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Parent/Legally Acceptable Representative Information Sheet and Consent Form (UK)-Part 1

NAME OF STUDY:	A Phase I/II Open Label Study in Previously Studied, SBC-103 Treatment Naïve MPS IIIB Subjects to Investigate the Safety, Pharmacokinetics, and Pharmacodynamics/Efficacy of SBC-103 Administered Intravenously
Short Title:	SBC-103 Intravenously in SBC-103 Treatment Naïve MPS IIIB (NGLU-CL01-T)
STUDY NUMBER:	NGLU-CL01-T
STUDY SPONSOR:	Alexion Pharmaceuticals, Inc. 100 College Street New Haven, CT 06510, United States
STUDY DOCTOR (INVESTIGATOR):	[Investigator Name] [Site Address] [Office Hours Tel] [Out of Hours Tel]

Why are you receiving this information?
Your child is being invited to take part in a research study because he/she has Mucopolysaccharidosis type IIIB ("MPS IIIB") and have previously participated in study NGLU-CL01. Before you decide whether to give permission for your child to participate in this research study, it is important for you to understand why the research study is being done and what it will involve. The following information describes the study and your child's role as a possible participant. Please read this information carefully and do not hesitate to ask the study doctor any questions to ensure that you are able to make an informed decision as to whether your child may participate. Please take as much time as you need to decide whether or not you think you would want your child to take part; you do not have to decide today. You may take this information sheet home with you and discuss participation with family, friends or your general practitioner (GP).

Part 1 tells you the purpose of this study and what will happen to your child if he/she takes part.
Part 2 gives you more detailed information about the conduct of the study.

Your child is under no obligation to take part in this study.

What is the purpose of this clinical research study?
The study sponsor is evaluating a drug called SBC-103. SBC-103 is an investigational drug. "Investigational" means the drug is not approved for use in the treatment of your child's disease by any regulatory authorities. This study is being done to learn more about the safety and effects of SBC-103. In this document, SBC-103 will be referred to as "study drug".

Mucopolysaccharidosis type IIIB (MPS IIIB) also known as Sanfilippo B Syndrome is a rare disease that causes build-up of sugars (heparan sulfate) in the brain and other parts of the body. This is due to the lack of the enzyme called NAGLU (or N-acetylglucosaminidase). The build-up causes serious health problems that include changes in behaviour, mental retardation and severe physical disability. There are currently no effective or approved treatments for MPS IIIB. In studies with animals that also lack the NAGLU enzyme, SBC-103 has

been shown to reduce the build-up of sugars in the brain and liver of these animals. The effects of the study drug in humans are currently being studied in one other study of 11 children. The study will help provide information on whether similar reduction of sugars can be observed in participants with MPS IIIB.

Does your child have to take part?
No. Participation is entirely voluntary and you may refuse for your child to participate or withdraw him/her from the trial at any time without penalty or loss of benefits to which he/she is otherwise entitled. If you would like your child to participate you will need to read this information sheet and sign a declaration form to show you would like your child to take part.

Depending on your child's age and level of understanding, he/she may be given an age-specific information sheet and assent form to sign. Your child may decide not to take part in the study, even if you have agreed for him/her to take part.

How many participants will take part in this study?
It is expected that approximately 5 participants in the United Kingdom will participate in this study.

How long will your child be in the study?
If your child takes part in the study, your child's participation could last for approximately 3 years (164 weeks). This will include a Screening period that may last up to 4 weeks, a treatment period that will last up to 156 weeks, and a follow-up phone call 4 weeks after the last dose of study drug.

How many visits and what procedures are involved?
If you decide to allow your child to participate in this study and your child is considered eligible, your child will have visits every other week for up to 156 weeks (3 years). Most visits will take approximately 5-7 hours. Some visits will take approximately 10 hours. Two visits will require an overnight stay at the clinic/hospital. At your child's visit at Week 24 (6 month) he/she will have a complete evaluation similar to the screening visit. The number of days your child visits the clinic may be more if the study doctor schedules procedures over several days.

Your child will have a follow-up telephone call within 24 hours of dosing from Week 2 through Week 6 (after your child's 2nd, 3rd and 4th dose), and 4 weeks after your child's last dose of the study drug. During these calls, we will ask you how your child is feeling and if there have been any changes in your child's medications.

What will happen at your child's first study doctor visit (Screening)?
The following tests and procedures will be performed to determine if your child qualifies to take part in this study. This study visit may take place over more than one day:

- **Informed Consent**- Before any study procedures are done, you will be asked to sign the Consent Form. You should read and understand the form before signing. Your child's study doctor will discuss with you any questions you may have.
- **Medical History**- We will ask you about your child's past health history since the completion of the NGLU-CL01 study. Data on your child's siblings (under age of 16) medical history will be obtained from the NGLU-CL01 database. Any changes in sibling's medical history since your child's participation in the NGLU-CL01 study will be recorded.
- **Medication History**- We will ask you about the medicine(s) your child takes now or has taken in the past 30 days and will record this, including all current medications (use of prescription and over-the-counter medications), any supplements your child takes such as herbal preparations, vitamins and mineral supplements.
- **Electrocardiogram (ECG)** - This test is a painless way of looking at how your child's heart is working.

- **Physical Examination**- The study doctor will examine your child's body, and their height and weight will be measured.
- **Vital Signs-** The study doctor will check your child's temperature, blood pressure, heartbeat and breathing rate.
- B**lood tests-** Some blood will be taken for tests that check and monitor your child's general health, as well as for tests related to MPS IIIB. The amount of blood taken on this first visit will be about 20 milliliters (ml), or 4 teaspoons. Blood samples will be taken approximately 40 times throughout the course of the study. Approximately 790 mL of blood, (about 3 cups), will be collected throughout the study. On average this is 30-35 mLs of blood per draw over the course of 3 years. This is safe and well within the recommended/accepted limit for blood sampling volumes. Additional blood samples may be required if any of your child's lab test results are abnormal. It is possible that more than one attempt to obtain a blood sample may be necessary.
- **Urine Tests**- Some urine will be collected for tests related to MPS IIIB. If your child is a female who can become pregnant, a urine pregnancy test will be performed. If a urine sample is not able to be provided, a serum pregnancy test will be performed. The test result must be negative in order for your child to join this study.
- **Questionnaires**- We will ask you and your child some questions and will ask you to fill out several questionnaires that will help us to understand how MPS IIIB affects you and your child's life. You can skip any questions you do not want to answer.
- **Photo**- The build-up of sugars in this disease can change the appearance of your child's face. As part of the study, we will ask to take a photograph of your child's face. Your child's picture will only have his/her study-specific identification linked to it and his/her name or other personal identifiers will not be attached. Your child's picture will be used with photographs from other children in the study to look for specific changes in facial characteristics which are linked to the onset and progression of MPS IIIB. This information may contribute to a method for earlier diagnosis in the future. The photos will also be used to see if there are changes over time. This will be done by a vendor contracted by the study sponsor. Images will be sent using secure (encrypted) means of connection between the mobile device and the vendor database. All photos are stored in an encrypted, secure way and are not accessible by third parties. You may refuse to have your child's picture taken and still be able to participate in this study.
- If you are not familiar with any of these procedures, please ask your child's study doctor to explain why and how they are performed. Any of the procedures or tests above, such as blood sampling, may need to be repeated if the results of the tests are unclear. For additional information regarding the procedures mentioned above, refer to the section "Risk associated with study procedure".

What happens after the Screening visit?
If the results of the tests performed at the Screening visit show that your child qualifies for this study, and the study doctor agrees, he/she will be accepted to participate in this study and will be scheduled to come back for more visits every 2 weeks for up to 156 weeks (3 years).

What will happen at the second study doctor visit (Week 0)?
At your child's second visit**,** which will require an overnight stay at the clinic/hospital, the following procedures will be performed. Please note that some of these procedures may be spread over a few days.

- The study doctor will examine your child's body, and check his/her heartbeat, temperature, blood pressure and breathing.
- An electrocardiogram (ECG) test will be performed.

- A urine pregnancy test for all female participants who can get pregnant will be performed. If it is not possible to collect urine, a blood pregnancy test will be performed. The test result must be negative in order for your child to stay in the study.
- **Lumbar Puncture-** We will ask you to allow your child to have a test called a Lumbar Puncture. We will give your child medicines to make him/her sleepy where he/she is unable to move or to feel pain. While he/she is sleeping, the study doctor will use another needle to get a small amount of spinal fluid from your child's back. A total of 10ml of fluid (2 teaspoons) will be collected. For safety, the study team will watch your child after the lumbar puncture and take his/her vital signs before he/she is permitted to leave the hospital.
- **Magnetic Resonance Imaging (MRI) -** We will ask you to allow your child to have a test called an MRI. An MRI scanner is a large tube that uses magnetic waves to make detailed pictures of the inside of the body. In this study your child will have an MRI of his/her head to take these pictures of the brain. Because the strong magnet in the machine attracts some metals and affects some electronic devices, please tell your child's study doctor if he/she has any metal implants, a pace-maker or any metal dental fillings. Your child may not be able to have an MRI if he/she has metal in his/her body. MRIs will be performed while your child is still asleep from the general anaesthesia.
- **Anaesthesia/Sedation** - During the lumbar puncture procedure and the MRI your child will need to lie almost perfectly still. Because this can be hard to do, especially for patients with your child's disease, the study doctor may decide to give your child anaesthesia or medication to make him/her sleepy. Medication for general anaesthesia is either given intravenously (through a vein) or inhaled through a mask in order to help your child go into a kind of deep sleep where he/she is unable to move or to feel pain. In general, participants will breathe by themselves during the kind of general anaesthesia that will be used. However, if needed assistance with a breathing machine (ventilator) might be applied. More information about general anaesthesia is given later in this Information Sheet.
- **Intravenous (IV) infusion of Study Drug (SBC-103)** - Starting at this visit, your child will be given his/her first dose of study drug by IV infusion. Your child will be awake while he/she is given the study drug, which is given through a vein in the arm, hand or chest. A small tube called an IV catheter will be placed in your child's arm or hand. This tube will make it easier to give your child the study drug. Instead of inserting a tube in your child's arm, your child's study doctor may decide to place a central venous catheter. This is a tube inserted in a large vein in your child's chest. This is a surgical procedure which may require general anesthesia (your child will be given medicine to help him/her go into a deep sleep) or sedation. The infusion of study drug will take about 2 hours. Before any infusion, you should tell your child's study doctor if your child has been feeling sick (a cold, flu or fever), so that he can decide whether to give your child study drug on that day. Your child's vital signs will be taken before the infusion and several times during and after the injection.
- Blood and urine will be taken for other tests, including tests to see how much study drug is in your child's blood during and up to 24 hours after the infusion. The amount of blood taken at this visit will be about 35 mL (approximately 7 teaspoons) from approximately 18 blood samples. Depending on your child's age and body weight, less blood may be taken. Some tests may be postponed to the next visit. Blood and urine samples that are left over may be used for additional testing for markers of MPS IIIB.
- After your child's first infusion of study drug, he/she will stay at the hospital/clinic overnight to see if he/she is showing signs or symptoms of any negative effects from the infusion.

What to expect at the overnight stay?
During the overnight stay, all of your child's meals will be provided. You may bring books, magazines, electronic devices such as laptops, tablet computers, smartphones, etc. to the clinic. You may bring comfortable clothing and personal items, but please leave any valuables, such as jewellery, at home.

The day after your child's first infusion the study team will take blood for tests before your child goes home. The amount of blood taken on the day after your child's infusion will be about 5 ml (1 teaspoon). Depending on your child's age and body weight, less blood may be taken.

What will happen at the next study visits?
Every 2 weeks for the next 156 weeks (3 years) your child will come to the hospital/clinic. We will give your child study drug approximately every 2 weeks for a total of approximately 79 doses administered. Visits will usually last between 5-7 hours.

At every visit your child will have the following:
- We will ask you or your child how he/she is feeling now, and since the last visit.
- We will ask you about the medicines your child is taking.
- We will call you after each visit at Week 2, Week 4 and Week 6 to ask you and your child how he/she has been feeling.
- Your child's vital signs will be taken before the infusion and several times during and after the infusion.
- Your child will be given a dose of study drug by IV infusion.

Every 4 weeks (1 month) your child will have the following:
- A physical exam will be completed.
- Blood and urine will be taken for tests before your child's infusion. The amount of blood taken on these visits will be about 27 mL (a little more than 4 teaspoons). Depending on your child's age and size, less blood may be taken.

Every 12 – 16 weeks your child will have the following:
- An electrocardiogram (ECG) test will be performed.
- Anaesthesia/Sedation will be given for the lumbar puncture procedure.
- Lumbar Puncture will be done to get some cerebrospinal fluid from your child's back. A total of 10ml of fluid (2 teaspoons) will be collected.
- Blood tests to check levels of enzyme will be taken before, during and after study drug infusion at Week 12, Week 24, Week 52, Week 78, Week 104, Week 130, and Week 156/End of Treatment. Some of these visits will require your child to stay after the infusion is completed.

Every 6 months to 1 year your child will have the following:
- Anesthesia/Sedation will be given for the MRI procedure.
- A MRI will be performed.
- Questionnaires- We will ask you and your child some questions and will ask you to fill out several questionnaires that will help to understand how MPS IIIB affects you or your child's life. You can skip any questions you do not want to answer.
- Photo- To assess possible changes in your child's appearance during the study, we will take a picture of your child's face.

4 weeks (1 month) after your child's last visit your child will have a phone call:

- To discuss any changes in the medications your child is taking.
- To discuss how your child is feeling now, and since the last visit.

The study doctor will watch your child's health closely during the study. The study doctor may ask you to allow your child to have other tests if his/her health changes.

The following table shows you a summary of which tests to expect at each visit during the study:

	Screening	**Week 0**	**Day 1**	**Every 2 Weeks**	**Every 4 Weeks**	**Week 12**	**Week 24**
Eligibility	X	X					
Medical History	X						
Physical Exam	X	X	X		X	X	X
Vital Signs	X	X	X	X	X	X	X
Photograph	X						X
Blood and Urine Samples	X	X	X		X	X	X
ECG	X	X				X	X
Questionnaires	X						X
Lumbar puncture – Spinal Fluid Samples		X				X	X
General Anesthesia/Sedation		X				X	X
MRI		X					X
Questions about how your child is feeling	X	X		X			
Questions about medicines your child has taken	X	X		X			
Study Drug Infusion		X		X	X	X	X
Overnight Stay*		X					X

*There will be an overnight stay at week 24.

	Every 12-16 weeks	Every 12-28 weeks	Every 6 months – 1yr	Week 156/End of Treatment	Week 160
Physical exam/height and weight				X	
Vital signs				X	
Photograph			X	X	
Blood and urine samples				X	
Electrocardiogram (ECG)		X		X	
Questionnaires			X	X	
Lumbar puncture	X			X	
Medicine to make your child sleepy or to feel numb	X		X	X	
MRI			X	X	
Questions about how your child is feeling				X	
Questions on medications				X	
Infusion of SBC-103				X	
Phone call (4 weeks after last infusion of SBC-103)					X

Expenses and payments
You/ your child will not receive any payment, either directly or indirectly for your child's participation in this study. Reasonable expenses incurred in travelling to the hospital for study visits will be reimbursed. Bus/train/taxi fares and petrol will be reimbursed on production of a receipt.

Reasonable meal costs may also be reimbursed. The study staff will explain to you the reimbursement process, which may be provided by the MPS PACT (Patient Access to Clinical Trials). If this travel reimbursement is needed, a separate information sheet and consent form, explaining the process, will be provided to you.

What is expected from your child?
When deciding whether to have your child participate, consider whether you and your child are able and willing:
- To follow the study rules
- To commit the time required to keep appointments, including overnight visit(s)
- To tell the study doctor about your child's complete medical history
- To report any new problems, illnesses, or changes in medication during the study
- Please do not start your child on any new treatment without first asking your child's study doctor, not even over the counter drugs, herbs, or supplements that you can get without a prescription.

What are the alternatives to taking part in this study?
You can choose for your child not to take part in this study and continue with the normal care provided by the doctor. If you decide for your child not to participate in this study, the study doctor will discuss treatment options with you and your child and the associated risks/benefits. There are other experimental treatments currently under investigation in the UK for your child's disease. You should discuss the risks and potential benefits of this experimental therapy for your child with your doctor. However, there is currently no approved treatment for MPS-IIIB.

What will happen at the end of the study?
After the study drug is stopped, the study doctor will discuss what medical treatment your child should receive.

What are the potential risks and discomforts?
If your child holds private medical insurance, you should check with the company issuing the insurance before agreeing for your child to take part in this clinical study, as you will need to ensure that his/her taking part in the study will not affect the insurance.

Your child may have side effects while taking part in this study. At this time there may be unknown side effects which cannot be predicted. No clinical results of this study are available at this time. The study staff will watch your child carefully for any side effects. Some side effects may be mild, but others could make your child very sick or may be life-threatening. Your study doctor and staff will make every effort to prevent side effects or treat them quickly. **If you think your child has any side effects during the study, you should tell the study doctor right away.**

SBC-103 (Study drug)
To date, 14 participants have been treated with SBC-103.
Preliminary safety data has been reviewed by the study sponsor as of 29 June 2016. Eleven participants have received at least 1 year of study drug treatment. In addition three participants have received between 32 to 36 weeks of study treatment. Overall, data from 14 participants have been reviewed by the study sponsor. It was found that IV infusions of SBC-103 from 0.3 to 10 mg/kg administered every other week appear, overall, to be safe and well tolerated by all participants in the study. The most common side effects (adverse events) were fever, vomiting, diarrhoea, cough, runny nose, nasopharyngitis (symptoms of a common cold), hypervigilance

(an increased arousal or increased responsiveness to stimuli) and diaper rash. The majority of side effects were considered mild in intensity and were considered unlikely or not related to the study drug. There were some side effects considered by the investigator to be related or possibly related to treatment with SBC-103; the majority of these happen during the infusion (also referred to as infusion associated reactions or [IARs]), which are also commonly observed with other enzyme replacement therapies. The IARs occurred in three participants and included fever, fast heartbeat, elevated blood pressure, and chills. These side effects were all non-serious and mild in intensity. One participant experienced 3 IARs with signs and symptoms consistent with a hypersensitivity reaction. These 3 hypersensitivity IARs were considered serious by the investigator and reported as related to the study drug. The hypersensitivity reactions fully resolved following interruption of the study drug infusion and administration of medications.
As of 29 June 2016, there were 5 additional treatment-emergent serious adverse events in three participants (staphylococcal bacteria in blood, bacteria in blood, fever and device-related infection [2 events]). These events were assessed as mild to moderate in intensity, unrelated to the study drug, and were resolved at the time of the data review.

Enzyme Replacement Therapies

SBC-103 is an investigational enzyme replacement therapy. Since there are only 14 participants who have received SBC-103 to date, there is limited information available on the side effects of SBC-103. Larger numbers of patients with other lysosomal storage diseases (like other MPS diseases) have been treated with enzyme replacement therapies. It is possible that the risks and discomforts for SBC-103 may be similar to these drugs, and may include the following:

- Side effects of enzyme replacement therapy may include: flushing, rash, mild-moderate high blood pressure, fast heartbeat, fast breathing rate, headache, and a slight fever. These are common side effects with these types of drugs and they usually happen during the infusion. These side effects can usually be controlled by slowing the speed of the infusion or by giving some drugs like anti-histamines and acetaminophen.
- Severe infusion reactions and serious side effects related to enzyme replacement therapy administration are rare. These side effects include hypersensitivity, shortness of breath or difficulty breathing, very low or very high blood pressure, and very fast or very slow heartbeat. These types of reactions are usually controlled by stopping the infusion and by giving stronger prescription medications like steroids and/or adrenaline.

Allergic Reaction

As with any drug, particularly with enzyme replacement therapies, an allergic reaction can occur and can be life-threatening to some people. **It is very important that you tell the study doctor about past medical history, including any reaction your child has had to other drugs or foods. This will allow the study doctors to keep your child as safe as possible during his/her participation in this study.**

Allergic reactions can be mild or more serious and very rarely can result in death. Common allergic reactions are rash or itching. Less common allergic reactions are swelling of the face and throat, or trouble breathing. If your child has signs of a moderate to severe allergic reaction, your child may have additional evaluations such as skin testing (tiny puncture or pricks made in the skin), to determine if it is safe for him/her to continue in the study. Your child will be monitored during the infusion and for a period after the infusion to look for signs of an allergic reaction. As the study drug is made from eggs, please tell the study doctor if your child has had an allergic reaction to eggs.

If your child experiences any of the side effects listed above or any changes in his/her health, please tell your study doctor immediately without waiting for the next planned study visit. Please do not have your

child start any new treatment without first asking your study doctor, not even over the counter drugs, herbs, or supplements that you can get without a prescription.

Risk associated with the study procedures

There are possible risks due to some of the procedures to be performed:

Intravenous Infusion Risks

Intravenous Infusion (IV dosing) is where the drug solution is given through a needle into your child's hand, arm or chest vein. Medications administered into veins (intravenously) can sometimes cause pain, swelling and redness of the vein and surrounding tissues, which may not go away quickly, even if the medication is stopped. Infection and nerve injury can also occur.

IV Catheter

The placement of a thin tube inside the vein in your child's arm, hand or chest is necessary to give your child the study drug and to make taking blood samples easier. The following risks may be encountered with this procedure:

- ***Pain during placement*** - Discomfort can result from the needle stick and placement of the catheter at the time it is inserted. Doctors try to lessen the pain with a local numbing medicine (anaesthetic like novocaine). The discomfort is usually mild and goes away once the catheter is in place.
- ***Collapsed lung*** - This is called a pneumothorax. The lung is very close to the veins of the neck or chest. If the needle passes through the vein, it could pierce the lung causing it to leak and collapse on that side. If this happens, the doctor can place a tube between the ribs into the chest to suck out the air that is leaking from the lungs. This complication is particularly dangerous when a patient is on a breathing machine. Rarely, collapse of the lung can cause death. This complication can even happen when everything is done correctly.
- ***Infection*** - Any tube (catheter) entering the body can make it easier for bacteria to get in and infect the patient. The longer a catheter remains in the body, the more likely it is to become infected. Special care in bandaging the skin at the needle site and changing the connecting tubes and fluids help to decrease this risk. With great care, these catheters can remain in the body for several weeks without becoming infected.
- ***Bleeding*** - Bleeding around holes in the veins is usually mild and seals on its own. Since the major arteries run alongside the major veins, the arteries can be punctured by accident. Even bleeding from an artery can stop on its own before serious problems occur. Rarely, the chest fills with blood, which can be life-threatening. In that situation, it may be necessary to place a tube between the ribs to drain out the blood.
- ***Clotting around the catheter*** - Blood clots can commonly form in and around these catheters inside the veins. Such clots usually do not cause problems. Once the catheter is removed, the body can often dissolve the clot over time. Sometimes, clots can break off and travel out into the lungs. This is called a pulmonary embolism. A blood clot in the lungs can cause breathing problems and, very rarely, death.
- ***Air entering through the catheter*** - Rarely, air enters the catheter as it is being inserted. The air bubbles can travel through the heart and cause lung injury and low blood pressure. This problem is called an air embolism. Special care is taken to avoid air entry.

Please tell the study doctor or nurse if your child feels something strange is happening to him/her. If these things happen to your child, he/she may need to have other testing done to decide if he/she can keep getting study drug.

Blood Sampling – Your child may feel some pain, bruising, redness or itching where the needle pierced the skin. Very rarely your child might feel dizzy or faint, he/she may get an infection in the blood, an infection on

the spot where the needle went into his/her arm or a blood clot may form. In very rare cases, the needle might damage a nerve or a blood vessel. This will be performed by very experienced staff under sterile conditions so this is very unlikely to occur.

ECG - During the ECG test, the study staff will put sticky patches on your child's skin. Some people may get a slight skin irritation from the patches or from their removal, but this is usually mild and goes away within a few days.

MRI

During the MRI, your child will lie on a narrow table, which slides into a large tunnel-shaped scanner. An MRI exam causes no pain, but your child may have difficulty keeping still or may become nervous in the scanner. Your child may be given anaesthesia/sedation to help him/her to lie still. The sound of the MRI scanner can be quite loud; your child may be given special ear plugs to minimise the noise. If your child has metal objects in his/her body, this can be a safety risk to your child or affect the MRI image. Metal or electronic devices in the body can include the following: metallic joint prostheses, artificial heart valves, an implantable heart defibrillator, a pacemaker, metal clips to prevent veins from leaking, cochlear implants, body piercing, a bullet, shrapnel or any other type of metal fragment.

Lumbar puncture

Prior to the lumbar puncture, we will give your child some medicine that will help him/her feel sleepy and medicine to make it not hurt, but your child may still feel some pain. The skin on your child's back may be a little sore for a short time at the place where the fluid was taken. To help with this, we will use a special cream. Your child may also have a mild sore head for a short time. We will give your child medicine to help this get better.

Anaesthesia/Sedation

During procedures such as MRI and lumbar puncture your child may be sedated, which means that your child will be given some medicine that will help him/her go into a kind of deep sleep where he/she is unable to move or to feel pain. Medicines are usually given intravenously (through a vein) in your child's arm or leg or inhaled through a mask. Monitoring devices are used to watch your child's blood pressure, heart rhythm and breathing. Although common and generally safe, any sedation carries some degree of risk and it is important for you to be aware of these risks. Risks of sedation include excessive sleepiness, slow to wake up, low blood pressure, slowed breathing, apnea (no breathing), abnormal or irregular heartbeats, nausea, vomiting, aspiration (inhaling stomach contents into the lungs), or very rarely death. Usually, participants will breathe by themselves during the kind of general anaesthesia that will be used. However, the work of breathing may have to be performed artificially with assistance of a breathing machine (ventilator). In this case, a tube would be inserted into your child's airway ('breathing pipe') in order to safely and securely manage the breathing during the anaesthesia. The anaesthesia will be given and managed by an experienced paediatric anaesthetist. Your child will therefore be continuously and strictly monitored during the whole procedure until fully awake. This will be done under supervision of the anaesthesia team.

In the event that your child experiences any side effects during his/her participation in the study you should contact the study doctor as soon as possible.

Allergy Skin Test

The risk with skin testing is that allergy symptoms might occur during the test. The most common side effects of skin testing are itching and/or swelling of the skin where the test was done. The itching and/or swelling are usually most noticeable during the test and typically go away within a few hours, although it can last for 1 or 2 days. In rare cases, a more serious allergic reaction can occur.

Are there any reproductive risks?

Women: It is not known if the study treatment may affect an unborn child or nursing infant. For this reason, if your child is breast-feeding, pregnant or plans to become pregnant, your child may not participate in this study. If your child is capable of becoming pregnant, she must use an acceptable method of birth control throughout the entire study and for 30 days after her last dose of study drug.

Men: It is not known if the study treatment may affect your child's sperm or an unborn child. For this reason, your child must use an acceptable method of birth control throughout the entire study and for 30 days after your child's last dose of study drug.

Birth control methods considered acceptable for this study include hormonal contraception (pills, injections, contraceptive patch, implant), intrauterine device, and double-barrier methods (any double combination of male or female condom with spermicidal gel, diaphragm, sponge or cervical cap with spermicidal gel) or true abstinence. Please discuss this with your child's study doctor.

Your child must use birth control for the entire study and for at least 30 days after your child's last dose of study drug.

It is important that you tell the study doctor immediately if your child or his/her partner becomes pregnant during and up to 90 days after the study. The doctor will talk with you about what you should do. Your child's participation in the study may be stopped, and your child and/or his/her partner will be required to sign a separate informed consent form prior to collection of data about the pregnancy and associated outcome for scientific or security reasons and genetic risks.

What are the advantages and disadvantages of participation in the study?

Since this is the second study in patients, and the results of the first study are not yet available, it is not known if your child is likely to benefit. However, by taking part, your child will provide new information that may benefit other participants in the future. Potential disadvantages of participations include the risk of experiencing side effects from treatment with SBC-103, or from study-related procedures. These side effects and risks are described in the sections above.

What happens when the research study stops?

When the study stops the study doctor will discuss ongoing standard of care.

What if there is a problem?

Any complaint about the way you/ your child have been dealt with during the study or any possible harm your child might suffer will be addressed. The detailed information on this is given in Part 2.

Will taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about your child will be handled in confidence. The details are included in Part 2.

This completes Part 1.

If the information in Part 1 has interested you and you think you may like your child to take part, please read the additional information in Part 2.

What will happen if new information becomes available during the study?

Your child's study doctor will inform you in a timely manner of any new information learned during the study that may affect your willingness to continue your child's participation. If you decide not to have your child continue, the study doctor will discuss potential options for your child's care. If you decide for your child to continue in the study, you may be asked to sign an updated informed consent form.

What happens if you change your mind?

Your child's participation in this study is voluntary. Your child does not have to take part, or you may discontinue your child's involvement at any time without penalty or loss of benefits to which he/she is otherwise entitled. If you decide to have your child leave the study before the last study visit, tell the study doctor and follow instructions. It may be helpful to the study sponsor if you could explain your reasons, but you do not have to. Your child may receive standard treatment and no prejudice will be shown towards your child for medical care or participation in future research.

Can your child be withdrawn from the study?

Your child's study doctor or the study sponsor may withdraw your child from the study for any reason, even if you wish to have your child continue to participate for the following reasons:

- The study doctor thinks it is best for your child to stop taking the study drug.
- Your child experiences certain side effects.
- You or your child does not follow the study instructions.
- If your child is a female and becomes pregnant during the study.
- The study sponsor decides to stop the study for safety or business reasons.
- The responsible regulatory authority or Institution Review Board / Ethics Committee decide to stop the study.

If your child's participation in the study is stopped early, you may be asked to allow your child to complete end of study procedures (such as a final medical examination and laboratory tests) for your child's own safety.

If you choose to withdraw your child from the study or he/she is taken out of the study, your child will not continue to receive the study drug. The study doctor will discuss your child's options with you. If the study is terminated early, or when the study is ended, the study sponsor may not continue providing the study drug.

What if there is a problem?

Complaints

If you have a concern about any aspect of this study, you should ask to speak with the researchers who will do their best to answer your questions <<contact number>>. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. We recommend that you obtain a copy of the hospitals complaints procedure or policy if you intend to make a complaint.

Harm

Alexion Pharmaceuticals, Inc. has obtained insurance for compensation of injury caused by taking part in this study in accordance with the guidelines of the Association of the British Pharmaceutical Industry (ABPI).

This insurance will reimburse for injuries directly resulted from:

- Any test or procedure your child receives as part of the trial
- A drug being tested or administered as part of the trial protocol
- Any reimbursement would be without legal commitment. (Please ask if you wish more information on this)

Alexion Pharmaceuticals, Inc. would not be bound by these guidelines to reimburse where:

- The injury resulted from a drug or procedure outside the trial protocol.
- The protocol was not followed.

Copies of these guidelines are available from the study doctor on request.

If you think your child has had an injury/illness that is related to the study, you should immediately tell <<insert name>>, the investigator, or one of the staff members working on the study. The investigator and the study staff may be reached at <<insert address and telephone number>>.

How will your child's confidentiality be respected and the privacy of your child's personal information be maintained?

You have the right to control the use and disclosure of your child's personal information. Basic personal information will be recorded including your child's name, contact details, gender, height, weight and racial origin (to be used only for clinical purposes), as well as information on your child's medical history, and clinical data collected about your child's participation in the study. The following people may also access your child's medical records in addition to the study doctor and study personnel:

- Study monitors and auditors who may work for Alexion Pharmaceuticals, Inc. (the study sponsor) or its affiliates or authorised representatives, to check that the study is being performed correctly and that the information collected about your child is accurate;
- National and international regulatory authorities (including without limitation the Medicines and Healthcare products Regulatory Agency MHRA) and the United States Food and Drug Administration (FDA) involved in ensuring that the study is being performed correctly according to the study protocol and applicable laws.

All personnel accessing your child's records or your child's personal data are required to respect your child's confidentiality at all times in accordance with any applicable laws.

To ensure privacy, your child's name and other identifying information will not be attached to study data or samples released for research purposes. Instead, your child will only be identified by a code. Only the study doctor and authorised personnel will be able to connect this code to your child's name, by a list that will be kept securely by the study site for 15 years. This list will not be removed from the site by the study sponsor and its representatives or contracted third parties. After 15 years the link to the coded data will be destroyed. Once the code key is destroyed, it will not be possible to link the data collected about your child to his/her name, your child's data will become anonymous, and the study sponsor will only keep and use fully anonymous data.

Where allowable by local law, your child's date of birth may also be recorded to help identify your child's study record.

Your child's coded study data will be forwarded to the study sponsor and its representatives or contracted third parties for activities related to the study. The study sponsor may process, access, store, transfer, and use the coded study data collected from your child's medical records and health information as explained above. Once the code key is destroyed and your child's coded data becomes anonymous, the study sponsor may process, access, store, transfer, and use it indefinitely.

Study data will be transferred and stored into a computer database and processed to allow the results of this study to be processed, accessed, analysed and reported or published. If the results of the study are published, your child's identity will remain confidential.

Recipients of your child's information may be in countries that do not have data protection safeguards and rights. Alexion Pharmaceuticals, Inc. and its authorised representatives, and regulatory authorities, shall anyway

seek to maintain confidentiality within the limits of local laws in these countries. A list of companies to whom your child's coded information is transferred is available from Alexion Pharmaceuticals, Inc. via the study doctor.

Under data protection law UK Data Protection Act 1998 your child's study site and Alexion Pharmaceuticals, Inc. shall be jointly responsible as 'controllers' for ensuring that your child's information is safeguarded. Alexion Pharmaceuticals, Inc. has appointed PPD Global Ltd, Granta Park, Great Abington, Cambridge, CB21 6GQ, UK as its 'representative' in your child's country to fulfill its obligations under this law. You have the right to access, through the study doctor, all the information collected about your child and, if applicable, ask for corrections.

If your child should withdraw from the study, data collected prior to your child's withdrawal may still be accessed, used, stored, transferred and processed along with other data collected as part of the study. Normally no new information will be collected for the study database unless you specifically consent to that. However, the law does require that any side effects your child may suffer are documented and reported. You have the right to require that any previously retained samples are destroyed. If you require that your child's samples be destroyed, and your child's samples have already been tested, those results will still remain and continued to be accessed, used, stored, transferred and processed as part of the overall research data.

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

What will happen to your child's data?
This clinical study may only be performed by collecting and using your child's medical information. Data protection laws give you the right to control the use of your child's personal information. Therefore, by signing this form you specifically authorise your child's information to be checked, accessed, used, stored, transferred and processed as follows:

- The authorised representatives of Alexion Pharmaceuticals, Inc. and regulatory authorities' inspectors may review your child's medical information by direct access to your child's medical records.
- Study data, including your child's coded medical information, may be used, processed, stored, accessed, transferred and shared for legitimate study and scientific purposes, including (if you do not object), for future use in medical or pharmaceutical research.
- Study data may be transferred to other countries outside of the United Kingdom for access, use, storage and processing, including countries not covered by the data protection legislation.

Involvement of the General Practitioner/Family doctor (GP)
Your child's family doctor (general practitioner) will be notified of your child's involvement in this study and asked to provide details from his/her medical records including any treatment received during the study if you give permission to do so, by signing the consent form.

What will happen to any samples given?
Your biological samples may be collected, used, stored, accessed, transferred, processed (to other countries outside the United Kingdom) and reported as necessary for the purposes of the study.

Some of the spinal fluid samples collected during the lumbar puncture and some of the blood samples will be sent to the hospital's local laboratory <insert address> for testing and will be destroyed within 6 months after official release of study data reports. Blood, urine, spinal fluid samples and tissue samples will also be sent and stored at the following locations:

- Greenwood Genetic Center, 106 Gregor Mendel Circle, Greenwood, SC 29646, USA
- Blue Stream Laboratories, Inc. , 763 Concord Ave., Building E, Cambridge, MA 02138, USA
- Frontage Laboratories, Inc., 700 Pennsylvania Drive, Exton, PA 19341, USA
- Charles River Laboratories, 22022 Transcanadienne, Senneville, Quebec Canada H9X 3R3
- PPD Central Labs, 2 Tessenner Drive, Highland Heights, KY, USA 41076
- PPD Central Labs, Clusterpark, Kleine Kloosterstraat 19, Zaventem, Belgium
- Cleveland Clinic, 2119 E. 93rd St, L15, Cleveland, OH 44195, USA

The blood samples will be retained for a maximum of 15 years and will be destroyed afterwards. Only authorised representatives will have access to the samples and results.

You have the right to withdraw your child's consent to their samples being use and stored. You have the right to require that all of your child's previously retained identifiable samples are destroyed to prevent future analysis. Some samples may be stored for a maximum of 15 years after the end of this research, as required by applicable legislation. In case the study sponsor wants to use these samples after the 15 year storage period, in the future for new research, you will be informed and we will ask you for your permission again. You can then decide whether it can be used.

What will happen to the results of the study?
Information from this study may be presented at a professional meeting or published in a medical journal. Your child's name and other information that would identify your child will not be used.

Who is funding this research?
Alexion Pharmaceuticals, Inc., (a biopharmaceutical company) will be organising and funding this study. Alexion Pharmaceuticals, Inc. will pay the hospital trust to cover their costs of conducting this study. If applicable, the study doctor will disclose to you any financial links or other interests that he/she may have to the study sponsor.

Has the study received medical or ethical approval?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee to protect patient's safety, rights, well-being and dignity. This study has been reviewed and given favourable opinion by NRES Committee North West – Haydock.

Further information and contact details
You may freely ask questions about this form or the study now or at any time during this study. If your child experiences any side effects, or if you have any questions about this research during this study you may contact: <insert investigators name> on telephone number <insert telephone number> or support staff on <insert telephone number>

For any questions about your child's rights as a research participant, please direct enquiries to:
<Insert Contact Information>

Do not sign this declaration form unless you have had the chance to ask questions and have received satisfactory answers to all of your questions.

If you think you would like your child to participate in this study and you sign the declaration form, you will receive a signed and dated copy of this form for your records. Thank you for taking the time to read this information.

Site/ institution headed paper

Consent Form
(UK)

Principal Investigator: **Site/Institution:**

Participant Number:

Short Title: SBC-103 Intravenously in SBC-103 Treatment Naïve MPS IIIB (NGLU-CL01-T)

Please initial box

1. I confirm that I have read and understand the participant information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my child's participation is voluntary and that I am free to withdraw my child at any time without giving any reason, without my/my child's medical care or legal rights being affected ☐

3. I understand that relevant sections of my/my child's medical notes and data collected during the study, may be looked at by individuals from Alexion, from regulatory authorities or from the NHS Trust where it is relevant to their taking part in this research. I give permission for these individuals to have access to my/my child's records. ☐

4. I have no objection to, and authorize my/my child's personal information and blood samples collected during the study being sent outside the European Economic Area (EEA) as described in this information sheet. ☐

5. I have no objection to, and authorize my/my child's GP being informed of my/my child's participation in the study and providing information from my/my child's medical records to the study team as described in this information sheet. ☐

6. I agree for my child to take part in this study ☐

Do you additionally consent to the use of your child's remaining samples of blood, urine or CSF for exploratory biomarker testing in future medical or pharmaceutical research? If you check the "no" box it will not disqualify your child from participating in this study.

☐ Yes No ☐

Do you additionally consent to the use of your child's photo for the purposes described in the information sheet knowing that your child's identifying features will not be hidden? If you check the "no" box it will not disqualify your child from participating in this study.

☐ Yes No ☐

Site/ institution headed paper

Consent Form Continue
(UK)

Principal Investigator: **Site/Institution:**

Participant Number:

Short Title: SBC-103 Intravenously in SBC-103 Treatment Naïve MPS IIIB (NGLU-CL01-T)

I give permission for my child's sibling's (under age of 16) medical history to be obtained where relevant to the study.

☐ Yes ☐ No

_____

Participant
Printed Name

_____

Legally Acceptable Representative or Legal Guardian
Printed Name Signature Date

_____

Witness (if applicable)
Printed Name Signature Date

- I have presented the study and answered the participant's parent or legally acceptable representative's questions
- I will give the parent/legal representative a copy of this signed and dated Participant Information Sheet and Informed Consent

_____

Name of person taking consent (Investigator/Delegate)
Printed Name Signature Date

When completed, 1 copy for parent/guardian/legal representative; 1 for researcher site file; 1 to be kept in medical notes.