponsor does not have compelling legitimate grounds to continue processing which override yours and your child's interests, rights, and freedoms. You and your child can exercise your rights by contacting the study doctor (using the contact details on the first page), who will contact the Sponsor's data protection officer as needed.

You also have the right to lodge a complaint regarding how your personal data are being handled with the supervisory authority responsible for enforcing data protection legislation, the Information Commissioner's Office at https://ico.org.uk/.

Withdrawal:

If you wish to withdraw your consent to your child's participation in the research study, no further personal data will be collected about your child unless it is necessary for your child's safety or to maintain the integrity of the research. The Sponsor may, however, still use your

child's personal data that was collected and shared before you withdrew your consent, as described in this form. If you wish to withdraw your consent for your child's participation to the research study, you must notify the study doctor using the contact details on the first page.

Organisational and technical safeguards:

The Sponsor and study clinic have put in place appropriate security measures to prevent your child's personal data from being accidentally lost, used, altered, disclosed, or accessed in an unauthorised way. Specifically, your child's personal data will be coded or "pseudonymised" before it is stored, analysed, or transferred. The Sponsor and study clinic have also put in place procedures to deal with any personal data breach and will notify any applicable regulator of a breach as required by law. Furthermore, your study doctor will inform you and your child of any personal data breach as required by law.

Who can you contact with further questions?

You and your child may ask questions about this consent form or the study at any time (before or during the course of the study). If your child experiences any medical problems, suffer a research-related injury, or have questions, concerns, or complaints about the study, please contact the study doctor at the telephone number listed on page one of this information sheet.

If you seek emergency care for your child, or hospitalisation is required for your child, alert the treating doctor that you are participating in a research study being conducted by the study doctor listed on page one of this information sheet.

If you have any questions about your child's rights as a research participant or you would like to obtain information or offer input, or you wish to speak with someone not directly involved with the research study, or if you wish to make a complaint, you should contact:

[site to delete irrelevant sections and insert relevant contact details]

for England

the NHS Complaints Procedure / PALS (Patient Advice and Liaison Service)

<Insert Telephone Number>"

or for Scotland

the Patient Advice and Support Service

<Insert Telephone Number>"

or for Wales

enter the PI site details or the Community Health Council for the local health board <Insert Telephone Number>"

or Northern Ireland

the Patient and Client Council

<Insert Telephone Number>"

or for non-NHS sites the Private institutional arrangements

at: <Insert Telephone Number>"

Thank you for taking the time to read this information sheet and for considering your child taking part in this study. If you are interested in your child to take part in the study, please inform us and we will arrange a Screening visit.

PARENTAL INFORMATION SHEET AND CONSENT FORM

Study Title:	An Exploratory, Multicenter, Randomized, double-blind, placebo-controlled study evaluating the effect and safety of pitolisant in children and adolescents with autism spectrum disorders.
Protocol/Study Number	P21-01
IRAS ID:	1007904
STUDY SPONSOR:	Bioprojet Pharma, 9, rue Rameau, 75002 Paris, France
Study Doctor & Research Site Address:	*[Principal Investigator First and Last Name]* *[Site Name and Address]* *[Office Hours Tel]* *[Out of Hours Tel]* *to be added by the site*
Telephone:	*Insert Site (study team) Contact Number/s including 24hr Emergency Contact Phone Number and any relevant Instructions for emergency e.g., ask for registrar on call explaining that your child is participating in a clinical trial etc.* *to be added by the site*
Participant Number:	*to be added by the site*

Statement of Parental's Consent	Please initial each box
I have read the information in this Parental Information Sheet and Consent Form and its contents were explained to me. I have had the opportunity to ask questions and had these answered satisfactorily.	
I understand that my child's participation is voluntary and that I am free to withdraw at any time without giving any reason, without my child's medical care or legal rights being affected.	
I understand and agree that my child's coded medical data and coded biological samples that are relevant for this research study may be transferred within and outside of United Kingdom to Bioprojet Pharma and partners, to countries that may not have the same level of protection as in United Kingdom	
I understand that relevant sections of my child's medical records and data collected during the study may be looked at by individuals from the sponsor, Bioprojet Pharma , including persons or companies working for or with the sponsor, the clinical research organisation, from regulatory authorities and the Ethics Committee, where it is relevant to my child taking part in this research. I give permission for these individuals to have access to my child's records.	
I agree for my child's GP to be informed of my child's participation in this study and for exchange of information with the research site's study team	

I will be told about new findings the study doctor learns during the study that may affect my child's willingness to stay in the study. If I want to have this information sent to my child's GP, I should tell the study doctor listed on page one of this informed consent form.	
I agree to my child take part in this research study.	

I agree ☐/I do not agree ☐ to the storage of my child's blood samples for up to 10 years after the end of the study for future analyses as described in the information sheet.

I agree ☐/I do not agree ☐ to the reuse of my child's pseudonymised data for future analyses as described in the information sheet.

For the first parent/Legal Guardian(s)

_____ _____

Signature of the First Parent/Legal Guardian Date

_____

Printed Name of the First Parent/Legal Guardian

For the second parent/Legal Guardian(s)

_____ _____

Signature of the Second Parent/Legal Guardian Date

_____

Printed Name of the Second Parent/Legal Guardian

STATEMENT OF PERSON EXPLAINING CONSENT

I have carefully explained to the participant's parent(s)/legal guardian(s) the nature and purpose of the above study. There has been an opportunity for the participant's parent/legal guardian to ask questions about this research study. I have been available to answer any questions the participant's parent/legal guardian has had about this study.

Signature of Person Explaining Consent | Date

Printed Name of Person Explaining Consent

DATA PROTECTION

I confirm that I have read 'Section 12 - Will my child's personal data be kept private?' and its contents were explained to me. I have had the opportunity to ask questions and all my questions were answered to my satisfaction. I understand that my child's personal data will be collected, used, and shared for the purposes specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing this form.

Signature of Parent/Legal Guardian | Date

Printed Name of Parent/Legal Guardian

STATEMENT OF PERSON EXPLAINING AUTHORISATION

I have carefully explained to the participant's parent/legal guardian the nature and purpose of this form. I have been available to answer any questions the participant's parent/legal guardian has about this form.

Signature of Person Explaining Authorisation | Date

Printed Name of Person Explaining Authorisation

(When completed: 1 original to be filed in the Investigator Study File (ISF), 1 to be kept in the medical records, 1 for the participant)