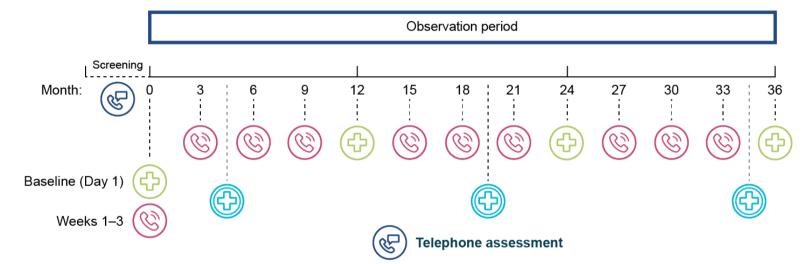
#### Supplementary Figure 1. Study designs of the PVO-1A-001, PVO-1A-201 and PVO-1A-202 studies

#### Supplementary Figure 1A. PVO-1A-001 natural history study



## **(2)**

#### Clinic visit

Low-dose WBCT scan (excluding head) at all planned clinic visits or at early termination (within 2 months of termination)

#### **Telephone contact**



Participants were asked to telephone the site with a suspected flare-up. In addition, telephone contact was performed every 3–6 months to determine whether new flare-ups occurred since the prior clinic visit or telephone contact.

#### Flare-up clinic visit



A maximum of one flare-up per year could be studied via a clinic visit within 14 days of the identification of the flare-up, with follow up assessments at Weeks 6 and 12

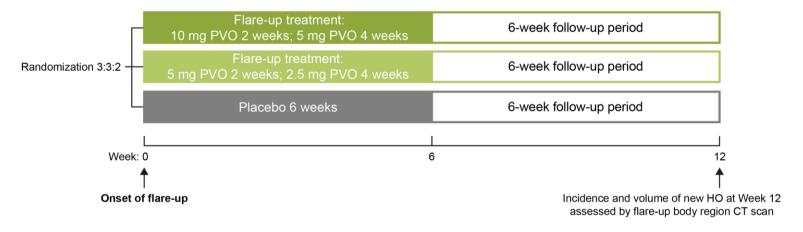
2

### **Supplementary Figure 1B. PVO-1A-201 randomized control trial**

#### Cohort 1 (Participants ≥15 years)



#### Cohort 2 (Participants ≥6 years)

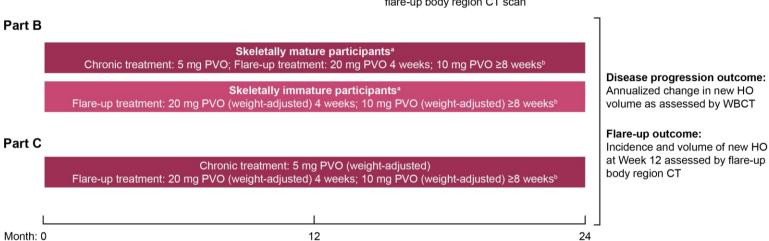


2

CT: computed tomography; HO: heterotopic ossification; PVO: palovarotene.

## Supplementary Figure 1C. PVO-1A-202 open-label extension trial Part A

# Flare-up treatment: 10 mg PVO 2 weeks; 5 mg PVO 4 weeks Week: 0 6 12 Onset of flare-up Incidence and volume of new HO at Week 12 assessed by flare-up body region CT scan



In Part D of PVO-1A-202, annual assessments were obtained after the last dose of palovarotene in participants who were skeletally immature at the time of treatment discontinuation to obtain longer-term safety data.  $^a$ Skeletally mature participants were  $\geq 18$  years of age or had  $\geq 90\%$  skeletal maturity on hand/wrist radiography [defined by a bone age of  $\geq 12$  years in female and  $\geq 14$  years in male participants] at screening. Skeletally immature participants were < 18 years of age and had < 90% skeletal maturity on hand/wrist radiography at screening.  $^b\geq 8$  weeks or until flare-up resolved. CT: computed tomography; HO: heterotopic ossification; PVO: palovarotene; WBCT: whole-body computed tomography.