CLINICAL TRIAL PROGRAM FOR FIBRODYSPLASIA OSSIFICANS PROGRESSIVA

TABLE OF CONTENTS

Who is Clementia? .................................................................................................................................. 2
What is the objective of Clementia's clinical trial program? ................................................................. 2
What is palovarotene? ........................................................................................................................... 3
What is the status of palovarotene for FOP? ......................................................................................... 3
Clementia has 3 clinical trials – all actively recruiting participants .................................................. 4
Clementia covers the costs associated with participating in its clinical trials ................................. 4
Phase 2 Clinical Trial ............................................................................................................................. 5
  What is the objective of this study? ................................................................................................. 5
  Who is eligible? ............................................................................................................................... 5
  How is the study designed? ............................................................................................................. 5
  What does participation in the study involve? .................................................................................. 6
  What types of assessments are involved? ......................................................................................... 6
  What are the potential side effects of palovarotene? ...................................................................... 7
Phase 2 Open-label Extension Trial ...................................................................................................... 8
  What is the objective of this study? ................................................................................................. 8
  Who is eligible? ............................................................................................................................... 8
Natural History Study .......................................................................................................................... 9
  What is the objective of this study? ................................................................................................. 9
  Who is eligible? ............................................................................................................................... 9
  What does participation in the study involve? .................................................................................. 9
What's next in the development of palovarotene for FOP? ............................................................... 10
Interested in participating? ................................................................................................................ 11
Message and thank you to the FOP community ................................................................................. 12
WHO IS CLEMENTIA?

Clementia is a group of dedicated people experienced in rare disease and orphan drug development. The company has offices in Canada and the U.S.

WHAT IS THE OBJECTIVE OF CLEMENTIA’S CLINICAL TRIAL PROGRAM?

The overall objective is to provide sufficient data to regulatory authorities for review and approval of palovarotene as a treatment for FOP.
WHAT IS PALOVAROTENE?

- Palovarotene is an oral therapy under investigation for the treatment of FOP
- In people with FOP, the ACVR1/ALK2 receptor in the BMP pathway is overactive resulting in heterotopic ossification
- Palovarotene may prevent heterotopic ossification by inhibiting signaling from the overactive ACVR1/ALK2 receptor
- Palovarotene blocked heterotopic bone in mouse models with FOP
- Clementia is investigating whether palovarotene has the same effect in humans with FOP

WHAT IS THE STATUS OF PALOVAROTENE FOR FOP?

All drugs must pass through a rigorous development process to get to regulatory review and approval by regulatory agencies such as the FDA in the United States and the EMA in Europe

- Palovarotene was previously studied in 800 subjects by Roche Pharmaceuticals
- Clementia is currently enrolling children with FOP ages 6 to 14 in a Phase 2 trial of palovarotene
CLEMENTIA HAS 3 CLINICAL TRIALS – ALL ACTIVELY RECRUITING PARTICIPANTS

- **PVO 201**
  - Phase 2 clinical trial of palovarotene in individuals with FOP*

- **PVO 202**
  - Phase 2 open-label, extension trial**

- **PVO 101**
  - Natural History Study

*currently enrolling children with FOP ages 6 to 14
**open to individuals who have completed the Phase 2 trial

CLEMENTIA COVERS THE COSTS ASSOCIATED WITH PARTICIPATING IN ITS CLINICAL TRIALS

- All reasonable costs associated with participating in the Phase 2, Open-label, or Natural History Study will be covered, including travel, meals and accommodations for the study participant and up to two caregivers

- Clementia works with patients and their families to minimize the challenges associated with traveling to clinical trial sites
  - Travel and accommodations are booked by an agency that specializes in travel planning for individuals with restricted mobility
  - Clinical trial sites work closely with families to minimize the burden on the patient
  - Some up front planning can be done even prior to flare-up onset
  - For more information, contact the clinical trial site
PHASE 2 CLINICAL TRIAL

WHAT IS THE OBJECTIVE OF THIS STUDY?

The purpose is to investigate whether palovarotene has an effect on new bone formation during and following a flare-up in patients with FOP, at what dose and with what associated side effects.

WHO IS ELIGIBLE?

- Clementia is currently enrolling children with FOP ages 6 to 14 who have an eligible flare-up
  - Clementia has completed enrollment of adults (age 15 or older) in this study
- There are a limited number of spots left for children experiencing a flare-up in the shoulders, chest, abdomen, arms, hips or legs

HOW IS THE STUDY DESIGNED?

- The Phase 2 trial is a randomized, double-blind placebo controlled study
- **Randomized** means that participants are randomly allocated to receive either palovarotene or a placebo as their study medication
  - There are two doses of palovarotene being tested
  - A placebo is a product with no therapeutic action and is used in order to determine whether an experimental compound provides any treatment benefit or has any side effects
- **Double-blind** means that neither the doctor nor the participant are aware of which study medication is being given
- Study participants have a 75% (3/4) chance of receiving palovarotene and a 25% (1/4) chance of receiving a placebo
WHAT DOES PARTICIPATION IN THE STUDY INVOLVE?

- Patients must travel to a clinical trial site within 7 days of the start of the flare-up for examination, imaging, and bloodwork
  - A flare-up can consist of warmth, redness, swelling, pain, and/or limited/loss of movement
  - Eligible flare-ups can be located in the shoulders, chest, abdomen, arms, hips, or legs
- If eligibility is confirmed, study duration is 12 weeks
  - Study medication is taken orally after breakfast for first 6 weeks
  - There is an additional 6 weeks of follow-up
  - In general, assessments at the clinical trial site will be performed at the time of enrollment, at week 6, and at week 12

WHAT TYPES OF ASSESSMENTS ARE INVOLVED?

- A complete history and physical examination
- Laboratory assessments (bloodwork)
- Imaging assessments including x-ray, CT scan, and MRI (or ultrasound) of the flare-up site
- Participant self-assessments include:
  - rating of flare-up site pain and swelling symptoms
  - assessment of movement at the flare-up site
  - range of motion at the flare-up site
- Questionnaires meant to assess physical limitations and other general health measures
- Side effects will be assessed
WHAT ARE THE POTENTIAL SIDE EFFECTS OF PALOVAROTENE?

✔ The Phase 2 trial is evaluating potential side effects of palovarotene

✔ The most frequent side effects associated with palovarotene include effects on skin and mucous membranes (e.g. the inside of your nose and mouth) such as dry skin, dry lips, itching, rash, redness of the skin, flaking and peeling skin, inflammation of the lips, dry mouth, and dry eyes.

✔ There are potential side effects associated with the class of medications of which palovarotene is a part - called retinoids
  
  ✔ These will be described in the informed consent process when being considered for enrollment in the clinical trial
  
  ✔ There will be an opportunity to discuss these potential health risks with the clinical trial personnel

✔ If a patient experiences a side effect during the clinical trial, he/she will be carefully evaluated by the clinical site physician and treated appropriately

✔ Patients can choose to stop participating in the clinical trial at any time
PHASE 2 OPEN-LABEL EXTENSION TRIAL

WHAT IS THE OBJECTIVE OF THIS STUDY?

The purpose is to evaluate the long term effects and safety of palovarotene in individuals with FOP who have completed the Phase 2 trial.

WHO IS ELIGIBLE?

- All participants who complete the Phase 2 trial are eligible to enroll in the Phase 2 Open-label Extension Trial
  - Open-label means that a participant experiencing a new, eligible flare-up is treated with palovarotene regardless of the study medication he/she received in the Phase 2 trial
  - There is no placebo in this trial
NATURAL HISTORY STUDY

WHAT IS THE OBJECTIVE OF THIS STUDY?

The purpose is to better understand the natural progression of FOP over time in order to advance current and future drug development.

Natural History Study data will be shared with the IFOPA to advance disease understanding.

WHO IS ELIGIBLE?

- Clementia is enrolling individuals with FOP age 0 to 65
- Up to 100 individuals with FOP will be enrolled

WHAT DOES PARTICIPATION IN THE STUDY INVOLVE?

- No investigational medication is administered
- Patients must travel to a clinical trial site once a year (every 12 months) for examination, imaging and bloodwork
  - There are additional visits if there is a flare-up
  - There is a phone call every 6 months between visits
- Study duration is up to 3 years
- Study participants who experience an eligible flare-up can transfer into the Phase 2 trial as long as it is still open for enrollment
WHAT’S NEXT IN THE DEVELOPMENT OF PALOVAROTENE FOR FOP?

The results of the current, ongoing trials will inform the design of a Phase 3 trial.
INTERESTED IN PARTICIPATING?

Contact the clinical trial site closest to you.

The Royal National site in England is enrolling children with FOP age 6 to 14 into the Phase 2 Study and individuals with FOP age 0 to 65 into the Natural History Study.
MESSAGE AND THANK YOU TO THE FOP COMMUNITY

We are committed to continue to develop palovarotene for FOP as efficiently and safely as possible
- Donna Grogan, MD, Chief Medical Officer

We appreciate your support, collaboration, encouragement and inspiration
- Clarissa Desjardins, PhD, CEO and Founder

Together, we will advance drug development through clinical trials and prepare the data for regulatory review and approval
- Jeff Packman, Chief Development Officer

Together, we will obtain a better understanding of FOP, which will inform the development of future therapies
- Eric Soliman, Director of Clinical Operations