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Chiesi Farmaceutici S.p.A.

Clinical Research Protocol CLI-06814AA1-01

A Single Arm, Open-Label, Multicenter, Registry Study of Revcovi™ (elapegademase-lvlr) Treatment in ADA-SCID Patients Requiring Enzyme Replacement Therapy

NCT03878069

Informed Consent Form Version 4.0, Dated 26October2021

INFORMED CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT

PROTOCOL TITLE: A Single Arm, Open-Label, Multicenter, Registry Study of Revcovi™ (elapegademase-lvlr) Treatment in ADA-SCID Patients Requiring Enzyme Replacement Therapy

PROTOCOL NO.: CLI-06814AA1-01

SPONSOR: Chiesi Farmaceutici S.p.A.
Parma, Italy

INVESTIGATOR: [name and telephone number]

STUDY-RELATED CONTACTS AND PHONE NUMBER(S):

For research questions: [name and telephone number]

For questions on research subject's rights: [name and telephone number]

For research-related injuries: [name and telephone number]

This consent form may contain words that you may not understand. Please ask the study doctor orthe study staff to explain any words or information that you do not clearly understand. You may takehome an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

1. INTRODUCTION

You are being asked to be in this study because you have adenosine deaminase severe combined immunodeficiency (ADA-SCID) and are being treated with Revcovi™.

Your study doctor is an investigator for this study, and as an investigator, is interested both in your health and in the conduct of this study. The study is being conducted for Chiesi Farmaceutici, S.p.A. (Chiesi). Your study doctor is being paid by Chiesi to conduct this study.

Taking part in a research study is voluntary and your decision whether or not to take part in this study will not affect the medical care you receive from your doctor. The purpose of this consent form is to help you decide if you want to be in this study. Before agreeing to take part in this research study, it is important that you read and understand the following explanation of this research study. This consent document describes the purpose, procedures, benefits, risks, discomforts and precautions of the study. It also describes the alternative procedures that are available to you and your right to withdraw from the study at any time. No guarantees or assurances can be made as to the results of the study.

After reading and discussing the information in this consent form you should know:

- Why this research study is being done;
- What will happen during the research;
- What drugs will be used;
- Any possible benefits and the possible risks to you;
- Your other options if you choose not to be in this research study; and
- How problems that may occur will be treated during the study and after the study is over.

Please ask your study doctor about any information you are unclear on and he/she will explain it to you.

If you volunteer to take part in this research study, after you have signed and dated this consent form, you will be given a copy.

2. PURPOSE OF THIS STUDY

Chiesi (the Sponsor) is conducting an observational study on Revcovi™. The purpose of this study is to collect information on patients with ADA-SCID receiving Revcovi™.

This study will include up to 30 subjects at approximately 13 study centers in the United States.

3. STUDY PROCEDURES

If you agree to take part, you will be volunteering information collected from your medical records and laboratories, Revcovi™ dosing, and how you feel while taking Revcovi™.

As a subject in this study, you are expected to:

- Adhere to the appointments suggested by the study doctor
- Communicate information on unexpected medical occurrences
- Provide information on how you took your Revcovi™
- Call the call center every few months to provide responses to age-based, health-related quality of life (QOL) questionnaires. Each call will take approximately 10-12 minutes to complete. Your study doctor will provide you with the paper version of the questionnaires to take home with you, so you know what questions will be asked during each call. Parental consent and attendance may be required during the calls. Note that the QOL data collection is only for the first 24 months after starting Revcovi™.

If you agree to take part in this study, you will be asked to sign this consent form. After you sign and date this form, your study doctor or their staff will retrieve information about the following from your medical records:

- Demographics, for example, your age, gender, race, and ethnicity
- Disease background and history
- Assessment of infections and hospitalizations that have occurred over the past year prior to being administered Revcovi™
- Medical history
- Medication history
- Perform a physical examination
- Vital signs, for example your pulse and blood pressure
- Height and weight measurements of growth assessment
- Information about your general health
- Safety labs (blood and urine samples) will be drawn as part of your standard treatment
- Side effects or health changes (recorded during your standard treatment assessments)

Important Monitoring Information:

Treatment with Revcovi™ should be monitored by measuring trough plasma ADA activity and trough

dAXP levels via blood draws for keeping helpful targets of your immunodeficiency. ADA, adenosine deaminase, is an enzyme found throughout the body but is most active in specialized white blood cells called lymphocytes. These cells protect the body against potentially harmful invaders.

The function of the adenosine deaminase enzyme is to eliminate a molecule called deoxyadenosine (dAXP), which is generated when DNA is broken down. Adenosine deaminase converts deoxyadenosine, which can be toxic to lymphocytes, to another molecule that is not harmful. Mutations in the ADA gene reduce or eliminate the activity of adenosine deaminase and allow the buildup of deoxyadenosine to levels that are toxic to lymphocytes.

If ADA activity drops, immune function and clinical status should be watched closely, and steps should be taken to minimize the risk of infection. Your doctor will determine the frequency of physician assessments based on standard of care for ADA-SCID patients and your specific needs.

The information listed above will be collected from your medical chart while you take part in the study. Your data will be collected until the last subject enrolled in this study has been followed for 2 years.

4. POSSIBLE RISKS AND DISCOMFORTS

There are no physical risks being in the study. There is a risk of loss of confidentiality of your personal health information. There may be risks in this study that are unknown.

There are risks taking Revcovi™. Please ask your study doctor for Revcovi™ Full Prescribing Information. The warnings, precautions, potential adverse reactions (side effects), and any concerns that you might have should be discussed with your study doctor.

Warnings and Precautions:

- Injection site bleeding in patients with thrombocytopenia (low blood platelet count): Revcovi™ should be used with caution in patients with thrombocytopenia and should not be used if thrombocytopenia is severe.
- Delay in improvement of immune function: Patients should maintain precautions to reduce exposure to infections until their immune system improves.

Adverse Reactions:

The most commonly reported adverse reactions were cough and vomiting.

In addition, based on reports of adverse reactions for the same class of enzyme replacement therapy for ADA-SCID, patients treated with Revcovi™ may also experience:

- Hematologic events: hemolytic anemia (lack of healthy red blood cells), autoimmune hemolytic anemia, thrombocythemia (excess blood platelets), thrombocytopenia and autoimmune thrombocytopenia
- Dermatological events: injection site erythema (skin redness), urticarial (hives)
- Lymphomas (cancers of the lymphatic system)

Should you experience any type of adverse reaction, please report them to your study doctor.

5. NEW INFORMATION

You will be given any new information about Revcovi™ that becomes known during the course of this study that may affect your willingness to continue to take part in the study.

You may be asked to sign a new consent form if this occurs.

6. PREGNANCY & BIRTH CONTROL

There is no information available on the effects of Revcovi™ on a pregnant woman, embryo, fetus, a breastfed infant or male sperm. If you, or your partner, become pregnant during participation in the study, please notify your study doctor. You, or your partner, may be asked to provide information on the pregnancy and its outcome.

7. BENEFITS

You will not receive any additional benefit from taking part in this study. Revcovi™ is expected to treat your ADA-SCID with no additional benefits anticipated. You may not experience any directhealth benefits during or after completing this study. Your participation in this study will provideinformation about Revcovi™ and ADA-SCID that may benefit others.

8. COSTS

There will be no charge to you for your participation in this study. The study-related procedures and any study visits will be provided at no charge to you or your insurance company.

The standard care that you were already receiving (including medical procedures and medications) prior to the study will continue and you will be charged in the normal way.

You or a third party (such as your insurance company) will be billed for the costs of all medications, doctor visits, physical exams, lab tests, x-rays, scans, and other procedures used in this study which are routine and customary costs for your ADA-SCID care. You will be billed for any deductibles or co-payments required by your insurance company or third-party payer. If your insurance company does not pay for these costs, you will be billed for them. You will be responsible for co-payments and deductibles.

If you have concerns or questions about what you will be asked to pay for or what your insurance company will pay for, you should discuss with your study doctor and contact your insurance company.

9. PAYMENT FOR STUDY PARTICIPATION

Most of the registry study data will be collected from your medical records of your standard of care treatment for ADA-SCID. You will not receive payment for this data. QOL assessment data will be collected for a maximum of 24 months after starting Revcovi™. If you meet the time window you will receive payment for calling into the call center and for providing your time, effort, and responses to the age-based health-related Quality of Life (QOL) questionnaires. You will be paid $25 for each questionnaire completed. Maximum payment for completion of all questionnaires is outlined below.

Max Payment	Naïve	Adagen-Transitioning
$100	5 years – 18 years age	1 year – 18 years age
$175	1month – 4 years age	1month – 12 months age
$200	> 18 years age	> 18 years age

10. TREATMENT AND COMPENSATION FOR INJURY

If you suffer any side effect, notify your study doctor immediately so that you can receiveappropriate medical treatment. Your insurance will be billed for this treatment.

You will not be paid for lost wages or other damages or losses or for medical expenses that have been covered by medical or hospital insurance or by third party or governmental programs providing such coverage. No other form of compensation is available from the study Sponsor except remedies available under the law. By signing this form, you do not give up any legal rights. Payment of medical expenses is not an admission of fault or liability by the study Sponsor or anyone else.

11. ALTERNATIVE TREATMENTS

You do not have to be in this study to be treated for ADA-SCID. If you decide not to enter this study, you can choose to receive the therapy prescribed by your physician. Consult with your personal doctor for further details.

12. VOLUNTARY PARTICIPATION AND WITHDRAWAL

Taking part in this study is voluntary. It is up to you whether to take part in this study or not. You may refuse to take part without penalty or loss of benefits to which you are otherwise entitled.

You may withdraw from this study at any time without penalty or loss of benefits to which you are otherwise entitled. If you want to withdraw from this study, please contact the study doctor at the number listed on the first page. However, please note that any information collected up to the point of your withdrawal cannot be removed from the study.

Your participation may be ended by your study doctor without your consent if:

- You become ineligible to continue in the study, i.e. your treatment with Revcovi™ is stopped
- You fail to follow the instructions of the study doctor

13. CONFIDENTIALITY OF RECORDS

Your study records will be reviewed by the representatives of the sponsor and may be reviewed by representatives of the United States (U.S.) Food and Drug Administration or other federal, state, or international regulatory agencies, and representatives of [*Site instruction: add name of reviewing IRB*]. All reasonable efforts will be made to keep your study-related information confidential, however total confidentiality cannot be guaranteed as unintentional, occasional lapses may occur. Information regarding your participation in this study may also be disclosed if required by state or federal law.

A description of this study will be available on http://www.clinicaltrials.gov This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

In addition, the results of this research study may be presented at meetings or in publications. Your identity will not be given out during those presentations.

14. AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCHPURPOSES

During your participation in this research study, the study doctor and study staff will collect or create personal health information about you and record it on study forms. The study doctor will keep this personal health information in your study-related records (your study records). In addition, the study doctor may obtain, and include in your study records, information regarding your past, present and/or future physical or mental health and/or condition. Your study doctor may ask you to sign a separate authorization to obtain some or all of your medical records from your doctor(s). Your study records may include other personal information (such as social security number, medical record numbers, date of birth, etc.), which could be

used to identify you. Health information that could identify you is called Protected Health Information (PHI).

Under federal law (the Privacy Rule), your PHI that is created or obtained during this research study cannot be "used" to conduct the research or "disclosed" (given to anyone) for research purposes without your permission. This permission is called an "Authorization." Therefore, you may not take part in this study unless you give your authorization to use and disclose your PHI by signing this consent form.

Please be mindful that the Sponsor, a European-based company, has to comply also with the European privacy law (the so-called GDPR) and your PHI will be processed and protected in compliance with the GDPR, to the extent applicable to the Sponsor.

What information may be used and given to others?

The study doctor will get your personal and medical information, including

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits
- Records about any study drug(s) you received
- Physical exams
- Laboratory, x-ray, and other test results
- Study diaries and questionnaires
- Other information gathered for this research

Who may use and give out information about you?

By signing the consent form, you are agreeing to allow the study doctor and staff to use your PHI to conduct this study.

Who might get this information?

By signing this consent form, you also are agreeing to allow the study doctor to disclose PHI as described below:

- The Sponsor of this study and anyone working on behalf of the Sponsor to conduct this study, including other companies within its group, with its service providers (such as CRO), its contractors, current and future commercial partners. The Sponsor will analyze and evaluate the PHI and may use it to develop new tests, procedures and commercial products. The study staff will assign a code number and/or letters to your records, which means you will not be identified in the records sent to the Sponsor ("coded data"), who will have access to your PHI only in a coded form, except as follows: the Sponsor will, however, look at your complete study records that identify you. In addition, the Sponsor will visit the study site to oversee the way the study is being conducted and may review your PHI during these visits to make sure the information is correct.
- The Institutional Review Board (IRB), which is a committee that approves, monitors and reviews this study, may have access to your PHI in relation to its responsibilities as an IRB.
- The Data Safety Monitoring Committee (DSMC), which is a committee that monitors and reviews the safety data for this study, may have access to your PHI in relation to its responsibilities as a DSMC.

The study doctor or Sponsor may disclose your PHI to the U.S. Food and Drug Administration (FDA), the U.S. Department of Health and Human Services (DHHS) or similar regulatory agencies in the US and/or foreign countries.

Furthermore, your coded data might be retained, used and processed by the Sponsor outside this study exclusively for scientific reasons and, more specifically, only for future Sponsor's scientific research relating to similar disorders.

How long will your personal data be stored?

Your coded data will be retained by the Sponsor as necessary to perform the contractual and legal obligations arising out of the study, for at least 25 years after the end of the research study.

In addition, the Sponsor will retain your coded data for the data retention period identified in the standards of Good Clinical Practice, whichever is the longest.

Your uncoded medical records and other source documentation will be kept for the maximum time permitted by the site and in accordance with national law.

Why will this information be used and/or given to others?

These disclosures also help ensure that the information related to the research is available to allparties who may need it:

- To do the research
- To study the results
- To see if research was done right

What if I decide not to give permission to use and give out my health information?

You may not take part in this study if you do not give your permission to use and disclose yourPHI.

May I review or copy my information?

You have a right to see and make copies of your PHI. You are agreeing, however, by signing thisform, not to see or copy some or all of your PHI until the Sponsor has completed all work related to this study. At that time, you may ask to see your records**.**

May I withdraw or revoke (cancel) my authorization?

This authorization has no expiration date. By signing and dating this form, you authorize the use of disclosure of your PHI as described in this section and for purposes of the study at any time in thefuture. This authorization will not automatically expire unless you request to withdraw it or take it away.

You have a right to withdraw or take away your authorization at any time. When you withdrawyour permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others. To revoke your authorization, you must write to the study doctor, stating that you are revoking your Authorization to Use or Disclose Protected Health Information. If you revoke this authorization,you will not be allowed to continue to be in this study.

Is my health information protected after it has been given to others?

Except for the disclosures described above, your PHI will not be shared with others unless required by law. If your PHI is given to the parties listed above and/or to others who are not required to comply with the federal law, your PHI will no longer be protected by this law and could possibly be used or disclosed in ways other than those listed here.

15. QUESTIONS

You should not sign this consent form unless you have had a chance to ask questions about the study and your questions have been answered to your satisfaction. You have the right to ask questions about this study at any time and are encouraged to do so.

- If you have any questions about this research study, ask the research study doctor or the research staff at [*telephone* #].

- If you experience an injury you believe is related to this study, contact [*person*] at [*telephone #]*.

The IRB is responsible for making sure that research with humans is ethical and that subject's rights and welfare are protected. This research study has been approved by your study doctor's IRB.

- If you have any questions about your rights as a research subject, you may contact [*name of IRB*] at [*telephone #*].

These contacts are also provided on the first page of this consent form.

16. CONSENT

By signing this consent form, I state that:

- I have read this consent form.
- I understand all the information in this consent form, including the potential risks and benefits, and the study procedures I am expected to have performed.
- I have been given the chance to discuss the study and ask questions.
- All my questions have been answered to my satisfaction.
- I do not know of any medical conditions that would prevent me from joining the study.
- I voluntarily consent to take part in this study.
- I understand I will receive a copy of this consent form.
- I understand that by signing this consent form, I have not given up any of the legal rights, which I otherwise would have as a subject in a research study.
- I authorize the collection, use and disclosure of my medical information in accordance with this form.

_____ _____

Signature of Subject Date

_____

Printed name of Subject

_____ _____

Signature of Parent/Guardian if Subject is not yet 18 years of age Date

_____

Printed name of Parent/Guardian

Signature of Person Administering this Consent | Date

Printed Name of Person Administering this Consent

As needed per IRB requirements:

Witness:

Signature of Witness | Date

Printed name of Witness

Investigator:

Signature of Investigator | Date

Printed name of Investigator