16.1.3 List of Institutional Review Boards and Sample Informed Consent Form

16.1.3.1 List of Institutional Review Boards

IRB (name/address)	Country/ Agency Type	Site Number
University of Witwatersrand Johannesburg - Human Research Ethics Committee: (Medical) Suite 189, Private Bag x2600, Houghton 2041, South Africa	South Africa/ Central	1001 1003 1004 1011
IEC of National Center for Tuberculosis and Lung Disease 8, Adzharskaya str., Tbilisi, 0101, Georgia	Georgia/ Local	1105
Local Ethics Committee at Central Research Institute of Tuberculosis 107564, Russia, Moscow, 2, Yauzskaya lane	Russia/ Local	1206
National Medical Research Centre of Phthisiopulmonology and Infectious Diseases 620039, Russia, Yekaterinburg , 22nd Partsesd Str, Bld 50	Russia/ Local	1207
Ethics Committee at FSBI "St.-Petersburg Research Institute of Phthisiopulmonology" 194064, Russia, Saint Petersburg, 32 Politekhicheskaya St.	Russia/ Local	1208
Ethics Committee at Ural Scientific Research Institution of Phthiziopulmonology 620039, Russia, Yekaterinburg , 22nd Partsesd Str, Bld 50	Russia/ Local	1209
Moscow City Independent Ethics Committee 125458, Russia, Moscow, Leningradskiy Prospekt, 51	Russia/ Local	1210
The RF MoH, Department of State Regulation of Circulation of Medicines, Ethics Council 125458, Russia, Moscow, Leningradskiy Prospekt, 51	Russia/ Central	1210
The National Committee for Ethical Review of Clinical Trials MD 2009, Chisinau Mun., 3 A. Cosmescu str.	Moldova/ Central	2201

16.1.3.2 Sample Consent Form

NC-007, Version 1.0, Addendum PIIC, 13JUN2018

NC-007, Version 1.0, Master Addendum Parent, 13JUN2018

NC-007, Version 1.0, Master Addendum Paeds, 13JUN2018

NC-007, Version 2.0, Master HIV PIIC, 13JUN2018

NC-007, Version 2.0, Master Main Paeds, 13JUN2018

NC-007, Version 2.0, Master Main PIIC, 13JUN2018

NC-007, Version 2.0, Master Parent PIIC, 13JUN2018

NC-007, Version 2.0, HIV Paeds, 13JUN2018

NC-007, Version 2.0, HIV Parent, 13JUN2018

ADDENDUM TO THE PARTICIPANT INFORMATION AND INFORMED CONSENT FORM

Protocol Number: NC-007
Protocol Title: A Phase 3 partially-blinded, randomized trial assessing the safety and efficacy of various doses and treatment durations of linezolid plus bedaquiline and pretomanid in participants with pulmonary infection of either extensively drug-resistant tuberculosis (XDR-TB), pre-XDR-TB or treatment intolerant or non-responsive multi-drug resistant tuberculosis (MDR-TB).

Participant Initials:_____ Participant Number:_____

Introduction

We previously invited you to take part in a study with a new combination of medicines. The names of the medicines are bedaquiline, linezolid, and pretomanid.

You have signed the **main informed consent form** before you agreed to take part in this study. It is important that you continue to read and understand the **main informed consent form**, at the same time as reading this new information.

The sponsor has made some changes to the study. This form will tell you what these changes are and will provide information to help explain the study better.

1. How will the study work? 1

The screening period, which is the time your study doctor is checking if you meet the requirements and if it is safe for you to be part of the study, is extended from 9 days to 14 days.

The study doctor may decide to pause all your medications at any time during the treatment period. The study doctor may also decide that your linezolid medicine dose needs to be reduced, paused, or just your linezolid medicine needs to be stopped. If your dose of linezolid is reduced any time during the study, the study doctor may increase your linezolid dosage at a later visit, but not higher than the dose you started on.

2. What will happen to me in the study? 2

In addition to the procedures listed in the previous main informed consent you signed, an additional eye exam will be performed on week 23 of your treatment period if you haven't already reached week 23 when you sign this consent.

We will record when you are discharged from the hospital.

If we collect sputum or TB bacteria from tests done before you are screened, it may be used to check the type of TB and what medication will work on that type of TB bacteria.

Early Withdrawal

There are different visits and procedures done depending on whether you withdrawal while you are still taking study medication or if you withdrawal during the follow-up after you complete the treatment. The main informed consent only listed what was done if you withdrew while you were getting treatment. What will be done in each situation is detailed below:

	Early Withdrawal During Treatment Period			
Procedures	**Early Withdrawal Visit During Treatment**	**Follow-up Week 12**	**Follow-up Week 26**	**Follow-up Week 78**
Demography				
Medical and smoking history				
Eligibility assessment				
Sputum collection	X			
Pregnancy Test	X			
CD4 Count	X			
Blood tests	X			
ECG	X			
Chest X-Ray				
TB Questionnaire/s	X			
Vital Signs	X			
Physical Exam	X			
Pharmacokinetic (PK) test	X			
Eye Exam	X	X		
Nerve Exam	X			
Study Medicine check	X			
Other medicines	X	X		
Adverse Events	X	X	X	X
Survival/TB outcome			X	X

If you haven't had all your follow-up visits when you are withdrawn from the study, we may request that you to come back for 1 more visit at the clinic so we can monitor your health as well.

	Early Withdrawal During Follow-up Period			
Procedures	**Early Withdrawal Visit During Follow-up**	**Follow-up Week 12 (If applicable)**	**Follow-up Week 26 (if applicable)**	**Follow-up Week 78**
Demography				
Medical and smoking history				
Eligibility assessment				
Sputum collection	X			
Pregnancy Test	X			
CD4 Count				
Blood tests	X			
ECG	X			
Chest X-Ray				
TB Questionnaire/s	X			
Vital Signs	X			
Physical Exam	X			
Pharmacokinetic (PK) test	X			
Eye Exam	X	X		
Nerve Exam	X			
Study Medicine check	X			
Other medicines	X	X		
Adverse Events	X	X	X	X
Survival/TB outcome			X	X

3. Are there things that I cannot do while I'm in the study? 3

Male participants and your female sex partners need to use at least 1 method of birth control for as long as you are taking the study medicine and for up to 12 weeks (instead of 6 months as noted in the main consent) after you have taken the last dose of study medicine. Methods of birth control for female partners are different from the main consent and from female participants. For female partners of male participants, hormone based contraceptives or IUDS can be used alone (at least one barrier method must be used with those methods for female participants).

Please note that it is your own responsibility to get the correct birth control for you from your family planning or birth control clinic. Please speak with your study doctor if you are unsure of where to get the correct birth control.

4. Whom can I contact if something worries me?

4

You can call the study doctor or another authorised person at any time of the day or night (24 hours) on Tel: <<add>> or <<add>>.	

Please refer to the main informed consent form for more information on whom to contact if you have complaints about this study.

5. How do I agree to continue to be in this study?

5

If you want to continue to take part in this study, please read the consent statement and sign on the next page.

PARTICIPANT INFORMED CONSENT FORM

By signing below, I agree that:

- I have read, or someone has read the information sheet and consent form for this study to me, and I understand it.
- I have had the chance to ask questions and I am happy with the answers.
- I have had time to discuss the information with others and to decide if I want to take part.
- I will get a signed and dated copy of this consent form on the day that I sign it.
- I agree of my own free will to take part in this study. I know I have the right to stop taking part at any time, without giving any reason. If I stop taking part, it will not change my medical care or legal rights.
- Site staff, representatives from the sponsor, including auditors, regulatory authorities and ethics committees can have direct access to my medical records. They will treat my information as confidential.
- Add information about data collected being used up to the point of withdrawal.
- <<Females only: "Follow up information on the outcome of my pregnancy can be collected, if needed.">>
- <<EU: "I consent to the processing/storing of my data and the transfer thereof to countries outside the EU.">>
- <<USA: I understand that I would additionally have to sign a HIPAA research data protection form.">>

Printed Name of Participant<</Legal Representative>>

Signature/mark/thumb print of Participant<</Legal Representative>>

Date

(Participant/witness must write date)

*Printed Name of Person Conducting Consent
(If other than investigator<</delegate>>)

*Signature of Person Conducting Consent

Date

(If other than investigator<</delegate>>)

(Person conducting consent must write date)

I, _____ (Insert name of investigator) hereby confirm that the above participant has been fully informed about the nature, conduct and risks of the above study.

Signature of Investigator

Date
(Investigator must write date)

By signing below, I verify that the above participant gave verbal informed consent. The participant has been informed about the risks and the benefits of the study, understands such risks and benefits and is able to agree to participation, without coercion, undue influence or inappropriate incentives.

*Printed Name of Witness

*Signature of Witness

Date
(Witness must write date)

* Where applicable

ADDENDUM TO THE PARENT OR LEGAL GUARDIAN INFORMATION AND INFORMED CONSENT FORM

Protocol Number: NC-007
Protocol Title: A Phase 3 partially-blinded, randomized trial assessing the safety and efficacy of various doses and treatment durations of linezolid plus bedaquiline and pretomanid in participants with pulmonary infection of either extensively drug-resistant tuberculosis (XDR-TB), pre-XDR-TB or treatment intolerant or non-responsive multi-drug resistant tuberculosis (MDR-TB).

Participant Initials:_____ Participant Number:_____

Introduction

We previously invited your child to take part in a study with a new combination of medicines. The names of the medicines are bedaquiline, linezolid, and pretomanid.

You have signed the **parent or legal guardian informed consent form** before you agreed for your child to take part in this study. It is important that you continue to read and understand the **parent or legal guardian informed consent form**, at the same time as reading this new information.

The sponsor has made some changes to the study. This form will tell you what these changes are and will provide information to help explain the study better.

1. How will the study work? 1

The screening period, which is the time your study doctor is checking if your child meets the requirements and if it is safe for him/her to be part of the study, is extended from 9 days to 14 days.

The study doctor may decide to pause all your medications for your child at any time during the treatment period. The study doctor may also decide that your child's linezolid medicine dose needs to be reduced, paused, or just your child's linezolid medicine needs to be stopped. If your child's dose of linezolid is reduced any time during the study, the study doctor may increase your child's linezolid dosage at a later visit, but not higher than the starting dose.

2. What will happen to my child in the study? 2

In addition to the procedures listed in the previous parent or legal guardian informed consent you signed, an additional eye exam will be performed on week 23 of the treatment period if your child hasn't already reached week 23 when this consent is signed

.

We will record when your child is discharged from the hospital.

If we collect sputum or TB bacteria from tests done before your child is screened, it may be used to check the type of TB and what medication will work on that type of TB bacteria.

Early Withdrawal

There are different visits and procedures done depending on whether your child withdrawals while he/she is still taking study medication or if your child withdrawals during the follow-up after he/she completes the treatment. The parent or legal guardian consent only listed what was done if your child withdrew while he/she was getting treatment. What will be done in each situation is detailed below:

	Early Withdrawal During Treatment Period			
Procedures	**Early Withdrawal Visit During Treatment**	**Follow-up Week 12**	**Follow-up Week 26**	**Follow-up Week 78**
Demography				
Medical and smoking history				
Eligibility assessment				
Sputum collection	X			
Pregnancy Test	X			
CD4 Count	X			
Blood tests	X			
ECG	X			
Chest X-Ray				
TB Questionnaire/s	X			
Vital Signs	X			
Physical Exam	X			
Pharmacokinetic (PK) test	X			
Eye Exam	X	X		
Nerve Exam	X			
Study Medicine check	X			
Other medicines	X	X		

Adverse Events	**X**	**X**	**X**	**X**
Survival/TB outcome			**X**	**X**

If your child hasn't had all of their follow-up visits when they are withdrawn from the study, we may request that your child come back for 1 more visit at the clinic so we can monitor their health as well.

	Early Withdrawal During Follow-up Period			
Procedures	**Early Withdrawal Visit During Follow-up**	**Follow-up Week 12 (If applicable)**	**Follow-up Week 26 (if applicable)**	**Follow-up Week 78**
Demography				
Medical and smoking history				
Eligibility assessment				
Sputum collection	**X**			
Pregnancy Test	**X**			
CD4 Count				
Blood tests	**X**			
ECG	**X**			
Chest X-Ray				
TB Questionnaire/s	**X**			
Vital Signs	**X**			
Physical Exam	**X**			
Pharmacokinetic (PK) test	**X**			
Eye Exam	**X**	**X**		
Nerve Exam	**X**			
Study Medicine check	**X**			
Other medicines	**X**	**X**		
Adverse Events	**X**	**X**	**X**	**X**
Survival/TB outcome			**X**	**X**

3. Are there things that my child cannot do while I'm in the study? 3

Male participants and your female sex partners need to use at least 1 method of birth control for as long as you are taking the study medicine and for up to 12 weeks (instead of 6 months as noted in the main consent) after you have taken the last dose of study medicine. Methods of birth control for female partners are different from the main consent and from female participants. For female partners of male participants, hormone based contraceptives or IUDS can be used alone (at least one barrier method must be used with those methods for female participants).

Please note that it is your own responsibility to get the correct birth control for you from your family planning or birth control clinic. Please speak with your study doctor if you are unsure of where to get the correct birth control.

4. Whom can I contact if something worries me or my child? 4

You can call the study doctor or another authorised person at the study site at any time of the day or night (24 hours) on Tel: <<add>> or <<add>>.

Please refer to the parent or legal guardian informed consent form for more information on whom to contact if you have complaints about this study.

5. How do I agree for my child to continue to be in this study? 5

If you want your child to continue to take part in this study, please read the consent statement and sign on the next page.

PARTICIPANT INFORMED CONSENT FORM

By signing below, I agree that:

- I have read, or someone has read the information sheet and consent form for this study to me, and I understand it.
- I have had the chance to ask questions and I am happy with the answers.
- I have had time to discuss the information with others and to decide if I want my child to take part.
- I will get a signed and dated copy of this consent form on the day that I sign it.
- I agree of my own free will to let my child take part in this study. I know my child has the right to stop taking part at any time, without giving any reason. If my child stops taking part, it will not change his/her medical care or legal rights.
- Site staff, representatives from the sponsor, including auditors, regulatory authorities and ethics committees can have direct access to my child's medical records. They will treat my child's information as confidential.
- If my child withdraws from the study, study data collected about him/her up to the point of his/her withdrawal can still be used to carry out this study.
- Girls only: "if my child becomes pregnant while on the study, follow-up information on the outcome of my child's pregnancy can be collected, if needed."
  <<EU: "I consent to the processing/storing of my data and the transfer thereof to countries outside the EU.">>

Printed Name of Parent/Legal Guardian

Signature/mark/thumb print of Parent/Legal Guardian

Date

(Parent or Legal Guardian/witness must write date)

*Printed Name of Person Conducting Consent
(If other than investigator/delegate)

*Signature of Person Conducting Consent (If other than investigator/delegate)	Date (Person conducting consent must write date)

I, _____ (Insert name of investigator) hereby confirm that the above Parent or Legal Guardian has been fully informed about the nature, conduct and risks of the above study.

Signature of Investigator	Date (Investigator must write date)

By signing below, I verify that the above Parent or Legal Guardian gave verbal informed consent. The Parent or Legal Guardian has been informed about the risks and the benefits of the study, understands such risks and benefits and is able to agree to participation, without coercion, undue influence or inappropriate incentives.

*Printed Name of Witness

*Signature of Witness	Date (Witness must write date)

* Where applicable

ADDENDUM TO THE PAEDIATRIC INFORMATION AND ASSENT FORM (14-17 YEARS AGE)

Protocol Number: NC-007
Protocol Title: A Phase 3 partially-blinded, randomized trial assessing the safety and efficacy of various doses and treatment durations of linezolid plus bedaquiline and pretomanid in participants with pulmonary infection of either extensively drug-resistant tuberculosis (XDR-TB), pre-XDR-TB or treatment intolerant or non-responsive multi-drug resistant tuberculosis (MDR-TB).

Participant Initials:_____ Participant Number:_____

Introduction

We previously asked you to take part in a study with a new medicines. The names of the medicines are bedaquiline, linezolid, and pretomanid.

You have signed the **paediatric informed assent form** before you agreed to take part in this study. It is important that you continue to read and understand the **paediatric informed assent form**, at the same time as reading this new information.

The sponsor has made some changes to the study. This form will tell you what these changes are and will provide information to help explain the study better.

1. How will the study work? 1

The screening period, which is the time your study doctor will check if you qualify meet the requirements and if it is safe for you to be part of the study, has been changed from 9 days to 14 days.

Your study doctor may decide to pause, reduce (lessen), or stop your linezolid. Your study doctor will tell you if you dose is changed. If your dose of linezolid is reduced anytime during the study, the study doctor may increase your linezolid dosage at a later visit- but not higher than the dose you started on.

Your study doctor may pause or stop **all** the study medicines.

2. What will happen to me in the study? 2

In addition to the procedures that you already know will happen from paediatric informed assent form you signed, another eye exam will be performed on week 23 of your treatment period if you haven't already reached week 23 when you sign this.

We will record when you are discharged from the hospital.

If we collect sputum or TB bacteria from tests done before you are screened, it may be used to check the type of TB and what medication will work on that type of TB bacteria.

Early Withdrawal

There are different visits and procedures done depending on whether you withdrawal while you are still taking study medication or if you withdrawal after you complete the treatment. The paediatric informed assent form only listed what was done if you withdrew while you were getting treatment. What will be done in each situation is below:

	Early Withdrawal During Treatment Period			
Procedures	**Early Withdrawal Visit During Treatment**	**Follow-up Week 12**	**Follow-up Week 26**	**Follow-up Week 78**
Demography				
Medical and smoking history				
Eligibility assessment				
Sputum collection	X			
Pregnancy Test	X			
CD4 Count	X			
Blood tests	X			
ECG	X			
Chest X-Ray				
TB Questionnaire/s	X			
Vital Signs	X			
Physical Exam	X			
Pharmacokinetic (PK) test	X			
Eye Exam	X	X		
Nerve Exam	X			
Study Medicine check	X			
Other medicines	X	X		
Adverse Events	X	X	X	X
Survival/TB outcome			X	X

If you haven't had all your follow-up visits when you are withdrawn from the study, we may request that you to come back for 1 more visit at the clinic so we can monitor your health as well.

	Early Withdrawal During Follow-up Period			
Procedures	**Early Withdrawal Visit During Follow-up**	**Follow-up Week 12 (If applicable)**	**Follow-up Week 26 (if applicable)**	**Follow-up Week 78**
Demography				
Medical and smoking history				
Eligibility assessment				
Sputum collection	X			
Pregnancy Test	X			
CD4 Count				
Blood tests	X			
ECG	X			
Chest X-Ray				
TB Questionnaire/s	X			
Vital Signs	X			
Physical Exam	X			
Pharmacokinetic (PK) test	X			
Eye Exam	X	X		
Nerve Exam	X			
Study Medicine check	X			
Other medicines	X	X		
Adverse Events	X	X	X	X
Survival/TB outcome			X	X

3. Are there things that I cannot do while I'm in the study? 3

We updated the assent Boys and now boys cannot take part in this study if you are planning to make someone pregnant during the treatment period or 12 weeks (instead of 6 months) after the last dose of study medicine

If you are a boy and you sometimes have sex, you and your girlfriend must either use 2 methods of birth control as we discussed above for the girls or use one form that your study doctor says you can use such as the birth control pill or an IUD.

Please talk to your study doctor if you are unsure of where to get the correct birth control. You are responsible for getting the correct birth control from your family planning or birth control clinic.

4. Whom can I contact if something worries me? 4

You can call the study doctor or another authorised person at the study site any time of the day or night (24 hours) on Tel: <<add>> or <<add>>.	

Please refer to the paediatric informed assent form for more information on who to contact if you have complaints about this study.

5. How do I agree to continue to be in this study? 5

If you want to continue to take part in this study, please read the statement and sign on the next page.

PARTICIPANT INFORMED CONSENT FORM

By signing below, I agree that:

- I have read the information sheet and consent form for this study, or someone has read it to me, and I understand it.
- I have had the chance to ask questions and I am happy with the answers.
- I have had time to discuss the information with others and to decide if I want to take part.
- I will get a signed and dated copy of this consent form on the day that I sign it.
- I agree of my own free will to take part in this study. I know I have the right to stop taking part at any time, without giving any reason. If I stop taking part, it will not change my medical care or legal rights.
- Site staff, representatives from the sponsor, including auditors, regulatory authorities and ethics committees can have direct access to my medical records. They will treat my information as confidential.
- If I withdraw from the study, study data collected about me up to the point of my withdrawal can still be used to carry out this study.
- Girls only: "If I become pregnant on the study, follow-up information on the outcome of my pregnancy can be collected, if needed."
  <<EU: "I consent to the processing/storing of my data and the transfer thereof to countries outside the EU.">>

Printed Name of Participant<</Legal Representative>>

Signature/mark/thumb print of Participant<</Legal Representative>> | Date

(Participant/witness must write date)

*Printed Name of Person Conducting Consent (If other than investigator<</delegate>>)

*Signature of Person Conducting Consent (If other than investigator<</delegate>>) | Date

(Person conducting consent must write date)

I, _____ (Insert name of investigator) hereby confirm that the above participant has been fully informed about the nature, conduct and risks of the above study.

_____ _____

Signature of Investigator Date

(Investigator must write date)

By signing below, I verify that the above participant gave verbal informed consent. The participant has been informed about the risks and the benefits of the study, understands such risks and benefits and is able to agree to participation, without coercion, undue influence or inappropriate incentives.

_____

*Printed Name of Witness

_____ _____

*Signature of Witness Date

(Witness must write date)

* Where applicable

PARTICIPANT INFORMATION AND INFORMED CONSENT FORM
TESTING FOR HIV

Protocol Name/Number: ZeNix/NC-007-(B-Pa-L)
Protocol Title: A Phase 3 partially-blinded, randomized trial assessing the safety and efficacy of various doses and treatment durations of linezolid plus bedaquiline and pretomanid in participants with pulmonary infection of either extensively drug-resistant tuberculosis (XDR-TB), pre-XDR-TB or treatment intolerant or non-responsive multi-drug resistant tuberculosis (MDR-TB).

Participant Initials:_____ Participant Number:_____

Introduction

This information sheet contains only information about testing for HIV in the study. Please read the **main consent form** that you have already signed for information about the **main clinical study**.

Please read this information sheet before you agree to have the HIV test done as part of the main study. This document will answer the following questions:

If you have any other questions that are not answered in this document, please ask someone from the study staff for more information. We explained some difficult medical terms in the **Glossary** on page <<XX>>.

It is very important that you understand this information sheet before you agree to have your HIV test done. We would like you to ask as many questions as you need. If there is anything that you do not understand, please discuss this with the study doctor, the study staff, your own doctor, or with your family.

Participant Notes

1. What is HIV? 1

The human immunodeficiency virus (HIV) is a virus that causes acquired immunodeficiency syndrome (AIDS). This is a condition in humans where the system that protects the body against diseases (immune system), begins to fail. This leads to other infections, which the body would normally be able to fight, being able to grow and thrive. These infections can be life-threatening and are known as opportunistic infections*.

How is HIV spread?

Infection with HIV occurs by the transfer of blood, semen or other similar fluid, vaginal fluid, or breastmilk in which HIV is present. The three major ways of getting HIV are:

- having sex without a condom,
- sharing needles, and
- a mother with HIV gives birth, or if she breastfeeds her baby.

How does HIV affect my body?

HIV mainly infects cells in the immune system*, called CD4 cells, and causes the number of CD4 cells to drop. When the number of CD4 cells drop below a certain amount, the body can no longer fight infection, and opportunistic infections may increase.

How is HIV treated?

If left untreated, most people who are HIV positive will get AIDS and die. However, about 1 in 10 people remain healthy for many years, with no obvious symptoms.

People with HIV are treated with anti-retrovirals (i.e. the medications used to fight the HIV virus). Using anti-retroviral medicine may help people to live longer.

2. Why are you testing me for HIV? 2

This study has nothing to with HIV/AIDS or its treatment. However, we need to test you for HIV as part of the study, and it may be unsafe for you to take part in the study if:

- your CD4 count is lower than a certain number (<100 cells/µL)
- you have had an existing TB and HIV diagnosis, you are taking HIV medicine and your viral load ("viral load" is a term that people living with HIV use to talk about how much of the virus is in their body) is higher than a certain number (>1000 copies/mL)
- you are diagnosed with tuberculosis and HIV and your study doctor recommends that the start of your HIV medicine should not be postponed until you have received at least 2 weeks of an anti-tuberculosis regimen. and/or
- you are currently receiving HIV medicine which cannot safely be taken with the study medicine and your study doctor decides it is not best for you to change your HIV medicine.

You can take part in the study if you meet the other criteria for the study and if you test positive for HIV, ***and***

- your CD4 count is equal to or more than a certain number (≥ 100 cells/µL)
- if you have previously been diagnosed with TB and your viral load is <1000 copies/mL
- you have a new TB and HIV diagnosis
- you are diagnosed with tuberculosis and HIV and your study doctor agrees that the start of your HIV medicine may be postponed until you have received at least 2 weeks of an anti-tuberculosis regimen
- HIV medicine that you will take during the study is safe to be taken with the study medicine;

OR if you are HIV negative.

3. How will you do the HIV test? 3

We will take an extra blood sample of 5 mL(about 1 teaspoon) in the main study. This extra blood sample will be taken at the same time as the routine blood samples in the clinical part of the study. It will not be necessary to prick you with a needle again.

4. What can go wrong with the HIV test? 4

The risk when we take a blood sample includes discomfort where we prick you with the needle or you may have a bruise, bleed, and only rarely, get an infection, or faint.

The following negative things may happen if you have an HIV test (especially if the result is that you are HIV positive):

- friends, family and colleagues may possibly reject you and discriminate against you;
- you may have emotional problems, feel more stressed and feel uncertain about the future.

5. How can the HIV test help me? 5

If you test negative, you may feel less worried after knowing your HIV status, and take steps to prevent yourself from getting HIV. If you know you are HIV positive, it may reduce the stress that comes with the uncertainty of not knowing. You can take advantage of treating your HIV early, monitoring your health, eating well and healthily. You will also know if you can infect others, and what to do to stop this from happening.

Women and their partners thinking about getting pregnant can take advantage of treatments that can help prevent their baby from getting HIV. You can also possibly plan for future care of your children.

6. What happens if I am injured during the HIV test? 6

The insurance that the TB Alliance has taken out as required by the laws and regulations of your country covers the extra blood samples. For more details, see the information sheet describing the **main clinical study**.

7. Will you keep my HIV test private? 7

We will respect your confidentiality* and only the study doctor and research team will know the results of the test. Selected people working for TB Alliance, as well as representatives of government regulatory authorities and ethics committees will also have access to the results. These persons know that they must keep your information private. You are giving permission for those people to see your medical records when you sign this document.

8. Will you pay me to do the HIV test? 8

No, we will not pay you for giving the blood sample to do the HIV test.
The TB Alliance or the study site will not be responsible for paying any costs related to your HIV treatment if you test positive. We will refer you to an HIV clinic for further testing and advice.

9. Will I have to pay for the HIV test? 9

No, the HIV test will not cost you anything,
<<If applicable add "You will receive HIV counseling before and after HIV test. The TB Alliance will pay for the test and the counseling."

10. Whom can I contact if something worries me? 10

You can call the study doctor or another authorised person at any time of the day or night (24 hours) on Tel: **<<add>>** or **<<add>>**.	

Please refer to the **main informed consent form** for more information on whom to contact if you have complaints about this study.

11. How do I agree to have the HIV test? 11

If you want to agree to do the HIV test, please read the statement on the following page and sign the form.

Participant Notes

Glossary

Technical term	Explanation
HIV	Human immunodeficiency virus
AIDS	Acquired immune deficiency syndrome
opportunistic infections	an infection that occurs when the immune system is weak
immune system	the system in your body that fights infections
pulmonary	of the lungs
confidentiality	a set of rules to keep information private

PARTICIPANT INFORMED CONSENT FORM FOR HIV TESTING

By signing below, I agree that:

- I have read, or someone has read the information sheet and consent form for this HIV testing to me, and I understand it.
- I have had the chance to ask questions and I am happy with the answers.
- I have had time to discuss the information with others and to decide if I want to do the test.
- I will get a signed and dated copy of this consent form on the day that I sign it.
- I voluntarily agree for HIV testing to be done.
- Site staff, representatives from the sponsor, regulatory authorities and ethics committees can have direct access to my medical records. They will treat my information as confidential.
- I hereby give up all rights to the test findings and I am not entitled to be paid anything because of the test findings.
- <<EU: "I consent to the processing/storing of my data and the transfer thereof to countries outside the EU.">>

_____
Printed Name of Participant

_____ _____
Signature/mark/thumb print of Participant Date
(Participant/witness must write date)

_____
*Printed Name of Person Conducting Consent
(If other than investigator /delegate)

_____ _____
*Signature of Person Conducting Consent Date
(If other than investigator /delegate)

(Person conducting consent must write date)

I, _____ (Insert name of investigator) hereby confirm that the above participant has been fully informed about the nature, conduct and risks of the HIV test.

Signature of Investigator	Date (Investigator must write date)

By signing below, I verify that the above participant gave verbal informed consent. The Participant has been informed about the risks and the benefits of the HIV test, understands such risks and benefits and is able to agree to have the HIV test, without coercion, undue influence or inappropriate incentives.

*Printed Name of Witness	

*Signature of Witness	Date (Witness must write date)

* Where applicable

PAEDIATRIC INFORMATION AND ASSENT FORM (14-17 YEARS AGE)

Protocol Name/Number: ZeNix/NC-007-(B-Pa-L)
Protocol Title: A Phase 3 partially-blinded, randomized trial assessing the safety and efficacy of various doses and treatment durations of linezolid plus bedaquiline and pretomanid in participants with pulmonary infection of either extensively drug-resistant tuberculosis (XDR-TB), pre-XDR-TB or treatment intolerant or non-responsive multi-drug resistant tuberculosis (MDR-TB).

Participant Initials:_____ Participant Number:_____

Introduction

My name is _____ and I do research studies to help us find out more about diseases or sicknesses and to help find better ways of helping, or treating children and adults who are sick.

I am going to give you information and invite you to be part of a study. You can choose whether or not you want to take part. We have discussed this research with your parent(s) / legal guardian and they know that we are also asking you for your agreement. If you are going to participate in the research, your parent(s) / legal guardian have to agree as well. If you do not want to take part in the research, you do not have to, even if your parents have agreed that you can.

There may be some words that you don't understand, or things that you want explained in more detail, because you are interested in it or worried about it. Please ask me to stop at any time and I will explain them to you.

This assent form has two parts:
- An information sheet that provides information about the study and
- A statement (this is where you sign if you agree to take part)

Write your notes or questions here:

You will be given a copy of the full assent form. This document will answer the following questions:

If you have any other questions that are not answered in this document, please ask someone from the study staff for more information. Difficult medical terms are marked with an (*) and are explained in the **Glossary** on page <<XX>>.

It is very important that you understand this information sheet before you agree to take part in this study. We would like you to ask as many questions as you need. If there is anything that you do not understand, please discuss this with your parent(s) / legal guardian, the study doctor, the study staff, your own doctor or with your family. You do not have to decide immediately.

1. Is the study safe? 1

The <<name of Ethics Committee as applicable>> and <<name of Regulatory Authority as applicable>> have checked this study and approved it because it complies with medical and ethical standards.

In addition, the study will be done according to the Declaration of Helsinki 2013, International Conference on Harmonisation-Good Clinical Practice (ICH-GCP) <<and list any other appropriate guidelines e.g. South African GCP Guidelines>>.

One of the purposes of these regulations is to make sure that the rights of people taking part in studies are protected. If you would like to read any of these guidelines and regulations, please ask your study doctor to give you a copy.

2. Do I have to take part? 2

Your participation in this study is totally out of free will. You may choose not to be in the study or leave the study at any time by telling your parent(s)/legal guardian and the study doctor.

If you decide not to be in the study or to leave the study, you will not lose any benefits that you would have had. The study doctor will give you a letter so that you can go to a place where they will give you the normal TB treatment.

3. Why are you doing the study? 3

Tuberculosis (TB) is a contagious* disease caused by bacteria. The bacteria can travel through the air and spread from one person to the next.

We are asking you to be in this study because the doctors found that you have a kind of TB [called extensively drug resistant pulmonary (i.e. in your lungs) TB (XDR-TB), pre-extensively drug resistant TB (pre-XDR-TB), or Multidrug Resistant TB (MDR-TB)]*, that is very hard to treat. The medicines used for this kind of TB must be taken for up to two years or more. New medicines are urgently needed to make the TB treatment time shorter and to treat the TB.

A previous study called the Nix-TB study has shown that three medicines called bedaquiline, linezolid and pretomanid taken together may treat your type of TB. These medicines have been tested in the laboratory, on animals, on healthy human volunteers, and on over 70 humans who have TB and they may be effective against XDR-TB and MDR-TB. We want to do this study to see what dose and length of treatment of linezolid is the most effective in treating your type of TB while causing the least amount of side effects. The safety and effectiveness of the following three drugs together: bedaquiline, linezolid and pretomanid will also be tested.

4. How will the study work? 4

About 180 people (called participants) will take part in this study. All the participants will be open to male and female<<14 (update for specific age for each Country/site)>> years old and older. The study will be done at approximately 12

study centers around the world, including South Africa, Eastern Europe and Asia. We expect that you will be in this study for about 2 years. The study is split into 3 parts:

Part	Name	Length	Reason
1	Screening	Up to 14 days	During this time, the study doctor will check if you qualify to be in the study and if it is safe for you to be part of the study.
2	Treatment	26 weeks or 39 weeks	We will give you the study medicine for a total of 26 weeks (about 6 months), depending on how you respond to the medicines. You will visit the hospital/clinic at least 17 times. Some of these visits may be while you are a patient in the hospital. If your TB has not been cured after 26 weeks of treatment, your study doctor may decide to extend your treatment to a total of 39 weeks.
3	Follow Up	78 weeks	After you finish taking the study medicine, your study doctor will check on your health for the next 78 weeks (about one and a half years). During this time, you will not take any study medicine but you will visit the hospital/clinic at least 8 times.

If your study doctor decides that you may be in this study, and if you and your parent(s) / legal guardian agree by signing the necessary forms, the following will happen:

You will be assigned by chance (like flipping a coin) to be given 1 of 4 possible doses of linezolid and, at the same time, you will also be given bedaquiline and pretomanid.

Your study doctor may decide to pause, reduce (lessen), or stop your linezolid. Your study doctor will tell you if you dose is changed. If your dose of linezolid is reduced anytime during the study, the study doctor may increase your linezolid dosage at a later visit- but not higher than the dose you started on. If there is an emergency and the study doctor needs to know what linezolid treatment you are receiving, he/she can quickly and easily find this out.

Your study doctor may pause or stop **all** the study medicines.

We will give you the study medicines at each visit during the first part of the study and we will ask you to bring back all empty packets and unused medicines to your next visit.

5. What will happen to me in the study? 5

For this study to be successful and for your own safety, it is important that you do exactly what the study doctor tells you to do throughout your time in the study.

Below are lists of the visits and what will happen at each visit during the study. The meanings of each of the procedures are explained in the next pages. There may be some small changes if your study doctor finds that it is necessary. This is a list of all the study visits and what will happen at each visit:

	Screening Visits	Treatment Visits																	Post-Treatment Follow-up Visits							
Procedures	Up to 14 days before Treatment	Day 1 (Baseline)	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 10	Week 12	Week 14	Week 16	Week 18	Week 20	Week 23	End of Treatment	4 weeks	8 weeks	12 weeks	26 weeks	39 weeks	52 weeks	65 weeks	78 weeks
Demography	X																									
Medical and smoking history	X																									
Eligibility assessment	X	X																								
Sputum collection	X	X	X	X	X	X		X		X	X	X		X		X	X	X	X	X	X	X	X	X	X	X
Pregnancy Test	X	X								X				X				X								
HIV, CD4 Count and Viral Load	X																									
Blood tests	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X							
ECG	X	X	X			X				X				X				X								
Chest X-Ray	X																									
TB Questionnaire/s	X									X				X				X				X		X		X
Vital Signs	X	X	X	X		X		X		X		X		X		X		X			X	X	X	X	X	X
Physical Exam	X	X	X	X		X		X		X		X		X		X	X	X			X	X	X	X	X	X
Pharmacokinetic (PK) test		X		X						X		X						X								
Eye Exam	X					X				X		X		X		X	X	X	X		X					
Study Medicine check		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X								
Other medicines	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse Events	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

To help you understand what will happen at each visit, we have described these procedures below:

Demography	→	This is personal information about your date of birth, gender and race.
Medical and smoking history	→	You will be asked questions about your health history and whether you have ever smoked.
Eligibility assessment	→	This is a process of checking that you meet the study requirements to make sure it is safe for you to take part.
Sputum collection	→	You will be asked to cough up sputum (phlegm) into a small cup at different times in the study. The sputum is used to check whether you have TB, the type of TB you have, how many TB bacteria you have and what medicines will work on the TB bacteria. *<<Add as required per country:* If you have a stored sputum (or TB from your sputum) sample (which was collected before this visit) that could be used to allow you into this study or check the type of TB and what medication will work on that type of TB bacteria. If you and your parent/guardian both agree to it, this may be collected from the applicable laboratory and used if you check "yes" at the end of this consent>> The TB germs that have been taken out of your sputum will also be sent to laboratories in the United Kingdom (UK) every few months to test how they respond to the study medicines.
HIV, CD4 count test and Viral load	→	This is a test to see if you have HIV and, if you have, we will measure your CD4 count (a kind of cell that fights infection). You will be counselled on HIV before the blood tests are taken and again once the results are given to you, and you may be asked to sign a separate assent form give us permission to do this.
Blood tests	→	We will take some blood (about 20 millilitres or 4 teaspoons) from you by inserting a small needle into a vein in your arm. We will test the blood to check if you are healthy.
Urine tests	→	You will be asked to give a sample of your urine in a small cup when you are at the clinic. We will test the urine to check if you are healthy and to see if you have taken any drugs.

Pregnancy test	→	If you are a girl, we will test your urine to see if you are pregnant, whether you sometimes have sex or not.
ECG	→	This is a test that we do by placing 12 sensors (like stickers) to your skin for a short time to check how your heart is working.
Chest X-Ray	→	This is a photograph of your lungs.
TB and health questionnaire/s	→	We will ask you to tell your study doctor about your TB symptoms and general health to check how you are feeling.
Physical exam	→	This is checking your body for signs of disease.
Vital signs	→	We will measure your blood pressure, heart rate, breathing, body temperature, height and weight.
Pharmacokinetic (PK) test	→	At some visits we will take some blood to check what happens to the medicines once you swallow them. We will take blood (about 20 millilitres or 4 teaspoons) from you by inserting a small needle into a vein in your arm.
Eye exam	→	We will check how well you can see by asking you to read the letters or symbols off a chart, and to read numbers or symbols off cards with coloured patterns on them. We will also look at the lens of your eyes by using a machine that shines a small beam of light into your eye while the eye doctor looks into it with a type of magnifying glass. To test your lens, the eye doctor will need to put a couple of drops of medicine in your eyes that will make your pupil (the black part in the middle of your eye) get bigger for a short time. This allows the eye doctor to see into your eyes easily. This is the same as what happens to your eyes in the dark.
Study medicine check	→	We will ask you how much study medicine you have taken or not taken since the last time you were at the clinic.
Hospital admission	→	You may need to stay in the hospital if your study doctor thinks it will be safer for you.
Hospital check-out	→	Your study doctor will tell you when it is safe for you to not be in hospital all the time. We will record when you are checked-out of the hospital.

After you have stopped or completed the study medicines, the study doctor will decide if you need more TB treatment. If you do, your study doctor will give you a letter to go to another place where they can treat your TB. It is very important that you go there as soon as possible and get more anti-TB treatment if your doctor recommends that.

Treatment Extension

If the study doctor decides that your treatment should be extended, either due to treatment pause of all of your study treatment, or if your TB is not cured after 26 weeks of treatment, the following procedures will be performed at additional treatment visits.

	Optional Treatment Extension Visits
Procedures	**Every 3 weeks, for up to a total of 26 or 39 weeks of treatment**
Demography	
Medical and smoking history	
Eligibility assessment	
Sputum collection	**X**
Pregnancy Test	
HIV, CD4 Count and Viral Load	
Blood tests	**X**
ECG	
Chest X-Ray	
TB Questionnaire/s	
Vital Signs	**X**
Physical Exam	**X**
Pharmacokinetic (PK) test	
Eye Exam	**X**
Nerve Exam	**X**
Study Medicine check	**X**
Other medicines	**X**
Adverse Events	**X**

Early Withdrawal

If you decide of your own free will, or your study doctor decides you should stop treatment or withdraw from the study before you have finished the above visits, the procedures listed below may be performed at an Early Withdrawal Visit. If you have received more than 15 doses of the study medication and haven't had your 12 week follow-up visit when you are withdrawn from the study, we will request you to come back for 1 more visit at the clinic so we can monitor your health, and you will be contacted 2 more times for a visit that can take place at the clinic, your home or

on the phone with your study doctor where the following procedures may be performed.

	Early Withdrawal During Treatment Period			
Procedures	**Early Withdrawal Visit**	**Follow-up Week 12**	**Follow-up Week 26**	
Demography				
Medical and smoking history				
Eligibility assessment				
Sputum collection	X			
Pregnancy Test	X			
CD4 Count	X			
Blood tests	X			
ECG	X			
Chest X-Ray				
TB Questionnaire/s	X			
Vital Signs	X			
Physical Exam	X			
Pharmacokinetic (PK) test	X			
Eye Exam	X	X		
	Nerve Exam	X		
Study Medicine check	X			
Other medicines	X	X		
Adverse Events	X	X	X	X
Survival/TB outcome			X	X

If you haven't had all your follow-up visits when you are withdrawn from the study, we may request that you to come back for 1 more visit at the clinic so we can monitor your health as well.

	Early Withdrawal During Follow-up Period			
Procedures	**Early Withdrawal Visit During Follow-up**	**Follow-up Week 12 (If applicable)**	**Follow-up Week 26 (if applicable)**	**Follow-up Week 78**
Demography				
Medical and smoking history				
Eligibility assessment				
Sputum collection	X			
Pregnancy Test	X			
CD4 Count				
Blood tests	X			

ECG	X			
Chest X-Ray				
TB Questionnaire/s	X			
Vital Signs	X			
Physical Exam	X			
Pharmacokinetic (PK) test	X			
Eye Exam	X	X		
Nerve Exam	X			
Study Medicine check	X			
Other medicines	X	X		
Adverse Events	X	X	X	X
Survival/TB outcome			X	X

If the study doctor feels it is necessary, you may be asked to come in for extra (unscheduled) visits that do not appear on the above charts.

6. What can go wrong in the study? 6

There are some possible risks and inconveniences of being in the study. Tuberculosis is a serious disease that can kill you.

You should **not drink alcohol** while you are taking study medicine or other TB medicines because alcohol may damage your liver.

Details of the risks of taking the medicines in this study are noted below:

Liver problems	→	May be associated with symptoms such as nausea or vomiting, stomach pain, fever, weakness, itching, unusual tiredness, loss of appetite, light coloured bowel movements, dark coloured urine, yellowing of your skin or the white of your eyes. Liver problems may also be suggested by blood tests that show abnormalities in measures of your liver enzymes and other measures of how your liver is working. In rare cases liver problems may be serious and even lead to death.	Pretomanid, Linezolid, Bedaquiline,

Headache	→	pain in any part of the head	Pretomanid, Linezolid, Bedaquiline,
Stomach problems	→	Tenderness or pain of the stomach area Feeling like you want to throw up, or actually throwing up. Also not feeling hungry, having diarrhoea (loose bowel movements) or having an upset stomach.	Linezolid, Pretomanid, Bedaquiline
Dizziness	→	A feeling of being 'drunk' or 'light headed', especially when you stand up or sit down quickly.	Linezolid, Bedaquiline

The following are a list and description of side effects that are unique to each of the medicines:

Pretomanid

Besides the side effects mentioned above, the other side effects include:

Reproductive organ changes	→	Results from animal studies have shown that rats given pretomanid showed signs of damage to the male rats' reproductive organs. Recent studies in people have shown that there is no evidence that pretomanid damages the male reproductive organs. The potential for pretomanid to have an effect on the male reproductive organs will remain under evaluation.
Cataracts (clouding of the lens in the eye)	→	Other results from animal studies show that rats given Pretomanid developed cataracts at high doses over a 6-month period of taking the medicine. It is not known if the effect found in rats indicates any risk for human beings.
Fits (convulsions or seizures)	→	were seen in some animal studies and in 1 patient treated with Pretomanid
Skin problems	→	Inflamed areas on your skin, which may be red, itchy and/or painful.

Linezolid

Besides the side effects mentioned above, the other **most common** side effects seen in patients who took linezolid are:

Changes in taste	→	certain food or drinks may taste different to you
Tongue discolouration	→	the colour of your tongue changes
Fungal infections	→	when a fungus causes the infection
Vaginal moniliasis	→	a fungal infection in the vagina
Oral moniliasis	→	a fungal infection in the mouth
Fever	→	When your body temperature goes higher than 38 °C or 100.4 °F.
Signs of nerve disturbances	→	This is sometimes called 'peripheral neuropathy', which may be experienced as a painful burning, or stinging, tingling, sensation of pins and needles or numbness in your arms and legs. In some cases this can be permanent.
Convulsions or seizures	→	These are also commonly known as 'fits'. A **convulsion** is when the body muscles contract and relax quickly and repeatedly / uncontrolled shaking of the body. A **seizure** is when there is a change in the normal electrical activity of the brain.

Other side effects seen in patients who took linezolid include, but are not limited to:

Myelo-suppression	→	a lack of certain cells in your blood that your body needs to function.

		can make you feel tired and make your body being unable to fight off other illnesses or heal an injury. This could also make you bleed or bruise easily.
Lactic acidosis	→	a build-up of waste products in your blood that can cause constant nausea and vomiting.
Serotonin syndrome	→	this rare but serious condition may occur when linezolid is given with certain types of medications that affect a chemical in the brain called serotonin. Some of these medications include antidepressants. Be sure to tell your study doctor about all prescription and non-prescription medications you are taking. It can cause many different symptoms, for example: confusion, restlessness, tremors, blushing, sweating and fever.
Interactions with other medicines	→	causing a rise in blood pressure
Optic neuropathy	→	A type of damage to the nerves in your eye that can lead to blindness if it is not treated. This can be permanent.
Low blood sugar	→	This is often seen in patients with diabetes who have to take insulin or other medicines

Bedaquiline

From studies in 380 patients with TB who received Bedaquiline (312 of whom received Bedaquiline for as long as 6 months), we continued to see that Bedaquiline is generally safe and well tolerated. Besides the side effects mentioned above, the other **most common** side effects seen in patients who took bedaquiline are:

Serious side effects	→	9 out of 79 patients (11%) taking bedaquiline with other TB medicines died, versus 2 out of 81 (3%) taking just the other TB medicines and no bedaquiline.

		It is not known why more patients in the bedaquiline group died.
QTc interval increase	→	An increase in the measure of the heart's electrical activity. This was seen on the electrocardiogram in patients taking bedaquiline and in those taking other TB drugs. This may increase the risk that the heart does not beat in its normal, regular rhythm, which in rare cases cause death. However, no clinical side effects relating to heart rhythm problems were seen.
Effects on the pancreas		Studies in mice and dogs showed that bedaquiline caused damage to the pancreas. It is not known if the effect found in mice and dogs indicates any risk for humans.
Joint pain	→	One type of joint pain that may be caused or worsened by some medicines is called gout. Gout is caused by too much of a normal chemical in your body called uric acid. Uric acid is a chemical that is created when the body breaks down substances called purines. Purines are found in some foods (like seafood) and drinks (like beer).
Accumulation in the body	→	Bedaquiline leaves your body slowly after the last tablet is taken. It takes about a year for all the drug to be removed from your body.

In addition to the listed side effects your study doctor has information on side effects that may occur less often and your study doctor could discuss these with you.

These are possible risks and side effects of procedures that we will perform:

- Drawing blood is a normal part of routine medical care. There is a slight risk of discomfort. Drawing blood does not often cause fainting, inflammation of the vein, pain, bruising or bleeding at the place where the needle goes in. There

is also a small chance of infection. But experienced staff will draw your blood under germ-free conditions.

- When an ECG is done, the sensors, or stickers, may cause slight discomfort when they are removed from your skin.
- An x-ray is a common test that exposes you to a small amount of radiation. Radiation adds up over your lifetime, but small doses like the one we use to take a picture of your chest will probably not be a risk to your health.
- The eye tests are common. The drops we put into your eyes will make your eyes see blurry and be sensitive to light for a few hours after the examination, and during that time you should not drive. Very seldom eye tests can cause higher pressure in your eyes which can make you feel nauseous and can make your eyes hurt. If this happens, you should call the study doctor right away.

It is important that you must do exactly what your study doctor and/or study nurse says.

You must tell your study doctor immediately if:

- you take any local or herbal medicines, medicine that a doctor prescribed or that you can buy at a chemist,
- your medical condition changes,
- you have seen any other healthcare providers,
- you have any side effects*,
- you have any complications*, or
- you get hurt in any way while taking the study medicine.

Your study doctor and/or nurse will ask you at every visit about any other medicine you may have taken and how you are feeling.

Your condition may stay the same or get worse while you are in this study. However, the study doctor will watch you closely and if he/she feels that taking part in the study is not good for your health, he/she will immediately take you out of the study.

Using the study medicine may have risks that we do not yet know about. If we find out about any of these risks, we will tell you about any new important information that may make you want to change your mind about staying in the study.

7. Are there things that I cannot do while I am in the study? 7

Pregnancy

Boys: You cannot take part in this study if you are planning to make someone pregnant during the treatment period or 12 weeks after the last dose of study medicine
Girls: You cannot take part in this study if you think you may be pregnant, are pregnant, are breast feeding or are trying to get pregnant during the treatment period or 6 months after the last dose of study medicine

This is because there may be risks to a mother and her baby that we may not yet know about.

We need to know about anything unusual that happens to you. You must feel free to call us anytime about anything that you are worried about or questions that you have.

If you get sick or are worried about anything or have questions between visits to the clinic, you should tell your study doctor. You do not have to wait for your next visit.

If you are a girl and **can** have babies (started your period) you must not fall pregnant or breastfeed while taking part in this research. You will have to take a pregnancy test. If you sometimes have sex, you must use effective birth control while you are taking part in the research. Effective birth control is using 2 methods of birth control while you are taking the study medicine and for 6 months after you have taken the last dose of study medicine.

When you are taking the study medicine, birth control such as the pill and the contraceptive injection may not work as well as usual. Because of this, you must be willing not to have sex, or you will have to use 2 methods of birth control. Talk to your study doctor to explain the methods to you. If you can't get birth control, you must also speak to your study doctor. The study doctor may be able to tell you about the correct birth control.
If you become pregnant while you are taking part in the study, it is very important that you tell the study doctor immediately. If this happens, the study doctor will discuss with you what to do. Because there might be risks to an unborn child that we do not know about yet, you will be asked to stop taking part in the study. We may want to ask you some questions about your pregnancy and the baby and we may ask you to visit the study doctor at certain times while you are pregnant and after you have had your baby so that we can check how healthy you are and collect information about what happened to the baby.

If you are a boy and you sometimes have sex, you and your girlfriend must either use 2 methods of birth control as we discussed above for the girls or use one form that your study doctor says you can use such as the birth control pill or an IUD.

You must tell your study doctor if you (if you are a girl) become pregnant during the study or within 6 months after the last time you took the study medicine.

Please talk to your study doctor if you are unsure of where to get the correct birth control. You are responsible for getting the correct birth control from your family planning or birth control clinic.

Foods and drinks that you cannot eat or drink

- While you are taking your study medicine, you should not eat a lot of some foods or drinks that contain a lot of a protein called tyramine. Foods that contain a lot of tyramine include foods that may have had protein changes because they have been allowed to age, ferment, because they were pickled or smoked to improve their flavor. Examples are: aged cheeses, fermented or air-dried meats (cold cuts and biltong), sauerkraut, soy sauce, tap beers and red wines.

Other medicines that you cannot use

- You cannot use certain medicines for depression while you are using the study medicine.
- There are some HIV medicines you should not use if you are HIV positive. Your study doctor can tell you which HIV medicines you can use during this study.
- You should tell your doctor if you are taking any illegal drugs, because some illegal drugs can affect your safety or your ability to follow through with all the study procedures.

8. How can the study help me? 8

Your TB could get better because you are in this study, but we cannot be sure about this. If the study medicine does not work well, it will not help you. However, the information that we get from the study can help us to make treatments for TB in the future, and in it can help other TB patients later on.

The medical attention you will get because you are taking part in the study can help you to learn useful information about your health.

9. What other treatments can I choose? 9

You do not have to take part in this study. If you decide not to take part, you will not be punished and you will still get care and treatment for your TB at <<TB clinic or specialized unit in a hospitalist location>> for at least <<add time period>>, per your country's National TB Treatment Guidelines.

If you do not take part in the study, your doctor will make sure that you are sent to another place to get treatment.

10. What will happen if I get hurt in the study? 10

<< For ABPI Countries:

The sponsor has taken out insurance in case you get hurt in this study.
The sponsor will pay you for all reasonable medical expenses that you may have because you got hurt in this study according to the guidelines of the Association of the British Pharmaceutical Industry (ABPI guidelines). These guidelines say that the sponsor of the study should pay you if you get hurt because you took the study medicine or because of other procedures that were carried out according to the protocol for this study. You will not have to prove that it was the sponsor's fault that you got hurt. Your study doctor has a copy of the ABPI guidelines if you would like to see them.

The APBI guidelines say that the sponsor does not have to pay you if:

- *you got hurt because you took medicine or had a procedure that the study does not need or if you did not stick to the rules of the study;*
- *the injury was not a serious injury that will last a long time and disable you.*

The ABPI guidelines say that the sponsor may pay you less, or may not have to pay you at all depending on the following reasons:

- *how serious the disease is that you are being treated for, how likely it is that something unpleasant will happen to you if you take the medication and any warnings that were given to you;*
- *the risks and benefits of normal or standard treatments compared to the risks and benefits that we know the study medicine have or think that it may have;*
- *if somebody who is not in the study did something wrong, or if the study doctor does not give you the right help if you have a bad reaction;*
- *if you have been careless.*

Any money that the sponsor pays to you because of the ABPI guidelines does not mean that the sponsor is legally responsible for your injury. You will not lose any of the legal rights you have if you are hurt just because the sponsor has agreed to follow the ABPI guidelines. Please ask if you want more information about this.>>

*<<Country regulatory authorities that **DO NOT require compliance to the ABPI clinical trial insurance guidelines**,*

Text will be provided on an 'as needed' basis in consultation with TB Alliance Legal.>>

11. What will happen to my personal information? 11

We won't tell other people that you are taking part in this research, and we won't give information about you to anyone who does not work in the study.

We will keep information about you that we collected during the research in a safe place and no-one except the researchers will be able to see it. Any information about you will have a number on it, and not your name. Only the researchers will know what your number is, and we will keep that information in a locked cupboard. We won't give it to anyone, except the research sponsor, your study doctor and the people that look at the information on behalf of the sponsor.

12. Will I be paid to take part in this study? 12

You will not be paid to take part in this study. However, the sponsor will pay your parent(s) / legal guardian back for expenses such as for transport to and from the study site and other costs that you may have because of taking part in the study.

13. Do I need to pay anything to be in this study? 13

The sponsor will pay all costs related to the study such as the study medicine, treatment, tests, examinations, and procedures specified in the protocol (study plan).

Not you, your parents/legal guardian, nor your <<medical insurance/aid,>> healthcare provider will have to pay for these expenses. In other words, you will not have to pay for anything that is needed for your participation in this study.

14. Who is in charge of the study? 14

The study is sponsored by the Global Alliance for TB Drug Development (TB Alliance), a not-for-profit organization based in New York in the United States.

15. What happens if I do not want to or cannot be in the study anymore? 15

You may stop participating in the study for the following reasons:

- Testing comes back that shows your TB won't respond to the study medicines.
- You do not do what the study doctor tells you to do.
- You do not take the study medicine as the doctor tells you to.
- Testing comes back that shows your TB won't respond to the study drugs.
- The study doctor decides that it is best for you.
- If you ask to stop (you don't have to explain why).
- If the TB Alliance asks you to stop.
- If the TB Alliance stops the study or closes the study site.
- If you become pregnant (girls who can get pregnant).

If you decide to leave the study, please tell us immediately.

If you leave the study, the doctor would like to ask you some questions and check your health to make sure that you are safe and any possible side effects from the study medicine are treated. Your study doctor/site staff may need to perform certain procedures previously mentioned in the "**5. What will happen to me in the study?**" section.

16. Whom can I contact if something worries me? 16

You can call the study doctor or another authorised person at the study site any time of the day or night (24 hours) on Tel: **<<*add*>>** or **<<*add*>>**.	

For questions about <u>your rights</u> as a participant in a study:

If you want any information about your rights as a study participant, or if you have complaints about this study, you may contact the <<add name of Ethics Committee>>, which is an independent committee established to help protect the rights of research participants. Their contact details are as follows:

<<Add name, address and contact telephone/fax numbers>>

For <u>complaints</u>, if you think that the study doctor or ethics committee did not help you:

<<include per country as appropriate>>

17. How do I agree to be in this study? 17

If you want to take part in this study, please read the statement and sign on page <<XX>>.

Personal doctor / specialist notification option:

Please mark below, by writing your initials in the correct block, if you want me to tell your personal doctor or your specialist that you are taking part in this study:

☐ **YES**, I want my study doctor to tell my personal doctor / specialist that I am taking part in this study.

☐ **NO**, I do not want my study doctor to tell my personal doctor / specialist that I am taking part in this study.

☐ **I do not have** a personal doctor / specialist.

Collection of Pre-screening Stored Sputum (or TB from your sputum) Sample agreement:

Please mark below, by writing your initials in the correct block, if you agree for your stored sputum sample or TB from your sputum (taken before this visit/reading and signing this form) to be collected from the storing laboratory:

☐ **YES**, I agree if available, for my stored sputum sample or TB from your sputum to be collected from the laboratory and used for this study.

☐ **NO**, I do not want my stored sputum sample or TB from your sputum to be collected from the laboratory and used for this study.

Participant Notes

Glossary

Technical term	Explanation
complications	another disease or condition that makes your TB worse
contagious	can be spread to other people
adverse events	unwanted events

PAEDIATRIC INFORMED ASSENT FORM

By signing below, I agree that:

- I have read the information sheet and consent form for this study, or someone has read it to me, and I understand it.
- I have had the chance to ask questions and I am happy with the answers.
- I have had time to discuss the information with others and to decide if I want to take part.
- I will get a signed and dated copy of this consent form on the day that I sign it.
- I agree of my own free will to take part in this study. I know I have the right to stop taking part at any time, without giving any reason. If I stop taking part, it will not change my medical care or legal rights.
- Site staff, representatives from the sponsor, including auditors, regulatory authorities and ethics committees can have direct access to my medical records. They will treat my information as confidential.
- If I withdraw from the study, study data collected about me up to the point of my withdrawal can still be used to carry out this study.
- Girls only: "If I become pregnant on the study, follow-up information on the outcome of my pregnancy can be collected, if needed."
  <<EU: "I consent to the processing/storing of my data and the transfer thereof to countries outside the EU.">>

Printed Name of Participant

Signature/mark/thumb print of Participant

Date
(Participant/witness must write date)

*Printed Name of Person Conducting Consent
(If other than study doctor/delegate)

*Signature of Person Conducting Consent
(If other than study doctor/delegate)

Date
(Person conducting consent must write date)

I, _____ (Insert name of investigator) hereby confirm that the above participant has been fully informed about the nature, conduct and risks of the above study.

_____ _____

Signature of Investigator (study doctor) Date

(Investigator must write date)

By signing below, I verify that the above participant gave verbal informed consent. The participant has been informed about the risks and the benefits of the study, understands such risks and benefits and is able to agree to participation, without coercion, undue influence or inappropriate incentives.

_____

*Printed Name of Witness

_____ _____

*Signature of Witness Date

(Witness must write date)

* Where applicable

PARTICIPANT INFORMATION AND INFORMED CONSENT FORM

Protocol Name/Number: ZeNix/NC-007-(B-Pa-L)
Protocol Title: A Phase 3 partially-blinded, randomized trial assessing the safety and efficacy of various doses and treatment durations of linezolid plus bedaquiline and pretomanid in participants with pulmonary infection of either extensively drug-resistant tuberculosis (XDR-TB), pre-XDR-TB or treatment intolerant or non-responsive multi-drug resistant tuberculosis (MDR-TB).

Participant Initials:_____ Participant Number:_____

Introduction

We invite you to take part in a study with a new combination of medicines. The names of the medicines are bedaquiline, linezolid, and pretomanid.

Please read this information sheet before you agree to take part. This document will answer the following questions:

If you have any other questions that are not answered in this document, please ask someone from the study staff for more information. Difficult medical terms are marked with an (*) and are explained in the **Glossary** on page <x>.

It is very important that you understand this information sheet before you agree to take part in this study. We would like you to ask as many questions as you need. If there is anything that you do not understand, please discuss this with the study doctor, the study staff, your own doctor or with your family.

Participant Notes

1. Is the study safe? 1

The <<name of Ethics Committee as applicable>> and <<name of Regulatory Authority as applicable>>have checked and approved this study because it complies with medical and ethical standards.

In addition, the study will be done according to the Declaration of Helsinki 2013, International Conference on Harmonisation-Good Clinical Practice (ICH-GCP) <<and list any other appropriate guidelines e.g. South African GCP Guidelines>>.

One of the purposes of these regulations is to make sure that the rights of people taking part in research studies are protected. If you would like to read any of these guidelines and regulations, please ask your study doctor to give you a copy.

2. Do I have to take part? 2

Your participation in this study is totally voluntary (out of free will). You may choose not to be in the study or leave the study (withdraw your consent) at any time by telling the study doctor.

If you decide not to be in the study or if you withdraw your consent, you will not lose any benefits that you otherwise would have had. If you withdraw before you complete treatment, the study doctor will give you a referral letter to an MDR or XDR-TB unit, TB clinic, or hospital where they will give you the standard TB treatment as to all TB patients, according to your country's National TB Treatment Guidelines.

3. Why are you doing the study? 3

You have been diagnosed with extensively drug resistant pulmonary (i.e. in your lungs) TB (XDR-TB), pre-extensively drug resistant TB (pre-XDR-TB), or Multidrug Resistant TB (MDR-TB). This means that these forms of TB bacteria, or germs, are present in your lungs and they do not respond to treatment or require treatment that you can't tolerate. These forms of TB can be very hard to treat and medicines must be taken for up to two years or even longer.

It is possible that because people do not take the medicines correctly, TB resistance to these medicines is becoming more common. These forms of resistant TB can be very difficult to treat. New medicines are urgently needed to make the TB treatment time shorter and to treat resistant TB.

A previous study called the Nix-TB study has shown that three medicines called bedaquiline, linezolid and pretomanid taken together may treat your type of TB. To date, these medicines have been tested in the laboratory, on animals ,on healthy human volunteers, and on over 70 TB participants and have been shown to be possibly effective against XDR-TB and MDR-TB. We want to do this study to see what dose and length of treatment of linezolid is the most effective in treating your type of TB while causing the least amount of side effects. The safety and effectiveness of the following three drugs together: bedaquiline, linezolid and pretomanid will also be tested.

4. How will the study work? 4

About 180 people (called participants) will be taking part in this study. All the participants will be men and women <<14 (update for specific age for each Country/site)>> years old and older. The trial will be conducted globally and it is planned that participants will be from approximately 12 research centers around the world, including but not limited to <<Country specific to ICF>> and additional centers in South Africa <<delete South Africa if noted previously in Country specific>>, Eastern Europe and Asia. <<When required by EC, list known targeted countries within the regions>>. We expect that you will be in this study for about 2 years. The study is split into 3 parts:

Part	Name	Length	Reason

1	Screening	Up to 14 days	During this time, the study doctor is checking if you meet the requirements and if it is safe for you to be part of the study. This may be several visits and take up to 14 days. If you don't meet all of the requirements when you are screened, you may have the opportunity to be screened at a later time if the doctor thinks you would be able to meet the requirements then.
2	Treatment	26 weeks or 39 weeks	You will receive study medicine for a total of 26 weeks, depending on how you respond to the medicines. You will visit the hospital/clinic at least 17 times. Some of these visits may be while you are a patient in the hospital. If the study doctor determines that you need to pause your treatment for any reason, then your treatment may extend longer than 26 weeks. If your TB has not been cured after 26 weeks of treatment, your study doctor may decide to extend your treatment to a total of 39 weeks.
3	Follow Up	78 weeks	After you finish taking the study medicine, your study doctor will check on your health for the next 78 weeks. During this time, you won't be on the study medicine but you will visit the hospital/clinic at least 8 times during this part.

If your study doctor decides that you qualify to be in this study, and if you agree to be in this study by signing this consent form, the following will happen:

You will be randomly assigned (purely by chance, like flipping a coin) to receive one of the 4 possible linezolid doses below. This study is partially blinded, which means neither you nor your study doctor will know what dose you will receive or how long you will receive linezolid. This is done by giving everyone the same number of tablets, some participants receive tablets that look like the linezolid medication, but do not contain linezolid, these are called placebo. We can only tell you at the end of the study (i.e. when the treatment blind has been broken) to which of the treatments you were assigned. If there is an emergency and the study doctor needs to know what linezolid treatment you are receiving, he/she can quickly and easily find this out.

- Linezolid 1200 milligrams (mg) daily for 26 weeks plus linezolid placebo or;
- Linezolid 600 mg daily for 26 weeks plus linezolid placebo or;
- Linezolid 1200 mg daily for 9 weeks plus linezolid placebo, then linezolid placebo for 17 weeks or;
- Linezolid 600 mg daily for 9 weeks plus linezolid placebo then linezolid placebo for 17 weeks.

In addition to linezolid and linezolid placebo, all participants will receive the following:

- bedaquiline 200 mg once daily for 8 weeks then 100 mg once daily for 18 weeks plus;
- pretomanid 200 mg once daily for 26 weeks

You and your study doctor will know how much bedaquiline and pretomanid you are receiving.

Pretomanid is a new medicine that has not been approved for the treatment of TB by any Government Regulatory Authority. Bedaquiline has been approved for treatment of MDR-TB in the United States of America and in Europe<<and has been approved by "specific regulatory authority when relevant" for treatment of MDR-TB in "Country">>. Linezolid has been approved around the world to treat many kinds of infections caused by germs. Linezolid is not approved for TB treatment, though it is sometimes used to treat TB patients if other approved medicines do not work.

You will take 5 whole tablets and one half tablet a day for the first 8 weeks of study treatment. You will then take 4 whole tablets and one half tablet a day for the remaining 18 weeks of study treatment.

The study doctor may decide to pause all your medications. The study doctor may also decide that your linezolid medicine dose needs to be reduced, paused, or just your linezolid medicine needs to be stopped. You will know if the study doctor decides to reduce, pause, or stop the linezolid. If your dose is reduced, neither you nor your doctor will know your current dose or the dose your linezolid medicine is reduced to. If your dose of linezolid is reduced anytime during the study, the study doctor may increase your linezolid dosage at a later visit, but not higher than the dose you started on. You will continue to receive the same number of tablets and half tablets, some or all the tablets with medicine will be replaced with placebos.

You will be given study medicines at each visit during the Treatment Period and asked to bring back all empty packets/bottles and unused medicines to your next visit.

5. What will happen to me in the study? 5

You must be willing to follow all study procedures and requirements. For this study to be successful and for your own safety, it is important that you co-operate fully with the study doctor and follow his/her instructions precisely throughout your time in the study.

Depending on your response to the medicine and study procedures, there may be some slight changes to the treatment visits and procedures, and how long you stay in the study. This is a list of all the study visits and what will happen at each visit:

	Screening Visits	Treatment Visits																	Post-Treatment Follow-up Visits							
Procedures	Up to 14 days before Treatment	Day 1 (Baseline)	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 10	Week 12	Week 14	Week 16	Week 18	Week 20	Week 23	End of Treatment	4 weeks	8 weeks	12 weeks	26 weeks	39 weeks	52 weeks	65 weeks	78 weeks
Demography	X																									
Medical and smoking history	X																									
Eligibility assessment	X	X																								
Sputum collection	X	X	X	X	X	X		X		X	X	X		X		X	X	X	X	X	X	X	X	X	X	X
Pregnancy Test	X	X								X				X				X								
HIV, CD4 Count and Viral Load	X																	X								
Blood tests	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X								
ECG	X	X	X			X				X				X				X								
Chest X-Ray	X																	X								
TB Questionnaire/s	X									X				X				X				X		X		X
Vital Signs	X	X	X	X		X		X		X		X		X		X		X			X	X	X	X	X	X
Physical Exam	X	X	X	X		X		X		X		X		X		X		X			X	X	X	X	X	X
Pharmacokinetic (PK) test		X		X						X		X				X		X								
Eye Exam	X					X				X		X		X		X	X	X	X		X					
Nerve Exam	X					X				X		X		X		X	X	X			X	X		X		X
Study Medicine check		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X								
Other medicines	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse Events	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

To help understand what will happen at each visit, we have described these below:

Demography	→	This is personal information about your date of birth, gender and race that you will be asked about.
Medical and smoking history	→	You will be asked about your medical (including alcohol and drug use) and smoking history and all other medicines, including prescription, herbal and traditional you may have taken in the last 30 days, or are currently still taking.
Eligibility assessment	→	This is a process of checking that you meet the study requirements to make sure it is safe for you to take part.
Sputum collection	→	You will be asked to cough up sputum (phlegm) into a small cup at different times in the study. The sputum is used to check that you have TB, the type of TB you have, how many TB bacteria you have and what medicines will work on the TB bacteria. *<<Add as required per country*: If you have a stored sputum (or TB from your sputum) sample (which was collected before this visit) that could be used to allow you into this study or check the type of TB and what medication will work on that type of TB bacteria. If you agree to it, this may be collected from the applicable laboratory and used if you check "yes" at the end of this consent>> The TB germs that have been taken out of your sputum will also be sent to laboratories in the United Kingdom (UK) every few months to test how they respond to the study medicines. They may also be used to research new testing methods for TB and/or study medicines. These germs will not contain any material from your body; only the TB germs. You will not receive the results from these tests or get any more benefit from these tests being done. The testing could be done for as long as five years after you take part.
HIV, viral load and CD4 count test	→	This is a test to see if you have been infected with HIV and, if you have, we will measure your CD4

		count (a kind of cell that fights infection) and the amount of HIV virus in your blood. You will be counselled on HIV before the blood tests are taken and again once the results are given to you, and you may be asked to sign a separate informed consent form.
Blood tests	→	Blood will be taken from you by inserting a small needle into a vein in your arm. The blood will be tested to check if you are healthy. A total of about 360 millilitres (72 teaspoons) of blood will be collected over the whole study, or about 20mL (4 teaspoons) at each study visit.
Urine tests	→	You will be asked to provide a sample of your urine in a small cup when you are at the clinic. The urine will be tested to check if you are healthy. Your urine will be tested to see if you have taken any drugs like cannabis, cocaine, amphetamines, opiates, benzodiazepines and barbiturates.
Pregnancy test	→	If you are a woman who is able to have children, your urine will be tested to see if you are pregnant, whether or not you are sexually active.
ECG	→	A test that is done by placing 12 sensors (like stickers) to your skin for a short time to check how your heart is working.
Chest X-Ray	→	This is a photograph of your lungs.
TB and health questionnaire/s	→	You will be asked to tell your study doctor about your TB symptoms and general health to check how you are feeling.
Physical exam	→	This is an assessment of your body to check for signs of disease.
Vital signs	→	A measurement of your blood pressure, heart rate, breathing rate, body temperature, height and weight.
Pharmacokinetic (PK) test	→	Blood will be taken at some visits to check what happens to the medicines once you swallow them. Blood will be taken from you by inserting a small needle into a vein in your arm. About 20 milliliters (4 teaspoons) of blood will be taken from you for this test.
Eye exam	→	This is a check of your vision by asking you to read the letters or symbols off a chart, and to read numbers or symbols off of cards with

		coloured patterns on them. There will also be an exam to look at the lens of your eyes using a machine that shines a thin beam of light into the eye while the eye doctor looks into it with a type of magnifying glass. To test your lens he/she will need to put a couple of drops of medicine in your eyes that will enlarge your pupil for a short time. This allows the eye doctor to see easily into your eyes. This is the same as what happens to your eyes in the dark.
Nerve Exam		You will be asked to answer some questions about whether you experience any feelings such as a painful burning, or stinging, tingling, sensation of pins and needles or numbness in your arms and legs. The doctor will test your legs to see what your reflexes are like and if you feel vibrations.
Study medicine check	→	You will be asked how much study medicine you have taken or not taken, since the last time you were at the clinic.
Hospital admission	→	You may need to stay in the hospital if your study doctor considers it safer for you.
Hospital check-out	→	Your study doctor will tell you when it is safe for you to not be in hospital all the time. We will record when you are checked out from the hospital.

If you are admitted to the hospital, but allowed to go home for the weekend, or if you are discharged from the hospital during the treatment period, used medicine containers/unused medicine should be returned when you return to the hospital.

After you have stopped or completed the study medicines, the study doctor will decide if you need more TB treatment. If you do, your study doctor will give you a referral letter to an MDR or XDR-TB unit or hospital. It is very important that you go to the hospital as soon as possible and continue anti-TB treatment if your doctor recommends that.

Treatment Extension

If the study doctor decides that your treatment should be extended, either due to a pause of all of your study treatment, or if your TB is not cured after 26 weeks of treatment, the following procedures will be performed at additional treatment visits.

	Optional Treatment Extension Visits
Procedures	**Every 3 weeks, for up to a total of 26 or 39 weeks of treatment**
Demography	
Medical and smoking history	
Eligibility assessment	
Sputum collection	X
Pregnancy Test	
HIV, CD4 Count and Viral Load	
Blood tests	X
ECG	
Chest X-Ray	
TB Questionnaire/s	
Vital Signs	X
Physical Exam	X
Pharmacokinetic (PK) test	
Eye Exam	X
Nerve Exam	X
Study Medicine check	X
Other medicines	X
Adverse Events	X

Early Withdrawal

If you decide of your own free will, or your study doctor decides you should stop treatment or withdraw from the study before you have finished the above visits, the procedures listed below may be performed at an Early Withdrawal Visit. If you have received more than 15 doses of the study medication and haven't had your 12 week follow-up visit when you are withdrawn from the study, we will request you to come back for 1 more visit at the clinic so we can monitor your health, and you will be contacted 2 more times for a visit that can take place at the clinic, your home or on the phone with your study doctor where the following procedures may be performed.

	Early Withdrawal During Treatment Period			
Procedures	**Early Withdrawal Visit During Treatment**	**Follow-up Week 12**	**Follow-up Week 26**	**Follow-up Week 78**
Demography				
Medical and smoking history				
Eligibility assessment				
Sputum collection	X			
Pregnancy Test	X			
CD4 Count	X			
Blood tests	X			
ECG	X			
Chest X-Ray				
TB Questionnaire/s	X			
Vital Signs	X			
Physical Exam	X			
Pharmacokinetic (PK) test	X			
Eye Exam	X	X		
Nerve Exam	X			
Study Medicine check	X			
Other medicines	X	X		
Adverse Events	X	X	X	X
Survival/TB outcome			X	X

If you haven't had all your follow-up visits when you are withdrawn from the study, we may request that you to come back for 1 more visit at the clinic so we can monitor your health as well.

	Early Withdrawal During Follow-up Period			
Procedures	**Early Withdrawal Visit During Follow-up**	**Follow-up Week 12 (If applicable)**	**Follow-up Week 26 (if applicable)**	**Follow-up Week 78**
Demography				
Medical and smoking history				
Eligibility assessment				
Sputum collection	X			
Pregnancy Test	X			
CD4 Count				
Blood tests	X			
ECG	X			

Chest X-Ray				
TB Questionnaire/s	X			
Vital Signs	X			
Physical Exam	X			
Pharmacokinetic (PK) test	X			
Eye Exam	X	X		
Nerve Exam	X			
Study Medicine check	X			
Other medicines	X	X		
Adverse Events	X	X	X	X
Survival/TB outcome			X	X

If the study doctor feels it is necessary, you may be asked to come in for extra (unscheduled) visits that do not appear on the above charts.

6. What can go wrong in the study? 6

There are some possible risks and inconveniences of being in the study.

Tuberculosis is a serious disease that can be fatal; all combinations of drugs used together in regimens to treat tuberculosis have rarely been associated with serious side effects, including death.

You should **not drink alcohol** while you are taking study medication or other TB drugs as alcohol may damage your liver.
You should tell your doctor if you have **heart problems**, including a slow heart rate, or if you have low thyroid hormone levels.
You will have ECGs from time to time to monitor the electrical activity of your heart, including the QT interval.

Details of the risks of taking the medicines in this study are noted below:

Liver problems	→	May be associated with symptoms such as nausea or vomiting, stomach pain, fever, weakness, itching, unusual tiredness, loss of appetite, light coloured bowel movements, dark coloured urine, yellowing of your skin or the white of your eyes. Liver problems may also be suggested by blood tests that show abnormalities in measures of your liver enzymes and other measures of how your liver is working. In	Pretomanid, Linezolid, Bedaquiline,

		rare cases liver problems may be serious and even lead to death.	
Headache	→	pain in any part of the head	Pretomanid, Linezolid, Bedaquiline,
Stomach problems	→	Tenderness or pain of the stomach area Feeling like you want to throw up, or actually throwing up. Also not feeling hungry, having diarrhoea (loose bowel movements) or having an upset stomach.	Linezolid, Pretomanid, Bedaquiline
Dizziness	→	A feeling of being 'drunk' or 'light headed', especially when you stand up or sit down quickly.	Linezolid, Bedaquiline

The following are a list and description of side effects that are unique to each of the medicines:

Pretomanid

Besides the side effects mentioned above, the other side effects include:

Reproductive organ changes	→	Results from animal studies have shown that rats given pretomanid showed signs of damage to the male rats' reproductive organs. Recent studies in people have shown that there is no evidence that pretomanid damages the male reproductive organs. The potential for pretomanid to have an effect on the male reproductive organs will remain under evaluation.
Cataracts (clouding of the lens in the eye)	→	Other results from animal studies show that rats given Pretomanid developed cataracts at high doses over a 6-month period of taking the medicine. It is not known if the effect found in rats indicates any risk for human beings.
Fits (convulsions or seizures)	→	were seen in some animal studies and in 1 patient treated with Pretomanid

Skin problems	→	Inflamed areas on your skin, which may be red, itchy and/or painful.

Linezolid

Besides the side effects mentioned above, the other **most common** side effects seen in patients who took linezolid are:

Changes in taste	→	certain food or drinks may taste different to you
Tongue discolouration	→	the colour of your tongue changes
Fungal infections	→	when a fungus causes the infection
Vaginal moniliasis	→	a fungal infection in the vagina
Oral moniliasis	→	a fungal infection in the mouth
Fever	→	When your body temperature goes higher than 38 °C or 100.4 °F.
Signs of nerve disturbances	→	This is sometimes called 'peripheral neuropathy', which may be experienced as a painful burning, or stinging, tingling, sensation of pins and needles or numbness in your arms and legs. In some cases this can be permanent.
Convulsions or seizures	→	These are also commonly known as 'fits'. A **convulsion** is when the body muscles contract and relax quickly and repeatedly / uncontrolled shaking of the body. A **seizure** is when there is a change in the normal electrical activity of the brain.

Other side effects seen in patients who took linezolid include, but are not limited to:

Myelo-suppression	→	a lack of certain cells in your blood that your body needs to function. can make you feel tired and make your body being unable to fight off other illnesses or heal an injury. This could also make you bleed or bruise easily.
Lactic acidosis	→	a build-up of waste products in your blood that can cause constant nausea and vomiting.
Serotonin syndrome	→	this rare but serious condition may occur when linezolid is given with certain types of medications that affect a chemical in the brain called serotonin. Some of these medications include antidepressants. Be sure to tell your study doctor about all prescription and non-prescription medications you are taking. It can cause many different symptoms, for example: confusion, restlessness, tremors, blushing, sweating and fever.
Interactions with other medicines	→	causing a rise in blood pressure
Optic neuropathy	→	A type of damage to the nerves in your eye that can lead to blindness if it is not treated. This can be permanent.
Low blood sugar	→	This is often seen in patients with diabetes who have to take insulin or other medicines

Bedaquiline

From studies in 380 patients with TB who received Bedaquiline (312 of whom received Bedaquiline for as long as 6 months), we continued to see that Bedaquiline is generally safe and well tolerated. Besides the side effects mentioned above, the other **most common** side effects seen in patients who took bedaquiline are:

Serious side effects	→	9 out of 79 patients (11%) taking bedaquiline with other TB medicines died, versus 2 out of 81 (3%) taking just the other TB medicines and no bedaquiline.

		It is not known why more patients in the bedaquiline group died.
QTc interval increase	→	An increase in the measure of the heart's electrical activity. This was seen on the electrocardiogram in patients taking bedaquiline and in those taking other TB drugs. This may increase the risk that the heart does not beat in its normal, regular rhythm, which in rare cases cause death. However, no clinical side effects relating to heart rhythm problems were seen.
Effects on the pancreas		Studies in mice and dogs showed that bedaquiline caused damage to the pancreas. It is not known if the effect found in mice and dogs indicates any risk for humans.
Joint pain	→	One type of joint pain that may be caused or worsened by some medicines is called gout. Gout is caused by too much of a normal chemical in your body called uric acid. Uric acid is a chemical that is created when the body breaks down substances called purines. Purines are found in some foods (like seafood) and drinks (like beer).
Accumulation in the body	→	Bedaquiline leaves your body slowly after the last tablet is taken. It takes about a year for all the drug to be removed from your body.

In addition to the listed side effects your study doctor has information on side effects that may occur less often and your study doctor could discuss these with you.

Possible risks and side effects of procedures to be performed:

- Drawing blood is normally done as part of routine medical care. There is a slight risk of discomfort. Drawing blood may rarely cause fainting, inflammation of

the vein, pain, bruising or bleeding at the site where the needle goes in. There is also a slight risk of infection. Your protection is that experienced staff will draw your blood under germ free conditions.

- When an ECG is done, the sensors, or stickers, may cause slight discomfort when they are removed from your skin.
- An x-ray is a common test exposing you to a small amount of radiation. The effect of radiation adds up over your lifetime, but small doses like the one used to take a picture of your chest is not likely to be a risk to your health.
- The eye tests are common. The drops put into your eyes will cause your vision to be blurred and sensitive to light for a few hours after the examination, during which time you should not drive. In very rare cases they can cause increased pressure in the eye with nausea and pain. If this happens, call the study doctor right away.

It is important that you follow your study doctor's and/or study nurses' instructions exactly.

You must inform your study doctor immediately if:

- you take any local or herbal remedies, prescribed or non-prescribed (over the counter) medicines,
- your medical condition changes,
- you have seen any other healthcare providers,
- you have any side effects,
- you have any complications*, or
- you have any injuries while taking the study medicine.

Your study doctor and/or nurse will ask you at every visit about any other medication you may have taken and how you are feeling.

It is possible that your condition will stay the same or get worse while you are in this study. However, the study doctor will watch you closely and if he/she feels that participating in the study is not good for your health, he/she will immediately take you off the study.

There may be risks with the use of the study medicine that we do not yet know of. If we become aware of these, we will tell you of any new important findings that may affect your willingness to stay in the study.

7. Are there things that I cannot do while I am in the study? 7

You cannot take part in this study if you are breastfeeding, pregnant or trying to get pregnant.

This is because there may be risks to becoming pregnant and to an unborn child that we may not yet know of. If you can get pregnant, we will test you before you take the study medicine and during the study to see if you are pregnant.

Women participants who CAN become pregnant:

You must use 2 methods of birth control. You need to use birth control for as long as you are taking the study medicine and for up to 6 months after you have taken the last dose of study medicine.

When taking the study medicine, birth control that are based on hormones only, such as the contraceptive pill or injection, may not work as well as usual. Because of this, either you must be willing not to have sex, or you must use 2 methods of birth control, for example:

a) Double (2 different types) barrier methods, which may include a male condom, diaphragm, cervical cap, or female condom; OR
b) 1 barrier method described above used together with a hormone-based birth control (tablet or injection), or an intra-uterine device

If you are a female participant and become pregnant while you are in the study, it is very important for you to tell the study doctor immediately. If this happens, the study doctor will discuss with you what to do.

Since there might be unknown risks to an unborn child, we will ask you to stop taking part in the study. We may have questions about your pregnancy and the baby and we may ask you to visit the study doctor at certain times during and after your pregnancy to check your health status and collect information on the outcome of your pregnancy.

Male participants' female sex partner who CAN become pregnant:

You and your female partner need to use at least 1 method of birth control for as long as you are taking the study medicine and for up to 12 weeks after you have taken the last dose of study medicine. Examples of methods of birth control are as follows:

Double barrier method, which can include a male condom, diaphragm, cervical cap, or female condom; OR

Hormone-based contraceptives or an intra-uterine device for your female partner.

Please note that it is your own responsibility to get the correct birth control for you from your family planning or birth control clinic. Please speak with your study doctor if you are unsure of where to get the correct birth control.

Women participants, and male participants' female sex partner, who CANNOT become pregnant:

You do not need to use birth control if you are:

a) Not an active heterosexual male or female participant, or you do not practice sex; OR
b) A female participant or male participants' female sex partner, and have had an operation to remove both ovaries, or both ovarian tubes have been tied or cut and or the uterus has been removed, or you have not had a period for at least 12 months in a row; OR
c) A male participant or female participants' male sex partner, who has had both testes tubes tied or cut, or have had both testes removed at least 3 months before the study.

Foods and drinks that you cannot eat or drink

- Large quantities of foods or beverages that contain a lot of a protein called tyramine should be avoided while taking your study medicine. Foods high in tyramine include those that may have had protein changes by aging, fermentation, pickling, or smoking to improve flavor, such as aged cheeses, fermented or air-dried meats, sauerkraut, soy sauce, tap beers and red wines. You should talk to your study doctor if you have questions about how you can avoid large quantities of tyramine.
- You should not drink alcohol while you are taking study medication as alcohol may damage your liver.

Other medicines that you cannot use

- You cannot use certain medications to treat depression while you are on the study medication.
- There are other medications that you cannot use while you are on the study drug because they may increase the risk of abnormal heart rhythms, or because they may affect what your body does to the study medication after you take them. Your study doctor can tell you which medications these are.
- If you are HIV positive, certain HIV medications should not be used. Your study doctor can tell you which HIV medications can be used during this study.

- You should inform your doctor if you are taking any illegal drugs, because some illegal drugs can affect your safety or your ability to follow through with all the study procedures.

8. How can the study help me? 8

There is a chance that your TB may get better because you are in this study, but we cannot guarantee this. If the study medicine does not work well you will not get any benefit from being in the study. However, the information that we get from the study can help in making future treatments for TB, and in the long run it will likely help other TB patients.

The close medical attention you will get by taking part in the study may help you to learn useful information about your health status.

9. What are my other choices for treatment? 9

You do not have to take part in this study. If you decide not to take part, you will not be disadvantaged and you will still receive care and treatment for your TB at <<TB clinic or specialized unit in a hospitalist location>> for at least <<add time period>>, per your country's National TB Treatment Guidelines.

If you do not take part in the study, your doctor will make sure you remain in or are sent to an MDR-TB unit or XDR-TB unit or hospital for treatment.

10. What will happen if I am injured in the study? 10

<< For ABPI Countries:

The sponsor has taken out insurance in case you get injured in this study.
The sponsor will pay you for all reasonable medical expenses you may have because you are injured in this study, according to the guidelines of the Association of the British Pharmaceutical Industry (ABPI guidelines). These guidelines recommend that the sponsor of the study, without any legal commitment, should pay you, without you having to prove that it is at fault, for any injury resulting from giving the study medicine or other procedures carried out in accordance with the protocol for this study. Your study doctor has a copy of the ABPI guidelines if you would like to see them.

The APBI guidelines do not require the sponsor to pay you if the injury:

- resulted from a medicine or procedure that is not required by the study or if you did not stick to the rules of the study;
- was not a serious injury that will last a long time and disable you.

Because of the following reasons, you may be paid less or the sponsor may not have to pay you at all under the ABPI Guidelines:

- how serious the disease is that is being treated, how likely you are to have adverse reactions and any warnings that were given to you;
- the risks and benefits of normal or standard treatments compared to the risks and benefits that we know the study medicine have or think that it may have;
- a wrongful act of someone outside the study, or if the study doctor does not properly deal with an adverse reaction;
- if you have been negligent.

Any payment that the sponsor makes to you because of the ABPI guidelines does not mean that the sponsor is legally responsible for your injury. You will not lose any of the legal rights you have if you are injured just because the sponsor has agreed to follow the ABPI guidelines. Please ask if you want more information on this.>>

*<<Country regulatory authorities that **DO NOT require compliance to the ABPI clinical trial insurance guidelines**,*

Text will be provided on an 'as needed' basis in consultation with TB Alliance Legal.>>

11. What will happen to my personal information? 11

All records with information that can identify you will be kept confidential and, as far as the applicable laws and regulations allow, will not be made publicly available.

The study doctor and research team will use personal information about you to carry out this study. This may include your name, address, medical history and information from your study visits. However, this personal information will stay at the study site and will not be included in the study data that we will send to the sponsor or representatives of the sponsor. You will only be identified by a coded number in reports or publications that are produced from this study (study data).

To confirm that the study data collected about you is correct and related to you, selected people working for the sponsor including auditors, as well as representatives of government regulatory authorities and ethics committees will have access to your personal information at the study site. These persons know that they must keep your information confidential. By signing this document, you are agreeing to let them have access to your information.

The sponsor may send your coded study data that were collected from your country to other countries. *<<EU: "Your data might be transferred to countries outside the EU".>>*However, they will obey all local and international laws and regulations on

data privacy to protect your personal and other information, even in countries where data privacy laws are less strict.

The sponsor or representatives may use this study data for the following purposes:

- To see if the study medicine works and is safe.
- To compare the study medicine to other medicines.
- For other activities related to the study medicine.

You have the right to ask the study doctor about the data we are collecting about you. You can ask the study doctor to allow you to see your personal information and you can ask him/her to make any corrections, if needed.

The results of the study will only be available once all participants have completed the study, the information has been collected and checked, and the results have been analyzed (looked at and a decision made about them). If you want to know the results of the study you may contact your study doctor and he/she will tell you the results if they are ready.

The results of this study will be made available to national and international medicine regulatory agencies to help them decide if the new treatments are helping to treat TB. In addition, the results may be published in international medical journals so that doctors and other health workers might learn from this work. You will not be named in any reports/publications.

A description of this clinical trial will be available on www.clinicaltrials.gov, as required by United States law<< and other countries as required, e.g. www.sanctr.gov.za, as required by South African law>>. This <these>> website<<s>> will not show information that can identify you. At most, the website<<s>> will include a summary of the results. You can search this<<these>> website<<s>> at any time.

12. Will I be paid to take part in this study? 12

You will not be paid to take part in this study. However, the sponsor will pay you back for out-of-pocket expenses such as for transport to and from the study site and other various costs that you may have because of your study participation.

You will get, depending on your out of pocket expenses, an amount of -*<<specify amount and frequency e.g. x per visit and add any pro-rata payments if applicable>>*. If your study related costs are more than the specified amount and you have proof of such costs, please discuss it with your study doctor.

13. Do I need to pay anything to be in this study? 13

The sponsor will pay all costs related to the study such as the study medicine, treatment, tests, examinations and procedures specified in the protocol. Not you, nor your <<medical insurance / aid,>> healthcare provider will have to pay for these expenses. In other words, you will not have to pay for anything that is needed for your participation in this study.

Should you need to visit any doctor, besides your study doctor, or you are hospitalized for any illness, including to treat your TB, then you will need to visit the doctor or hospital as allowed by your healthcare provider <<or medical insurance / aid>>. These medical visits, that are not part of the clinical study, are not paid for by the study.

14. Who is in charge of the study? 14

The study is sponsored by the Global Alliance for TB Drug Development (TB Alliance), a not-for-profit organization based in New York in the United States.

The TB Alliance will pay the study staff for doing this study. The study doctor will not benefit unduly if you are included in the study.

15. What happens if I do not want to or cannot be in the study anymore? 15

Your participation in the study may be stopped for the following reasons:

- Testing comes back that shows your TB won't respond to the study medicines
- You do not follow the study doctor's instructions.
- You do not take the study medicine as prescribed.
- Testing comes back that shows your TB will respond to medicines that treat drug sensitive TB
- The study doctor decides that it is in your best interest (e.g. you experience certain adverse events* during the study).
- If you ask to stop (you don't have to explain why).
- If the TB Alliance asks you to stop.
- If the TB Alliance stops the study or closes the study site.
- If you become pregnant (women who can get pregnant).

If you decide to withdraw from the study, please tell us immediately. If you withdraw from the study, it will not change your access to other medical care or the quality of the care.

If you leave the study, the doctor would like to ask you some questions and check your health to make sure that you are safe and any possible side effects from the study medicine are treated. If your study treatment is stopped, based on you and your study doctor's choice, you will be asked to continue to come to some of the study visits or be contacted in another way, unless you decide to withdraw from the study completely. If your treatment is stopped or you withdraw from the study completely, your study doctor/site staff may need to perform certain procedures previously mentioned in the "What will happen to me in the study" section.

We may ask you to come to the hospital/study site to complete these procedures.

Once you have left the study, the study doctor will give you a referral letter to an MDR or XDR-TB unit or hospital for further treatment of your TB or to another physician for routine medical care if your TB infection is cured.

16. Whom can I contact if something worries me? 16

You can call the study doctor or another person at the study site at any time of the day or night (24 hours) on Tel: **<<*add*>>** or **<<*add*>>**.	

For questions about <u>your rights</u> as a participant in a study:

If you want any information about your rights as a study participant, or if you have complaints about this study, you may contact the <<add name of Ethics Committee>>, which is an independent committee established to help protect the rights of research participants. Their contact details are as follows:

<<Add name, address and contact telephone/fax numbers>>

For <u>complaints</u>, if you think that the study doctor or ethics committee did not help you:

<<include per country as appropriate>>

17. How do I agree to be in this study? 17

If you want to take part in this study, please read the consent statement and sign on page <<XX>>.

<u>Personal doctor / specialist notification option:</u>

Please mark below, by writing your initials in the correct block, if you want me to tell your personal doctor or your specialist that you are taking part in this study:

☐ **YES**, I want my study doctor to tell my personal doctor / specialist that I am taking part in this study.

☐ **NO**, I do not want my study doctor to tell my personal doctor / specialist that I am taking part in this study.

☐ **I do not have** a personal doctor / specialist.

Collection of Pre-screening Stored Sputum (or TB from your sputum) Sample agreement:

Please mark below, by writing your initials in the correct block, if you agree for your stored sputum sample or TB from your sputum (taken before this visit/reading and signing this form) to be collected from the storing laboratory:

☐ **YES**, I agree if available, for my stored sputum sample or TB from your sputum to be collected from the laboratory and used for this study.

☐ **NO**, I do not want my stored sputum sample or TB from your sputum to be collected from the laboratory and used for this study.

Participant Notes

Glossary

Technical term	Explanation
complications	another disease or condition that makes your TB worse
diaphragm	A soft latex or silicone dome with a spring in the rim. The spring creates a seal against the wall of the vagina.
adverse events	unwanted events

PARTICIPANT INFORMED CONSENT FORM

By signing below, I agree that:

- I have read, or someone has read the information sheet and consent form for this study to me, and I understand it.
- I have had the chance to ask questions and I am happy with the answers.
- I have had time to discuss the information with others and to decide if I want to take part.
- I will get a signed and dated copy of this consent form on the day that I sign it.
- I agree of my own free will to take part in this study. I know I have the right to stop taking part at any time, without giving any reason. If I stop taking part, it will not change my medical care or legal rights.
- Site staff, representatives from the sponsor, including auditors, regulatory authorities and ethics committees can have direct access to my medical records. They will treat my information as confidential.
- If I withdraw from the study, study data collected about me up to the point of my withdrawal can still be used to carry out this study.
- Female participantsonly: "If I become pregnant while on the study, follow up information on the outcome of my pregnancy can be collected, if needed."
- <<EU: "I consent to the processing/storing of my data and the transfer thereof to countries outside the EU.">>

Printed Name of Participant/Legal Representative

Signature/mark/thumbprint of Participant/Legal Representative

Date

(Participant/witness must write date)

*Printed Name of Person Conducting Consent (If other than investigator/delegate)

*Signature of Person Conducting Consent (If other than investigator/delegate)	Date (Person conducting consent must write date)

I, _____ (Insert name of investigator) hereby confirm that the above participant has been fully informed about the nature, conduct and risks of the above study.

Signature of Investigator	Date (Investigator must write date)

By signing below, I verify that the above participant gave verbal informed consent. The participant has been informed about the risks and the benefits of the study, understands such risks and benefits and is able to agree to participation, without coercion, undue influence or inappropriate incentives.

*Printed Name of Witness

*Signature of Witness	Date (Witness must write date)

* Where applicable

PARENT OR LEGAL GUARDIAN INFORMATION AND INFORMED CONSENT FORM

Protocol Name/Number: ZeNix/NC-007-(B-Pa-L)
Protocol Title: A Phase 3 partially-blinded, randomized trial assessing the safety and efficacy of various doses and treatment durations of linezolid plus bedaquiline and pretomanid in participants with pulmonary infection of either extensively drug-resistant tuberculosis (XDR-TB), pre-XDR-TB or treatment intolerant or non-responsive multi-drug resistant tuberculosis (MDR-TB).

Participant Initials:_____ Participant Number:_____

Introduction

We invite your child to take part in a study with a new combination of medicines. The names of the medicines are bedaquiline, linezolid and pretomanid.

Please read this information sheet before you agree for your child to take part. This document will answer the following questions:

If you have any other questions that are not answered in this document, please ask someone from the study staff for more information. Difficult medical terms are marked with an (*) and are explained in the **Glossary** on page <<XX>>.

It is very important that you understand this information sheet before you agree for your child to take part in this study. We would like you to ask as many questions as you need. If there is anything that you do not understand, please discuss this with the study doctor, the study staff, your own doctor or with your family.

Parent or Legal Guardian Notes

1. Is the study safe? 1

The <<name of Ethics Committee as applicable>> and <<name of Regulatory Authority as applicable>> have checked this study and have approved it because it complies with medical and ethical standards.

In addition, the study will be done according to the Declaration of Helsinki 2013, International Conference on Harmonisation-Good Clinical Practice (ICH-GCP) <<and list any other appropriate guidelines e.g. South African GCP Guidelines>>.

One of the purposes of these regulations is to make sure that the rights of people taking part in research studies are protected. If you or your child would like to read any of these guidelines and regulations, please ask your child's study doctor to give you a copy.

2. Does my child have to take part? 2

Your child's participation in this study is totally voluntary (out of free will). Your child may choose not to be in the study or leave the study (withdraw his/her consent) at any time by telling the study doctor.

If you decide not to have your child take part in the study or if your child no longer wants to take part, he/she will not lose any benefits that he/she otherwise would have had. The study doctor will give you a referral letter to take your child to an MDR or XDR-TB unit, TB clinic, or hospital where they will give him/her the standard TB treatment according to your country's National TB Treatment Guidelines.

3. Why is your child doing the study? 3

Your child has been diagnosed with extensively drug resistant pulmonary (i.e. in the lungs) TB (XDR-TB), pre-extensively drug resistant TB (pre-XDR-TB), or Multidrug Resistant TB (MDR-TB). This means that these forms of TB bacteria, or germs, are present in your child's lungs and that these bacteria do not respond to treatment or requires treatment that he/she can't tolerate. These forms of TB can be very hard to treat and medicines must be taken for up to two years or even longer.

It is possible that because people do not take the medicines correctly, TB resistance to these medicines is becoming more common. These forms of resistant TB can be very difficult to treat. New medicines are urgently needed to make the TB treatment time shorter and to treat resistant TB.

A previous study called the Nix-TB study has shown that three medicines called bedaquiline, linezolid and pretomanid taken together may treat your child's type of TB. To date, these medicines have been tested in the laboratory, on animals, on healthy human volunteers, and on over 70 TB participants and have been shown to be possibly effective against XDR-TB and MDR-TB. We want to do this study is to see what dose and length of treatment of linezolid is the most effective in treating your child's type of TB while causing the least amount of side effects. The safety and effectiveness of the following three drugs together: bedaquiline, linezolid and pretomanid will also be tested.

4. How will the study work? 4

About 180 people (called participants) will be taking part in this study. All the participants will be male and female <<14 (update for specific age for each Country/site)>> years old and older. The trial will be conducted globally and it is planned that they will be from approximately 12 research centers around the world, including but not limited to <<Country specific to ICF>> and additional centers in South Africa <<delete South Africa if noted previously in Country specific>>, Eastern Europe and Asia. <<When required by EC, list known targeted countries within the regions>>. We expect that your child will be in this study for about 2 years. The study is split into 3 parts:

Part	Name	Length	Reason
1	Screening	Up to 14 days	During this time, the study doctor checks if your child meets the requirements and if it is safe for him/her to be part of the study. This may be over several visits and take up to 14 days. If your child doesn't meet all of the requirements when he/she is screened, your child may have the opportunity to be screened at a later time if the doctor thinks he/she would be able to meet the requirements then.
2	Treatment	26 weeks or 39 weeks	Your child will receive study medicine for a total of 26 weeks, depending on how he/she responds to the medicines. Your child will visit the hospital/clinic at least 17 times. Some of these visits may be while he/she is a patient in the hospital. If the study doctor determines that your child needs to pause his/her treatment for any reason, then his/her treatment may last longer than 26 weeks. If your child's TB has not been cured after 26 weeks of treatment, the study doctor may decide to extend your child's treatment to a total of 39 weeks.
3	Follow-up	78 weeks	After your child has finished taking the study medicine, the study doctor will check on your child's health for the next 78 weeks. During this time, your child won't be on the study medicine but he/she will visit the hospital/clinic at least 8 times during this part.

If your child's study doctor decides that he/she qualifies to be in this study, and if you and your child agree for him/her to be in this study by signing the consent and assent forms, the following will happen:

Your child will be randomly assigned (purely by chance, like flipping a coin) to receive one of the 4 possible linezolid doses below. This study is partially blinded, which means neither your child nor your child's study doctor will know what dose he/she will receive or how long he/she will receive linezolid. This is done by giving everyone the same number of tablets, some participants receive tablets that look like the linezolid medicine, but do not contain linezolid. These are called placebo. We can only tell you at the end of the study (i.e. when the treatment blind has been broken) to which of the treatments your child was assigned. If there is an emergency and the study doctor needs to know what linezolid treatment your child is receiving, he/she can quickly and easily find this out.

- Linezolid 1200 milligrams (mg) daily for 26 weeks plus linezolid placebo; or

- Linezolid 600 mg daily for 26 weeks plus linezolid placebo; or
- Linezolid 1200 mg daily for 9 weeks plus linezolid placebo, then linezolid placebo for 17 weeks; or
- Linezolid 600 mg daily for 9 weeks plus linezolid placebo then linezolid placebo for 17 weeks.

In addition to linezolid and linezolid placebo, all participants will receive the following:

- bedaquiline 200 mg once daily for 8 weeks then 100 mg once daily for 18 weeks plus;
- pretomanid 200 mg once daily for 26 weeks.

Your child and the study doctor will know how much bedaquiline and pretomanid he/she is receiving.

Pretomanid is a new medicine that has not been approved for the treatment of TB by any Government Regulatory Authority. Bedaquiline has been approved for treatment of MDR-TB in the United States of America and in Europe <<and has been approved by "specific regulatory authority when relevant" for treatment of MDR-TB in "Country">>. Linezolid has been approved around the world to treat many kinds of infections caused by germs. Linezolid is not approved for TB treatment, but it is sometimes used to treat TB patients if other approved medicines do not work. Your child will take 5 whole tablets and one half tablet a day for the first 8 weeks of study treatment. Your child will then take 4 whole tablets and one half tablet a day for the remaining 18 weeks of study treatment.

The study doctor may decide to pause all medication for your child. The study doctor may also decide that your child's linezolid medicine dose needs to be reduced, paused, or just your child's linezolid medicine needs to be stopped. You will know if the study doctor decides to reduce, pause or stop the linezolid. If your child's dose is reduced, neither you nor your child's doctor will know your child's current dose or the dose your child's linezolid medicine is reduced to. If your child's dose of linezolid is reduced anytime during the study, the study doctor may increase your child's linezolid dosage at a later visit, but not higher than the starting dose. Your child will continue to receive the same number of tablets and half tablets, some or all of the tablets with medicine will be replaced with placebos.

Your child will be given study medicines at each visit in the Treatment Period and asked to bring back all empty packets/bottles and unused medicines to his/her next visit.

If for any reason the study doctor decides that all of the study medicine needs to be interrupted, then your child's treatment period may be longer. If your child's TB has not been cured after 26 weeks of treatment, the study doctor may decide to extend your child's treatment to 39 weeks.

5. What will happen to my child in the study?

5

Your child must be willing to follow all study procedures and requirements. For this study to be successful and for his/her own safety, it is important that your child works together fully with the study doctor and follow his/her instructions precisely throughout your child's time in the study.

Depending on your child's reaction to the medicine and study procedures, there may be some slight changes to the treatment visits and procedures, and how long your child will have to stay in the study. This is a list of all the study visits and what will happen at each visit:

	Screening Visits	Treatment Visits																	Post-Treatment Follow-up Visits							
Procedures	Up to 14 days before Treatment	Day 1 (Baseline)	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 10	Week 12	Week 14	Week 16	Week 18	Week 20	Week 23	End of Treatment	4 weeks	8 weeks	12 weeks	26 weeks	39 weeks	52 weeks	65 weeks	78 weeks
Demography	X																									
Medical and smoking history	X																									
Eligibility assessment	X	X																								
Sputum collection	X	X	X	X	X	X		X		X	X	X		X		X	X	X	X	X	X	X	X	X	X	X
Pregnancy Test	X	X								X				X				X								
HIV, CD4 Count and Viral Load	X																									
Blood tests	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X							
ECG	X	X	X			X				X				X				X								
Chest X-Ray	X																									
TB Questionnaire/s	X									X				X				X				X		X		X
Vital Signs	X	X	X	X		X		X		X		X		X		X		X			X	X	X	X	X	X
Physical Exam	X	X	X	X		X		X		X		X		X		X	X	X			X	X	X	X	X	X
Pharmacokinetic (PK) test		X		X						X		X						X								
Eye Exam	X					X				X		X		X		X	X	X	X		X					
Study Medicine check		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X								
Other medicines	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse Events	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

To help understand what will happen at each of your child's visits, we have described these below:

Demography	→	This is personal information about your child's date of birth, gender and race that you will be asked about.
Medical and smoking history	→	You and your child will be asked about your child's medical and smoking history and all other medicines, including over-the-counter, prescription, herbal and traditional medicines your child may have taken in the last 30 days, or are currently still taking.
Eligibility assessment	→	This is a process of checking that your child meets the study requirements to make sure it is safe for him/her to take part.
Sputum collection	→	Your child will be asked to cough up sputum (phlegm) into a small cup at different times in the study. The sputum is used to check if your child has TB, the type of TB your child has, how many TB bacteria your child has and what medicines will work on the TB bacteria. <<*Add as required per country*: If your child has a stored sputum (or TB from his/her sputum) sample (which was collected before this visit) that could be used to allow him/her into this study or check the type of TB and what medication will work on that type of TB bacteria. If you and your child both agree to it, this may be collected from the applicable laboratory and used if you check "yes" at the end of this consent>> The TB germs that have been taken out of your child's sputum will also be sent to laboratories in the United Kingdom (UK) every few months to test how they respond to the study medicines. They may also be used to research new testing methods for TB and/or study medicines. These germs will not contain any material from your child's body; only the TB germs. You/your child will not receive the results from these tests or get any more benefit from these tests being done. The testing could be done for as long as five years after your child take part.

HIV, CD4 count test and Viral load	→	This is a test to see if your child has been infected with HIV and, if he/she has, we will measure your child's CD4 count (a kind of cell that fights infection). You and your child will be counselled on HIV before the blood tests are taken and again once the results are given to you, and you and your child may be asked to sign separate informed consent and assent forms.
Blood tests	→	Blood will be taken from your child by inserting a small needle into a vein in his/her arm. The blood will be tested to check if your child is healthy. Each blood draw is about 20 millilitres (4 teaspoons).
Urine tests	→	Your child will be asked to provide a sample of his/her urine in a small cup when he/she is at the clinic. The urine will be tested to check if your child is healthy. Your child's urine will be tested to see if he/she has taken any drugs like cannabis, cocaine, amphetamines, opiates, benzodiazepines and barbiturates.
Pregnancy test	→	If your child is a girl who is able to have children, your daughter's urine will be tested to see if she is pregnant, whether or not she is sexually active.
ECG	→	A test that is done by placing 12 sensors (like stickers) on your child's skin for a short time to check how his/her heart is working.
Chest X-Ray	→	This is a photograph of your child's lungs.
TB and health questionnaire/s	→	Your child will be asked to tell the study doctor about his/her TB symptoms and general health to check how he/she is feeling.
Physical exam	→	This is an assessment of your child's body to check for signs of disease.
Vital signs	→	A measurement of your child's blood pressure, heart rate, breathing, body temperature, height and weight.
Pharmacokinetic (PK) test	→	Blood will be taken at some visits to check what happens to the medicines once your child swallows them. Blood will be taken from your child by inserting a small needle into a vein in his/her arm. About 20 milliliters (4 teaspoons) of blood will be taken from your child for this test.
Eye exam	→	This is a check of your child's vision by asking him/her to read the letters or symbols off a chart,

		and to read numbers or symbols off cards with coloured patterns on them. There will also be an examination to look at the lens of your child's eyes using a machine that shines a thin beam of light into the eye while the eye doctor looks into it with a type of magnifying glass. To test your child's lens, the eye doctor will need to put a couple of drops of medicine in your child's eyes that will enlarge his/her pupil for a short time. This allows the eye doctor to see easily into your child's eyes. This is the same as what happens to your eyes in the dark.
Study medicine check	→	Your child will be asked how much study medicine he/she has taken or not taken, since the last time he/she was at the clinic.
Hospital admission	→	Your child may need to stay in the hospital if the study doctor considers it safer for him/her.
Hospital check-out	→	The study doctor will tell you when it is safe for your child to not be in hospital all the time. We will record when your child is discharged from the hospital.

If your child is admitted to the hospital, but allowed to go home for the weekend, used/unused medicine should be returned when he/she returns to the hospital.

After your child has stopped or completed the study medicines, the study doctor will decide if your child needs more TB treatment. If he/she does, the study doctor will give you a referral letter for your child to an MDR or XDR-TB unit or hospital. It is very important that your child goes to the hospital as soon as possible and continues anti-TB treatment if the doctor recommends that.

Treatment Extension

If the study doctor decides that your child's treatment should be extended, either due to treatment pause of all of your child's study treatment, or if your child's TB is not cured after 26 weeks of treatment, the following procedures will be performed at additional treatment visits.

	Optional Treatment Extension Visits
Procedures	**Every 3 weeks, for up to a total of 26 or 39 weeks of treatment**
Demography	
Medical and smoking history	
Eligibility assessment	

Sputum collection	X
Pregnancy Test	
CD4 Count	X
Blood tests	X
ECG	
Chest X-Ray	
TB Questionnaire/s	
Vital Signs	X
Physical Exam	X
Pharmacokinetic (PK) test	
Eye Exam	X
Nerve Exam	X
Study Medicine check	X
Other medicines	X
Adverse Events	X

Early Withdrawal

If your child decides of his/her own free will, or your child's study doctor decides he/she should stop treatment or withdraw from the study before he/she has finished the above visits, the procedures listed below may be performed at an Early Withdrawal Visit. If your child received more than 15 doses of the study medication and has not had his/her 12 week follow-up visit when he/she is withdrawn from the study, we will request your child to come back for 1 more visit at the clinic so we can monitor his/her health, and your child will be contacted 2 more times for a visit that can take place at the clinic, your child's home or on the phone with your child's study doctor where the following procedures may be performed.

	Early Withdrawal During Treatment Period			
Procedures	**Early Withdrawal Visit During Treatment**	**Follow-up Week 12**	**Follow-up Week 26**	**Follow-up Week 78**
Demography				
Medical and smoking history				
Eligibility assessment				
Sputum collection	X			
Pregnancy Test	X			
CD4 Count	X			
Blood tests	X			
ECG	X			
Chest X-Ray				
TB Questionnaire/s	X			
Vital Signs	X			
Physical Exam	X			

Pharmacokinetic (PK) test	X			
Eye Exam	X	X		
Nerve Exam	X			
Study Medicine check	X			
Other medicines	X	X		
Adverse Events	X	X	X	X
Survival/TB outcome			X	X

If your child hasn't had all of his/her follow-up visits when he/she is withdrawn from the study, we may request that your child come back for 1 more visit at the clinic so we can monitor his/her health as well.

	Early Withdrawal During Follow-up Period			
Procedures	**Early Withdrawal Visit During Follow-up**	**Follow-up Week 12 (If applicable)**	**Follow-up Week 26 (if applicable)**	**Follow-up Week 78**
Demography				
Medical and smoking history				
Eligibility assessment				
Sputum collection	X			
Pregnancy Test	X			
CD4 Count				
Blood tests	X			
ECG	X			
Chest X-Ray				
TB Questionnaire/s	X			
Vital Signs	X			
Physical Exam	X			
Pharmacokinetic (PK) test	X			
Eye Exam	X	X		
Nerve Exam	X			
Study Medicine check	X			
Other medicines	X	X		
Adverse Events	X	X	X	X
Survival/TB outcome			X	X

If the study doctor feels it is necessary, you may be asked to come in for extra (unscheduled) visits that do not appear on the above charts.

6. What can go wrong in the study? 6

There are some possible risks and inconveniences of being in the study.

Tuberculosis is a serious disease that can be deadly; all combinations of medicines used together in treatment plans to treat tuberculosis have rarely been associated with serious side effects, including death.

Your child should **not drink alcohol** while he/she is taking study medicine or other TB medicines as alcohol may damage his/her liver.
You should tell the doctor if your child has **heart problems**, including a slow heart rate, or if your child has low thyroid hormone levels.
Your child will have ECGs from time to time to monitor the electrical activity of his/her heart, including the QT interval.

Details of the risks of taking the medicines in this study are noted below:

Liver problems	→	May be associated with symptoms such as nausea or vomiting, stomach pain, fever, weakness, itching, unusual tiredness, loss of appetite, light coloured bowel movements, dark coloured urine, yellowing of your skin or the white of your eyes. Liver problems may also be suggested by blood tests that show abnormalities in measures of your liver enzymes and other measures of how your liver is working. In rare cases liver problems may be serious and even lead to death.	Pretomanid, Linezolid, Bedaquiline,
Headache	→	pain in any part of the head	Pretomanid, Linezolid, Bedaquiline,
Stomach problems	→	Tenderness or pain of the stomach area Feeling like you want to throw up, or actually throwing up. Also not feeling hungry, having diarrhoea (loose bowel movements) or having an upset stomach.	Linezolid, Pretomanid, Bedaquiline
Dizziness	→	A feeling of being 'drunk' or 'light headed', especially when you stand up or sit down quickly.	Linezolid, Bedaquiline

The following are a list and description of side effects that are unique to each of the medicines:

Pretomanid

Besides the side effects mentioned above, the other side effects include:

Reproductive organ changes	→	Results from animal studies have shown that rats given pretomanid showed signs of damage to the male rats' reproductive organs. Recent studies in people have shown that there is no evidence that pretomanid damages the male reproductive organs. The potential for pretomanid to have an effect on the male reproductive organs will remain under evaluation.
Cataracts (clouding of the lens in the eye)	→	Other results from animal studies show that rats given Pretomanid developed cataracts at high doses over a 6-month period of taking the medicine. It is not known if the effect found in rats indicates any risk for human beings.
Fits (convulsions or seizures)	→	were seen in some animal studies and in 1 patient treated with Pretomanid
Skin problems	→	Inflamed areas on your skin, which may be red, itchy and/or painful.

Linezolid

Besides the side effects mentioned above, the other **most common** side effects seen in patients who took linezolid are:

Changes in taste	→	certain food or drinks may taste different to you
Tongue discolouration	→	the colour of your tongue changes
Fungal infections	→	when a fungus causes the infection
Vaginal moniliasis	→	a fungal infection in the vagina
Oral moniliasis	→	a fungal infection in the mouth

Fever	→	When your body temperature goes higher than 38 °C or 100.4 °F.
Signs of nerve disturbances	→	This is sometimes called 'peripheral neuropathy', which may be experienced as a painful burning, or stinging, tingling, sensation of pins and needles or numbness in your arms and legs. In some cases this can be permanent.
Convulsions or seizures	→	These are also commonly known as 'fits'. A **convulsion** is when the body muscles contract and relax quickly and repeatedly / uncontrolled shaking of the body. A **seizure** is when there is a change in the normal electrical activity of the brain.

Other side effects seen in patients who took linezolid include, but are not limited to:

Myelo-suppression	→	a lack of certain cells in your blood that your body needs to function. can make you feel tired and make your body being unable to fight off other illnesses or heal an injury. This could also make you bleed or bruise easily.
Lactic acidosis	→	a build-up of waste products in your blood that can cause constant nausea and vomiting.
Serotonin syndrome	→	this rare but serious condition may occur when linezolid is given with certain types of medications that affect a chemical in the brain called serotonin. Some of these medications include antidepressants. Be sure to tell your study doctor about all prescription and non-prescription medications you are taking.

		It can cause many different symptoms, for example: confusion, restlessness, tremors, blushing, sweating and fever.
Interactions with other medicines	→	causing a rise in blood pressure
Optic neuropathy	→	A type of damage to the nerves in your eye that can lead to blindness if it is not treated. This can be permanent.
Low blood sugar	→	This is often seen in patients with diabetes who have to take insulin or other medicines

Bedaquiline

From studies in 380 patients with TB who received Bedaquiline (312 of whom received Bedaquiline for as long as 6 months), we continued to see that Bedaquiline is generally safe and well tolerated. Besides the side effects mentioned above, the other **most common** side effects seen in patients who took bedaquiline are:

Serious side effects	→	9 out of 79 patients (11%) taking bedaquiline with other TB medicines died, versus 2 out of 81 (3%) taking just the other TB medicines and no bedaquiline. It is not known why more patients in the bedaquiline group died.
QTc interval increase	→	An increase in the measure of the heart's electrical activity. This was seen on the electrocardiogram in patients taking bedaquiline and in those taking other TB drugs. This may increase the risk that the heart does not beat in its normal, regular rhythm, which in rare cases cause death. However, no clinical side effects relating to heart rhythm problems were seen.

Effects on the pancreas		Studies in mice and dogs showed that bedaquiline caused damage to the pancreas. It is not known if the effect found in mice and dogs indicates any risk for humans.
Joint pain	→	One type of joint pain that may be caused or worsened by some medicines is called gout. Gout is caused by too much of a normal chemical in your body called uric acid. Uric acid is a chemical that is created when the body breaks down substances called purines. Purines are found in some foods (like seafood) and drinks (like beer).
Accumulation in the body	→	Bedaquiline leaves your body slowly after the last tablet is taken. It takes about a year for all the drug to be removed from your body.

In addition to the listed side effects, the study doctor has information on side effects that may occur less often and the study doctor could discuss these with you and your child.

Possible risks and side effects of procedures to be performed:

- Drawing blood is normally done as part of normal medical care. There is a slight risk of discomfort. Drawing blood may rarely cause fainting, inflammation of the vein, pain, bruising or bleeding at the place on the skin where the needle goes in. There is also a slight risk of infection. Your child's protection is that experienced staff will draw his/her blood under germ free conditions.
- When an ECG is done, the sensors, or stickers, may cause slight discomfort when they are removed from your child's skin.
- An x-ray is a common test exposing a person to a small amount of radiation. The effect of radiation adds up over your lifetime, but small doses like the one used to take a picture of your child's chest, is not likely to be a risk to your child's health.
- The eye tests are common. The drops put into your child's eyes will cause his/her vision to be blurry and sensitive to light for a few hours after the examination, during which time your child should not drive (if applicable). In very rare cases they can cause increased pressure in the eye, with nausea and pain. If this happens, call the study doctor right away.

It is important that your child follows the study doctor's and/or study nurses' instructions precisely.

You and/or your child must inform the study doctor immediately if:

- your child takes any local or herbal remedies, prescribed or non-prescribed (over the counter) medicines,
- your child's medical condition changes,
- your child has seen any other healthcare providers,
- your child has any side effects,
- your child has any complications*, or
- your child has any injuries while taking the study medicine.

The study doctor and/or nurse will ask your child at every visit about any other medicine he/she may have taken and how he/she is feeling.

It is possible that your child's condition will stay the same or get worse while he/she is in this study. However, the study doctor will watch your child closely and if he/she feels that participating in the study is not good for your child's health, he/she will immediately take your child off the study.

Using the study medicine may have risks that we do not know about yet. If we become aware of these, we will tell you and your child of any new important findings that may influence his/her willingness to stay in the study.

7. Are there things that my child cannot do while he/she is in the study? 7

Your child cannot take part in this study if she is breastfeeding, pregnant or trying to get pregnant.

This is because there may be risks to becoming pregnant and to an unborn child that we may not yet know of. If your daughter is participating in the study and can get pregnant, we will test her before she takes the study medicine and during the study to see if she is pregnant.

Girl participants who CAN become pregnant:

Your daughter must use 2 methods of birth control. Your daughter need to use birth control for as long as she is taking the study medicine and for up to 6 months after she has taken the last dose of study medicine.

When taking the study medicine, birth control that are based on hormones only, such as the contraceptive pill or injection, may not work as well as usual. Because of

this, either your daughter must be willing not to have sex, or she must use 2 methods of birth control, for example:

a) Double (2 different types) barrier methods, which may include a male condom, diaphragm, cervical cap, or female condom; OR
b) 1 barrier method described above used together with a hormone-based birth control (tablet or injection), or an intra-uterine device

If your daughter becomes pregnant while she is participating in the study, it is very important for you and your daughter to tell the study doctor immediately. If this happens, the study doctor will discuss with you and your daughter what to do.

Since there might be unknown risks to an unborn child, we will ask your child to stop taking part in the study. We may have questions about your daughter's pregnancy and the baby and we may ask your daughter to visit the study doctor at certain times during and after your daughter's pregnancy to check her health status and collect information on the outcome of her pregnancy.

Boy participants' female sex partner who CAN become pregnant:

Your son and his female sex partner need to use at least 1 method of birth control for as long as he is taking the study medicine and for up to 12 weeks after he has taken the last dose of study medicine. Examples of methods of birth control are as follows:

Double barrier (2 different types) method, which can include a male condom, diaphragm, cervical cap, or female condom; OR

Hormone-based contraceptives, or an intra-uterine device for son's your female partner.

Talk to the study doctor if your child is unable to obtain birth control. The study doctor may be able to advise your child about the correct birth control.

Girl participants, and boy participants' female sex partner, who CANNOT become pregnant:

Your child does do not need to use birth control if he/she is:

a) Not an active heterosexual boy or girl participant, or he/she does not practice sex; OR
b) A girl participant or boy participants' female sex partner, and have had an operation to remove both ovaries, or both ovarian tubes have been tied or cut and or the uterus has been removed; OR

c) A boy participant or girl participants' male sex partner, who has had both testes tubes tied or cut, or have had both testes removed at least 3 months before the study.

Foods and drinks that your child cannot eat or drink during the study

- Your child should not eat or drink large amounts of foods or drinks that contain a lot of a protein called tyramine. Foods high in tyramine include those that may have had protein changes by aging, fermentation, pickling, or smoking to improve flavour. This include foods such as aged cheeses, fermented or air-dried meats (cold cuts and biltong), sauerkraut, soy sauce, tap beers and red wines. You and your child should talk to the study doctor if either of you have questions about how your child can avoid large amounts of tyramine.
- Your child should not drink alcohol while he/she is taking study medicine as alcohol may damage his/her liver.

Other medicines that your child cannot use

- Your child cannot use certain medicines to treat depression while he/she is on the study medicine. There are other medicines that your child cannot use while he/she is on the study medicine because they may possibly cause abnormal heart rhythms, or because they may change the way your child's body reacts to the study medicine after he/she takes them. The study doctor can tell you and your child which medicines these are.
- If your child is HIV positive, certain HIV medicines should not be used. The study doctor can tell you and your child which HIV medicines can be used during this study.
- You/your child should inform the study doctor if your child is taking any illegal drugs, because some illegal drugs can affect your child's safety or your child's ability to follow through with all the study procedures.

8. How can the study help my child? 8

There is a chance that your child's TB may get better because he/she is in this study, but we cannot guarantee this. If the study medicine does not work well, your child will not get any benefit from being in the study. However, the information that we get from the study can help in making future treatments for TB, and in the long run it will likely help other TB patients.

The close medical attention your child will get by taking part in the study may help you and your child to learn useful information about his/her health status.

9. What are my child's other choices for treatment? 9

Your child does not have to take part in this study. If your child decides not to take part, he/she will not be disadvantaged and he/she will still receive care and treatment for his/her TB at <<TB clinic or specialized unit in a hospitalist location>> for at least <<add time period>>, per your country's National TB Treatment Guidelines.

If your child does not take part in the study, the doctor will make sure your child remain in or is sent to an MDR-TB unit or XDR-TB unit or hospital for treatment.

10. What will happen if I my child is injured in the study? 10

<< For ABPI Countries:

The sponsor has taken out insurance in case you get injured in this study.
The sponsor will pay you for all reasonable medical expenses you may have because you are injured in this study, according to the guidelines of the Association of the British Pharmaceutical Industry (ABPI guidelines). These guidelines recommend that the sponsor of the study, without any legal commitment, should pay you, without you having to prove that it is at fault, for any injury resulting from giving the study medicine or other procedures carried out in accordance with the protocol for this study. Your study doctor has a copy of the ABPI guidelines if you would like to see them.

The APBI guidelines do not require the sponsor to pay you if the injury:

- resulted from a medicine or procedure that is not required by the study or if you did not stick to the rules of the study;
- was not a serious injury that will last a long time and disable you.

Because of the following reasons, you may be paid less or the sponsor may not have to pay you at all under the ABPI Guidelines:

- how serious the disease is that is being treated, how likely you are to have adverse reactions and any warnings that were given to you;
- the risks and benefits of normal or standard treatments compared to the risks and benefits that we know the study medicine have or think that it may have;
- a wrongful act of someone outside the study, or if the study doctor does not properly deal with an adverse reaction;
- if you have been negligent.

Any payment that the sponsor makes to you because of the ABPI guidelines does not mean that the sponsor is legally responsible for your injury. You will not lose any of the legal rights you have if you are injured just because the sponsor has agreed to follow the ABPI guidelines. Please ask if you want more information on this.>>

*<<Country regulatory authorities that **DO NOT require compliance to the ABPI clinical trial insurance guidelines**,*

Text will be provided on an 'as needed' basis in consultation with TB Alliance Legal.>>

11. What will happen to my child's personal information? 11

All records with information that can identify your child will be kept confidential and, as far as the applicable laws and regulations allow, will not be made publicly available.

The study doctor and research team will use personal information about your child to carry out this study. This may include your child's name, address, medical history and information from your child's study visits. However, this personal information will stay at the study site and will not be included in the study data that we will send to the sponsor or representatives of the sponsor. Your child will only be identified by a coded number in reports or publications that are produced from this study (study data).

To confirm that the study data collected about your child is correct and related to him/her, selected people working for the sponsor, including auditors, as well as representatives of government regulatory authorities and ethics committees will have access to your child's personal information at the study site. These persons know that they must keep your child's information confidential. By signing this document, you are agreeing to let them have access to your child's information.

The sponsor may send your child's coded study data that were collected from your child's country to other countries. *<<EU: "Your child's data might be transferred to countries outside the EU".>>* However, they will obey all local and international laws and regulations on data privacy to protect your child's personal and other information, even in countries where data privacy laws are less strict.

The sponsor or representatives may use this study data for the following purposes:

- To see if the study medicine works and is safe.
- To compare the study medicine to other medicines.
- For other activities related to the study medicine.

You and your child have the right to ask the study doctor about the data we are collecting about your child. Your child can ask the study doctor to allow him/her to see your child's personal information and your child can ask the study doctor to make any corrections, if needed.

The results of the study will only be available once all participants have completed the study, the information has been collected and checked, and the results have been analysed (looked at and a decision made about them). If your child wants to know the results of the study, he/she may contact the study doctor and the study doctor will tell your child the results if they are ready.

The results of this study will be made available to national and international medicine regulatory agencies to help them decide if the new treatments are helping to treat TB. In addition, the results may be published in international medical journals so that doctors and other health workers might learn from this work. Your child will not be named in any reports/publications.

A description of this clinical study will be available on www.clinicaltrials.gov, as required by United States law << and other countries as required, e.g. www.sanctr.gov.za, as required by South African law>>. This <these>> website<<s>> will not show information that can identify your child. At most, the website<<s>> will include a summary of the results. You and your child can search this website<<these>> at any time.

12. Will my child be paid to take part in this study? 12

Your child will **not** be paid to take part in this study. However, the sponsor will pay you/your child back for out-of-pocket expenses, such as for your child's transport to and from the study site and other various costs that your child may have because of his/her study participation.

You/your child will get, depending on the out-of-pocket expenses, an amount of - *<<specify amount and frequency e.g. x per visit and add any pro-rata payments if applicable>>*. If your child's study-related costs are more than the specified amount and you have proof of such costs, please discuss it with the study doctor.

13. Do I need to pay anything for my child to be in this study? 13

The sponsor will pay all costs related to the study, such as the study medicine, treatment, tests, examinations and procedures specified in the study plan. Not you, nor your and/or your child's <<medical insurance / aid>>, healthcare provider will have to pay for these expenses. In other words, you will not have to pay for anything that is needed for your child's participation in this study.

Should your child need to visit any doctor, besides the study doctor, or if your child is hospitalised for any illness, including to treat his/her TB, then your child will need to visit the doctor or hospital as allowed by your/ your child's healthcare provider <<or medical insurance / aid>>. These medical visits, that are not part of the clinical study, are not paid for by the study.

14. Who is in charge of the study? 14

The study is sponsored by the Global Alliance for TB Drug Development (TB Alliance), a not-for-profit organisation based in New York in the United States.
The TB Alliance will pay the study staff for doing this study. The study doctor will not benefit unduly if your child is included in the study.

15. What happens if my child does not want to or cannot be in the study any more? 15

Your child's participation in the study may be stopped for the following reasons:

- Testing comes back that shows your child's TB won't respond to the study medicines
- If your child does not follow the study doctor's instructions.
- If your child does not take the study medicine as prescribed.
- Testing comes back that shows your child's TB will respond to medicines that treat drug sensitive TB.
- If the study doctor decides that it is in your child's best interests (e.g. your child experiences certain adverse events* during the study).
- If your child asks to stop (your child doesn't have to explain why).
- If the TB Alliance asks your child to stop.
- If the TB Alliance stops the study or closes the study site.
- If your child becomes pregnant (girls who can get pregnant).

If your child decides to withdraw from the study, please tell us immediately. If your child withdraws from the study, it will not change his/her access to other medical care or the quality of the care.

If your child leaves the study, the doctor would like to ask him/her some questions and check his/her health to make sure that your child is safe and any possible side effects from the study medicine are treated. If your child's study treatment is stopped, based on your/your child's and your child's study doctor's choice, your child will be asked to continue to come to some of the study visits or be contacted in another way, unless your child decides to withdraw from the study completely. If your child's treatment is stopped or he/she withdraws from the study completely, your study doctor/site staff may need to perform certain procedures previously mentioned in the "**5. What will happen to my child in the study?**" section.

We may ask your child to come to the hospital/study site to complete these procedures.

Once your child has left the study, the study doctor will give you a referral letter for your child to go to an MDR or XDR-TB unit or hospital for further treatment of his/her TB or to another physician for routine medical care if your TB infection is cured.

16. Whom can I contact if something worries me or my child? 16

You can call the study doctor or another authorised person at the study site at any time of the day or night (24 hours) on Tel: **<<*add*>>** or **<<*add*>>**.	

For questions about <u>your child's rights</u> as a participant in a study:

If you or your child wants any information about your child's rights as a study participant, or if you or your child has complaints about this study, you may contact the <<add name of Ethics Committee>>, which is an independent committee established to help protect the rights of research participants. Their contact details are as follows:

<<Add name, address and contact telephone/fax numbers>>

For <u>complaints</u>, if you or your child thinks that the study doctor or ethics committee did not help him/her:

<<include per country as appropriate>>

17. How do I agree for my child to be in this study? 17

If your child wants to take part in this study and you agree, please read the consent statement and sign on page <<XX>>.

<u>Personal doctor / specialist notification option:</u>

Please mark below, by writing your initials in the correct block, if you want us to tell your child's personal doctor or his/her specialist that your child is taking part in this study:

☐ **YES**, I want the study doctor to tell my child's personal doctor / specialist that he/she is taking part in this study.

☐ **NO**, I do not want the study doctor to tell my child's personal doctor / specialist that he/she is taking part in this study.

☐ **My child does not have** a personal doctor / specialist.

Collection of Pre-screening Stored Sputum (or TB from your child's sputum) Sample agreement:

Please mark below, by writing your initials in the correct block, if you agree for your child's stored sputum sample (taken before this visit/reading and signing this form) to be collected from the storing laboratory:

☐ **YES**, I agree if available, for my child's stored sputum sample or TB from your child's sputum to be collected from the laboratory and used for this study.

☐ **NO**, I do not want my child's stored sputum sample or TB from your child's sputum to be collected from the laboratory and used for this study.

Parent or Legal Guardian Notes

Glossary

Technical term	Explanation
complications	another disease or condition that makes your TB worse
diaphragm	a soft latex or silicone dome with a spring in the rim. The spring creates a seal against the wall of the vagina.
adverse events	unwanted events

PARENT/LEGAL GUARDIAN INFORMED CONSENT FORM

By signing below, I agree that:

- I have read the information sheet and consent form for this study, or someone has read it to me, and I understand it.
- I have had the chance to ask questions and I am happy with the answers.
- I have had time to discuss the information with others and to decide if I want my child to take part.
- I will get a signed and dated copy of this consent form on the day that I sign it.
- I agree of my own free will to let my child take part in this study. I know my child has the right to stop taking part at any time, without giving any reason. If my child stops taking part, it will not change his/her medical care or legal rights.
- Site staff, representatives from the sponsor, including auditors, regulatory authorities and ethics committees can have direct access to my child's medical records. They will treat my child's information as confidential.
- If my child withdraws from the study, study data collected about him/her up to the point of his/her withdrawal can still be used to carry out this study.
- Girls only: "if my child becomes pregnant while on the study, follow-up information on the outcome of my child's pregnancy can be collected, if needed."
  <<EU: "I consent to the processing/storing of my data and the transfer thereof to countries outside the EU.">>

Printed Name of Parent/Legal Guardian

Signature/mark/thumb print of Parent/Legal Guardian

Date

(Parent or Legal Guardian/witness must write date)

*Printed Name of Person Conducting Consent
(If other than investigator/delegate)

*Signature of Person Conducting Consent
(If other than investigator/delegate)

Date

(Person conducting consent must write date)

I, _____ (Insert name of investigator) hereby confirm that the above Parent or Legal Guardian has been fully informed about the nature, conduct and risks of the above study.

_____ _____

Signature of Investigator Date

(Investigator must write date)

By signing below, I verify that the above Parent or Legal Guardian gave verbal informed consent. The Parent or Legal Guardian has been informed about the risks and the benefits of the study, understands such risks and benefits and is able to agree to participation, without coercion, undue influence or inappropriate incentives.

_____

*Printed Name of Witness

_____ _____

*Signature of Witness Date

(Witness must write date)

* Where applicable

PAEDIATRIC INFORMATION AND INFORMED ASSENT FORM
TESTING FOR HIV

Protocol Name/Number: ZeNix/NC-007-(B-Pa-L)
Protocol Title: A Phase 3 partially-blinded, randomised trial assessing the safety and efficacy of various doses and treatment durations of linezolid plus bedaquiline and pretomanid in participants with pulmonary infection of either extensively drug-resistant tuberculosis (XDR-TB), pre-XDR-TB or treatment intolerant or non-responsive multi-drug resistant tuberculosis (MDR-TB).

Participant Initials:_____ Participant Number:_____

Introduction

This information sheet contains only information about testing for HIV in the study. Please read the **main assent form** that you have already signed for information about the **main medical study**.

Please read this information sheet before you agree to have the HIV test done as part of the main study. This document will answer the following questions:

If you have any other questions that are not answered in this document, please ask someone from the study staff for more information. We explained some difficult medical terms in the **Glossary** on page <<XX>>.

It is very important that you understand this information sheet before you agree to have your HIV test done. We would like you to ask as many questions as you need. If there is anything that you do not understand, please discuss this with the study doctor, the study staff, your own doctor, or with your family.

Participant Notes

1. What is HIV? 1

The human immunodeficiency virus (HIV) is a virus that causes Acquired Immunodeficiency Syndrome (AIDS). This is a condition in humans where the system that protects the body against getting sick (the immune system), stops working. This means that other infections can get worse. Normally, the immune system will help the body to fight against these infections so that you don't get sick. These infections can be life-threatening and are called opportunistic infections*.

How is HIV spread?

Infection with HIV happens when you come into contact with blood, semen or another similar fluid, vaginal fluid or breastmilk which have HIV in (from a person who has HIV). The 3 most common ways of getting HIV are:

- having sex without a condom,
- sharing needles, and
- when a mother who has HIV gives birth, or if she breastfeeds her baby.

How does HIV affect my body?

HIV mainly infects cells in the immune system* that are called CD4 cells, and it causes the number of CD4 cells to drop. When the number of CD4 cells drop below a certain amount, your body can no longer fight infection, and opportunistic infections may increase.

How is HIV treated?

If people who have HIV do not get treatment, most of them will get AIDS and die. However, about 1 in 10 people stay healthy for many years, with no obvious

symptoms. People with HIV are treated with anti-retrovirals* (i.e. the medications used to fight the virus that causes HIV). Using anti-retroviral medicine can help people to live longer.

2. Why are you testing me for HIV? 2

This study has nothing to with HIV/AIDS or its treatment. However, we need to test you for HIV as part of the study, because it may be unsafe for you to take part in the study if:

- your CD4 count is lower than a certain number (<100 cells/µL)
- you have had an existing TB and HIV diagnosis, you are taking HIV medicine and your viral load ("viral load" is a term that people living with HIV use to talk about how much of the virus is in their body) is higher than a certain number (>1000 copies/mL)
- you are diagnosed with tuberculosis and HIV and your study doctor recommends that the start of your HIV medicine should not be postponed until you have received at least 2 weeks of an anti-tuberculosis regimen and/or;
- you are currently receiving HIV medicine which cannot safely be taken with the study medicine and your study doctor decides it is not best for you to change your HIV medicine.

You can take part in the study if you meet the other requirements for the study and if you test positive for HIV, ***and***

- your CD4 count is equal to or more than a certain number (≥ 100 cells/µL)
- if you have previously been diagnosed with TB and your viral load is <1000 copies/mL
- you have a new TB and HIV diagnosis
- you are diagnosed with tuberculosis and HIV and your Study Doctor agrees that the start of your HIV medicine may be postponed until you have received at least 2 weeks of an anti-tuberculosis regimen
- HIV medicine that you will take during the study is safe to be taken with the study medicine;

OR if you are HIV negative.

3. How will you do the HIV test? 3

We will take an extra blood sample of 5 ml (about 1 teaspoon) in the main study. We will take this extra blood sample at the same time as the routine blood samples in the clinical part of the study. It will not be necessary to prick you with a needle again.

4. What can go wrong with the HIV test? 4

The risk when we take a blood sample includes discomfort where we prick you with the needle. You may get a bruise, bleed, and very rarely, you could get an infection, or you may faint.

The following unpleasant things may happen if you have an HIV test (especially if the result is that you are HIV positive):

- Friends, family and other students may reject you and discriminate against you.
- You may have emotional problems, feel more stressed and feel uncertain about the future.

5. How can the HIV test help me? 5

If you test negative, you may feel less worried after knowing your HIV status, and you could take steps to stop yourself from getting HIV. If you know you are HIV positive, it may reduce the stress that you get because of not knowing. You can treat your HIV early, and check your health, by eating well and healthily. You will also know if you can infect others, and what to do to stop this from happening.
Women who are thinking about getting pregnant and their partners can get treatments that can help to prevent their baby from getting HIV. You can also plan how to care for your children in the future.

6. What happens if I get hurt during the HIV test? 6

The insurance that the TB Alliance has taken out as required by the laws and regulations of your country covers the extra blood samples. For more details, see the information sheet describing the **main clinical study**.

7. Will you keep my HIV test private? 7

We will respect your confidentiality* and only the study doctor and the research team will know the results of the test. Some people working for TB Alliance, as well as representatives of government regulatory authorities and ethics committees will also be able to see the results. These persons know that they must keep your information private. You are giving permission for those people to see your medical records when you sign this document.

8. Will you pay me to do the HIV test? 8

No, we will not pay you for giving the blood sample to do the HIV test.
The TB Alliance or the study site will not be responsible for paying any costs for your HIV treatment if you test positive. We will send you to a specialist HIV clinic for further testing and advice.

9. Will I have to pay for the HIV test? 9

No, the HIV test will not cost you anything,
<<If applicable add "You will receive HIV counseling before and after HIV test. The TB Alliance will pay for the test and the counseling."

10. Who can I contact if something worries me? 10

You can call the study doctor or another authorised person at any time of the day or night (24 hours) on Tel: **<<add>>** or **<<add>>**.	

Please refer to the **main informed consent form** for more information on whom to contact if you have complaints about this study.

11. How do I agree to have the HIV test? 11

If you want to agree to have the HIV test, please read the statement on the following page and sign the form.

Participant Notes

Glossary

Technical term	Explanation
HIV	Human immunodeficiency virus
AIDS	Acquired immune deficiency syndrome
opportunistic infections	an infection that occurs when the immune system is weak
immune system	the system in your body that fights infections
pulmonary	of the lungs
confidentiality	a set of rules to keep information private

PAEDIATRIC INFORMED ASSENT FORM FOR HIV TESTING

By signing below, I agree that:

- I have read the information sheet and consent form for this HIV testing, or someone has read it to me, and I understand it.
- I have had the chance to ask questions and I am happy with the answers.
- I have had time to discuss the information with others and to decide if I want to do the test.
- I will get a signed and dated copy of this consent form on the day that I sign it.
- I voluntarily agree for HIV testing to be done.
- Site staff, representatives from the sponsor, regulatory authorities and ethics committees can have direct access to my medical records. They will treat my information as confidential.
- I hereby give up all rights to the test findings and I am not entitled to be paid anything because of the test findings.
- <<EU: "I consent to the processing/storing of my data and the transfer thereof to countries outside the EU.">>

_____
Printed Name of Participant

_____ _____
Signature/mark/thumb print of Participant Date
(Participant/witness must write date)

_____
*Printed Name of Person Conducting Consent
(If other than investigator / delegate)

_____ _____
*Signature of Person Conducting Consent Date
(If other than investigator / delegate)

(Person conducting consent must write date)

I, _____ (Insert name of investigator) hereby confirm that the above participant has been fully informed about the nature, conduct and risks of the HIV test.

Signature of Investigator

Date
(Investigator must write date)

By signing below, I verify that the above participant gave verbal informed consent. The Participant has been informed about the risks and the benefits of the HIV test, understands such risks and benefits and is able to agree to have the HIV test, without coercion, undue influence or inappropriate incentives.

*Printed Name of Witness

*Signature of Witness

Date
(Witness must write date)

* Where applicable

PARENT OR LEGAL GUARDIAN INFORMATION AND INFORMED CONSENT FORM TESTING FOR HIV

Protocol Name/Number: ZeNix/NC-007-(B-Pa-L)
Protocol Title: A Phase 3 partially-blinded, randomized trial assessing the safety and efficacy of various doses and treatment durations of linezolid plus bedaquiline and pretomanid in participants with pulmonary infection of either extensively drug-resistant tuberculosis (XDR-TB), pre-XDR-TB or treatment intolerant or non-responsive multi-drug resistant tuberculosis (MDR-TB).

Participant Initials:_____ Participant Number:_____

Introduction

This information sheet contains only information about testing your child for HIV in the study. Please read the **main Parent or Legal Guardian consent form** that you have already signed for information about the **main clinical study**.

Please read this information sheet before you agree to have your child's HIV test done as part of the main study. This document will answer the following questions:

If you have any other questions that are not answered in this document, please ask someone from the study staff for more information. We explained some difficult medical terms in the **Glossary** on page <<XX>>.

It is very important that you understand this information sheet before you agree for your child to have his/her HIV test done. We would like you to ask as many questions as you need. If there is anything that you do not understand, please discuss this with the study doctor, the study staff, your own doctor, or with your family.

Parent or Legal Guardian Notes

1. What is HIV? 1

The human immunodeficiency virus (HIV) is a virus that causes acquired immunodeficiency syndrome (AIDS). This is a condition in humans where the system that protects the body against diseases (immune system), begins to fail. This leads to other infections, which the body would normally be able to fight, being able to grow and thrive. These infections can be life-threatening and are known as opportunistic infections*.

How is HIV spread?

Infection with HIV occurs by the transfer of blood, semen or other similar fluid, vaginal fluid, or breastmilk in which HIV is present. The three major ways of getting HIV are:

- having sex without a condom,
- sharing needles, and
- a mother with HIV gives birth, or if she breastfeeds her baby.

How does HIV affect my body?

HIV mainly infects cells in the immune system*, called CD4 cells, and causes the number of CD4 cells to drop. When the number of CD4 cells drop below a certain amount, the body can no longer fight infection, and opportunistic infections may increase.

How is HIV treated?

If left untreated, most people who are HIV positive will get AIDS and die. However, about 1 in 10 people remain healthy for many years, with no obvious symptoms. People with HIV are treated with anti-retrovirals (i.e. the medications used to fight the HIV virus). Using anti-retroviral medicine may help people to live longer.

2. Why are you testing my child for HIV? 2

This study has nothing to with HIV/AIDS or its treatment. However, we need to test your child for HIV as part of the study, and it may be unsafe for your child to take part in the study if:

- your child's CD4 count is lower than a certain number (<100 cells/µL)
- your child has an existing TB and HIV diagnosis, your child is taking HIV medicine and your child's viral load ("viral load" is a term that people living with HIV use to talk about how much of the virus is in their body) is higher than a certain number (>1000 copies/mL)
- your child diagnosed with tuberculosis and HIV and your child's study doctor recommends that the start of his/her HIV medicine should not be postponed until your child has received at least 2 weeks of an anti-tuberculosis regimen and/or;
- your child is currently receiving HIV medicine which cannot safely be taken with the study medicine and the study doctor decides it is not best for your child to change his/her HIV medicine.

Your child can take part in the study if he/she meets the other criteria for the study and if your child tests positive for HIV, ***and***

- your child's CD4 count is equal to or more than a certain number (≥ 100 cells/µL)
- if your child had previously been diagnosed with TB and your child's viral load is <1000 copies/mL
- your child has a new TB and HIV diagnosis
- your child is diagnosed with tuberculosis and HIV and your child's Study Doctor agrees that the start of his/her HIV medicine may be postponed until he/she has received at least 2 weeks of an anti-tuberculosis regimen. HIV medicine that your child will take during the study is safe to be taken with the study medicine;

OR if your child is HIV negative.

3. How will you do the HIV test? 3

We will take an extra blood sample of 5 ml (about 1 teaspoon) in the main study. This extra blood sample will be taken at the same time as the routine blood samples in the clinical part of the study. It will not be necessary to prick your child with a needle again.

4. What can go wrong with the HIV test? 4

The risk when we take a blood sample includes discomfort where we prick your child with the needle or your child may have a bruise, bleed, and only rarely, get an infection, or faint.

The following negative things may happen if your child has an HIV test (especially if the result is that he/she is HIV positive):

- friends, family and colleagues may possibly reject your child and discriminate against him/her;
- your child may have emotional problems, feel more stressed and feel uncertain about the future.

5. How can the HIV test help my child? 5

If your child tests negative, he/she may feel less worried after knowing their HIV status, and take steps to prevent him-/herself from getting HIV. If your child knows he/she is HIV positive, it may reduce the stress that comes with the uncertainty of not knowing. Your child can take advantage of treating his/her HIV early, monitoring his/her health, eating well and healthily. Your child will also know if he/she can infect others, and what to do to stop this from happening.

Women and their partners thinking about getting pregnant can take advantage of treatments that can help prevent their baby from getting HIV. Your child can also possibly plan for future care of his/her children.

6. What happens if my child is injured during the HIV test? 6

The insurance that the TB Alliance has taken out as required by the laws and regulations of your country covers the extra blood samples. For more details, see the information sheet describing the **main clinical study**.

7. Will you keep my child's HIV test private? 7

We will respect your child's confidentiality* and only the study doctor and research team will know the results of the test. Selected people working for TB Alliance, as well as representatives of government regulatory authorities and ethics committees will also have access to the results. These persons know that they must keep your child's information private. You are giving permission for those people to see your child's medical records when you sign this document.

8. Will you pay my child to do the HIV test? 8

No, we will not pay your child for giving the blood sample to do the HIV test.
The TB Alliance or the study site will not be responsible for paying any costs related to your HIV treatment if your child tests positive. We will refer your child to an HIV clinic for further testing and advice.

9. Will I have to pay for my child's HIV test? 9

No, the HIV test will not cost you anything,
<<If applicable add "You will receive HIV counseling before and after HIV test. The TB Alliance will pay for the test and the counseling."

10. Whom can we contact if something worries me or my child? 10

You can call the study doctor or another authorised person at any time of the day or night (24 hours) on Tel: **<<add>>** or **<<add>>**.	

Please refer to the **main informed consent form** for more information on whom to contact if you or your child have complaints about this study.

11. How do I agree for my child to have the HIV test? 11

If you want to agree to do the HIV test, please read the statement on the following page and sign the form.

Parent or Legal Guardian Notes

Glossary

Technical term	Explanation
HIV	Human immunodeficiency virus
AIDS	Acquired immune deficiency syndrome
opportunistic infections	an infection that occurs when the immune system is weak
immune system	the system in your body that fights infections
pulmonary	of the lungs
confidentiality	a set of rules to keep information private

PARENT/LEGAL GUARDIAN INFORMED CONSENT FORM FOR HIV TESTING

By signing below, I agree that:

- I have read, or someone has read the information sheet and consent form for this HIV testing of my child to me, and I understand it.
- I have had the chance to ask questions and I am happy with the answers.
- I have had time to discuss the information with others and to decide if I want my child to do the test.
- I will get a signed and dated copy of this consent form on the day that I sign it.
- I voluntarily agree for HIV testing to be done on my child.
- Site staff, representatives from the sponsor, regulatory authorities and ethics committees can have direct access to my child's medical records. They will treat my child's information as confidential.
- I hereby give up all rights to the test findings and my child is not entitled to be paid anything because of the test findings.
- <<EU: "I consent to the processing/storing of my child's data and the transfer thereof to countries outside the EU.">>

_____
Printed Name of Parent/Legal Guardian

_____ _____
Signature/mark/thumb print of Parent/Legal Guardian | Date

(Parent or Legal Guardian/witness must write date)

_____
*Printed Name of Person Conducting Consent
(If other than investigator /delegate)

_____ _____
*Signature of Person Conducting Consent
(If other than investigator /delegate) | Date

(Person conducting consent must write date)

I, _____ (Insert name of investigator) hereby confirm that the above Parent or Legal Guardian has been fully informed about the nature, conduct and risks of the above study.

Signature of Investigator

Date
(Investigator must write date)

By signing below, I verify that the above Parent or Legal Guardian gave verbal informed consent. The Parent or Legal Guardian has been informed about the risks and the benefits of his/her child's HIV test, understands such risks and benefits and is able to agree for his/her child to have the HIV test, without coercion, undue influence or inappropriate incentives.

*Printed Name of Witness

*Signature of Witness

Date
(Witness must write date)

* Where applicable