CLAIMS

1. Use of palovarotene, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing heterotopic ossification in a subject with fibrodysplasia ossificans progressiva, wherein: (i) during a period when the subject is not experiencing any flare-up symptom, an amount of 3 ± 2.0 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject, and (ii) during a period when the subject is experiencing at least one flare-up symptom, 2-fold to 6-fold the amount to be administered daily during the period when the subject is not experiencing any flare-up symptom is to be orally administered daily to the subject, wherein during the period when the subject is experiencing at least one flare-up symptom the palovarotene, or a pharmaceutically acceptable salt thereof, is to be initially administered for a period of 20 to 40 days in a daily dose of 3.5-fold to 6-fold the amount to be administered daily during the period when the subject is not experiencing any flare-up symptom, and after the period of 20 to 40 days, a dose of 2-fold to 3-fold the amount to be administered daily during the period when the subject is not experiencing any flare-up symptom is to be administered daily for a period of 14 to 112 days.

2. The use of claim 1, wherein the amount to be administered during the period when the subject is not experiencing any flare-up symptom is 5 ± 0.5 mg daily and the amount to be administered during the period when the subject is experiencing at least one flare-up symptom comprises an amount of 20 ± 1.0 mg daily for the period of 20 to 40 days, and after the period of 20 to 40 days, an amount of 10 ± 1.0 mg daily for the period of 14 to 112 days.

3. The use of claim 2, wherein the subject weighs greater than 60 kg.

4. The use of claim 1, wherein the amount to be administered during the period when the subject is not experiencing any flare0up symptom is 3 ± 0.5 mg daily and the amount to be administered during the period when the subject is experiencing at least one flare-up symptom comprises an amount of 12.5 ± 1.0 mg daily for the period of 20 to 40 days, and after the period of 20 to 40 days, an amount of 6.0 ± 1.0 mg daily for the period of 14 to 112 days.

5. The use of claim 4, wherein the subject weighs from 20 to 40 kg.

6. The use of claim 1, wherein the amount to be administered during the period when the subject is not experiencing any flare-up symptom is 4 ± 0.5 mg daily and the amount to be administered during the period when the subject is experiencing at least one flare-up symptom comprises an amount of 15 ± 1.0 mg daily for the period of 20 to 40 days, and after the period of 20 to 40 days,an amount of 7.5 ± 1.0 mg daily for the period of 14 to 112 days.

7. The use of claim 6, wherein the subject weighs from 40 to 60 kg.

8. The use of claim 1, wherein the amount to be administered during the period when the subject is not experiencing any flare-up symptom is 2 ± 0.5 mg daily and the amount to be administered during the period when the subject is experiencing at least one flare-up symptom comprises an amount of 10 ± 1.0 mg daily for the period of 20 to 40 days, and after the period of 20 to 40 days, an amount of 5 ± 1.0 mg daily for the period of 14 to 112 days.

9. The use of claim 8, wherein the subject weighs less than 20 kg.

10. The use of any one of claims 1-9, wherein the amount of palovarotene, or a pharmaceutically acceptable salt thereof, to be administered for the period of 14 to 112 days is to be administered for at least a period of 14 to 84 days.

11. The use of claim 10, wherein at the end of 84 days the amount of palovarotene, or a pharmaceutically acceptable salt thereof, to be administered for the period of 84 days is to be administered daily for an additional 28 days if the subject continues to experience at least one flare-up symptom.

12. The use of claim 10 wherein during the period when the subject is experiencing at least one flare-up symptom an amount of 20 mg is to be administered daily for a period of 28 days, and after the period of 28 days, an amount of 10 mg is to be administered daily for 56 days and the daily amount to be administered during the period when the subject is not experiencing any flare-up symptom is 5 mg/day.

13. Use of palovarotene, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing the severity of flare-ups in a subject with fibrodysplasia ossificans progressiva, wherein: (i) during a period when the subject is not experiencing any flare-up symptom, an amount of 3 ± 2 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject, and (ii) during a period when the subject is experiencing at least one flare-up symptom, 2-fold to 6-fold the amount to be administered daily during the period when the subject is not experiencing any flare-up symptom is to be orally administered daily to the subject, wherein during the period when the subject is experiencing at least one flare-up symptom the palovarotene, or a pharmaceutically acceptable salt thereof, is to be initially administered for a period of 20 to 40 days in a daily dose of 3.5-fold to 6-fold the amount to be administered daily during the period when the subject is not experiencing any flare-up symptom, and after the period of 20 to 40 days, a dose of 2-fold to 3-fold the amount to be administered daily during the period when the subject is not experiencing any flare-up symptom is to be administered daily for a period of 14 to 112 days.

14. The use of claim 13, wherein the amount to be administered during the period when the subject is not experiencing any flare-up symptom is 5 ± 0.5 mg daily and the amount to be

administered during the period when the subject is experiencing at least one flare-up symptom comprises an amount of 20 ± 1.0 mg daily for the period of 20 to 40 days, and after the period of 20 to 40 days, an amount of 10 ± 1.0 mg daily for the period of 14 to 112 days.

15. The use of claim 14, wherein the subject weighs greater than 60 kg.

16. The use of claim 13, wherein the amount to be administered during the period when the subject is not experiencing any flare-up symptom is 3 ± 0.5 mg daily and the amount to be administered during the period when the subject is experiencing at least one flare-up symptom comprises an amount dose of 12.5 ± 1.0 mg daily for the period of 20 to 40 days, and after the period of 20 to 40 days, an amount of 6.0 ± 1.0 mg daily for the period of 14 to 112 days.

17. The use of claim 16, wherein the subject weighs from 20 to 40 kg.

18. The use of claim 13, wherein the amount to be administered during the period when the subject is not experiencing any flare-up symptom is 4 ± 0.5 mg daily and the amount to be administered during the period when the subject is experiencing least one flare-up symptom comprises an amount of 15 ± 1.0 mg daily for the period of 20 to 40 days, and after the period of 20 to 40 days, an amount of 7.5 ± 1.0 mg daily for the period fo 14 to 112 days.

19. The use of claim 18, wherein the subject weighs from 40 to 60 kg.

20. The use of claim 13, wherein the amount to be administered during the period when the subject is not experiencing any flare-up symptom is 2 ± 0.5 mg daily and the amount to be administered during the period when the subject is experiencing at least one flare-up symptom comprises an amount of 10 ± 1.0 mg daily for the period of 20 to 40 days, and after the period of 20 to 40 days, an amount of 5 ± 1.0 mg daily for the period of 14 to 112 days.

21. The use of claim 20, wherein the subject weighs less than 20 kg.

22. The use of any one of claims 13-21, wherein the amount of palovarotene, or a pharmaceutically acceptable salt thereof, to be administered for the period of 14 to 112 days is to be administered for at least a period of 14 to 84 days.

23. The use of claim 22, wherein at the end of 84 days the amount of palovarotene, or a pharmaceutically acceptable salt thereof, to be administered for the period of 84 days is to be administered daily for an additional 28 days if the subject continues to experience at least one flare-up symptom.

24. Use of palovarotene, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing heterotopic ossification in a subject with fibrodysplasia ossificans progressiva, wherein during a period when the subject is experiencing at least one flare-up symptom: (i) an amount of from 9 to 21 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered to the subject daily for a period of 20 to 40 days and (ii) following the period of 20 to 40 days, an amount of 40% to 60% of the daily amount to be administered during the period of20 to 40 days is to be orally administered daily to the subject for period of 14 to 112 days.

25. The use of claim 24, wherein an amount of 20 ± 1.0 mg palovarotene, or a pharmaceutically acceptable salt thereof, is to be administered daily for the period of 20 to 40 days and an amount of 10 ± 1.0 mg palovarotene, or a pharmaceutically acceptable salt thereof, is to be administered daily for the period of 14 to 112 days.

26. The use of claim 25, wherein the subject weighs greater than 60 kg.

27. The use of claim 24, wherein an amount of 12.5 ± 1.0 mg palovarotene, or a pharmaceutically acceptable salt thereof, is to be administered daily for the period of 20 to 40 days and an amount of 6.0 ± 1.0 mg palovarotene, or a pharmaceutically acceptable salt thereof, is to be administered daily for the period of 14 to 112 days.

28. The use of claim 27, wherein the subject weighs from 20 to 40 kg.

29. The use of claim 24, wherein an amount of 15 ± 1.0 mg palovarotene, or a pharmaceutically acceptable salt thereof, is to be administered daily for a period of 20 to 40 days and an amount of 7.5 ± 1.0 mg palovarotene, or a pharmaceutically acceptable salt thereof, is to be administered daily for the period of 14 to 112 days.

30. The use of claim 29, wherein the subject weighs from 40 to 60 kg.

31. The use of claim 24, wherein an amount of 10 ± 1.0 mg palovarotene, or a pharmaceutically acceptable salt thereof, is to be administered daily for the period of 20 to 40 days and an amount of 5 ± 1.0 mg palovarotene, or a pharmaceutically acceptable salt thereof, is to be administered daily for the period of 14 to 112 days.

32. The use of claim 31, wherein the subject weighs less than 20 kg.

33. The use of any one of claims 24-32, wherein the amount of palovarotene, or a pharmaceutically acceptable salt thereof, to be administered for the period of 14 to 112 days is to be administered for at least a period of 14 to 84 days.

34. The use of claim 33, wherein at the end of 84 days the amount of palovarotene, or a pharmaceutically acceptable salt thereof, to be administered for the period of 84 days is to be administered daily for an additional 28 days if the subject continues to experience at least one flare-up symptom.

35. The use of any one of claims 1-34, wherein the subject has not achieved 90% skeletal maturity.

36. The use of any one of claims 1-35, wherein an antihistamine is to be administered to the subject.

37. The use of claim 36, wherein the antihistamine is to be administered topically.

38. The use of claim 36, wherein the antihistamine is to be administered systemically.

39. The use of any one of claims 1-35, wherein an emollient is to be administered to the skin of the subject.

40. Use of palovarotene, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing heterotopic ossification in a subject with fibrodysplasia ossificans progressiva, wherein : (i) during a period when the subject is not experiencing any flare-up symptom, an amount of 5 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject, and (ii) during a period when the subject is experiencing at least one flare-up symptom, an amount of 20 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for 28 days, and after the 28 days, ana mount of 10 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for at least 56 days.

41. Use of palovarotene, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing heterotopic ossification in a subject with fibrodysplasia ossificans progressiva, wherein the subject weighs from 10 to 20 kg, wherein: (i) during a period when the subject is not experiencing any flare-up symptom, an amount of 2.5 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject, and (ii) during a period when the subject is experiencing at least one flare-up symptom, an amount of 10 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for 28 days, and after the 28 days, an amount of 5 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for at least 56 days.

42. Use of palovarotene, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing heterotopic ossification in a subject with fibrodysplasia ossificans progressiva, wherein the subject weighs from 20 to 40 kg, wherein: (i) during a period when the

subject is not experiencing any flare-up symptom, an amount of 3 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject, and (ii) during a period when the subject is experiencing at least one flare-up symptom, an amount of 12.5 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for 28 days, and after the 28 days, an amount of 6 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for at least 56 days.

43. Use of palovarotene, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing heterotopic ossification in a subject with fibrodysplasia ossificans progressiva, wherein the subject weighs from 40 to 60 kg, wherein: (i) during a period when the subject is not experiencing any flare-up symptom, an amount of 4 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject, and (ii) during a period when the subject is experiencing at least one flare-up symptom, an amount, an amount of 15 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for 28 days,and after the 28 days, an amount of 7.5 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for at least 56 days.

44. Use of palovarotene, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing heterotopic ossification in a subject with fibrodysplasia ossificans progressiva, wherein the subject weighs 60 kg or more, wherein: (i) during a period when the subject is not experiencing any flare-up symptom, an amount of 5 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject, and (ii) during a period when the subject is experiencing at least one flare-up symptom, an amount of 20 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily for the subject for 28 days, and after the 28 days, an amount of 10 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for at least 56 days.

45. Use of palovarotene, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing heterotopic ossification in a subject with fibrodysplasia ossificans progressiva, wherein: (i) during a period when the subject is not experiencing any flare-up symptom, an amount of 4 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject, and (ii) during a period when the subject is experiencing at least one flare-up symptom, an amount of 15 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for 28 days, and after the 28 days, an amount of 7.5 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for at least 56 days.

46. Use of palovarotene, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing heterotopic ossification in a subject with fibrodysplasia ossificans progressiva, wherein the subject weighs from 10 to 20 kg, wherein: (i) during a period when the

subject is not experiencing any flare-up symptom, an amount of 1 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject, and (ii) during a period when the subject is experiencing at least one flare-up symptom, an amount of 7.5 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be administered daily to the subject for 28 days, and after the 28 days, an amount of 3 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for at least 56 days.

47. Use of palovarotene, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing heterotopic ossification in a subject with fibrodysplasia ossificans progressiva, wherein the subject weighs from 20 to 40 kg, wherein: (i) during a period when the subject is not experiencing any flare-up symptom, an amount of 2.5 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject, and (ii) during a period when the subject is experiencing at least one flare-up symptom, an amount of 10 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for 28 days, and after the 28 days, an amount of 5 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for at least 56 days.

48. Use of palovarotene, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing heterotopic ossification in a subject with fibrodysplasia ossificans progressiva, wherein the subject weighs from 40 to 60 kg, wherein: (i) during a period when the subject is not experiencing any flare-up symptom, an amount of 3 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject, and (ii) during a period when the subject is experiencing at least one flare-up symptom, an amount of 12.5 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for 28 days, and after the 28 days, an amount of 6 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for at least 56 days.

49. Use of palovarotene, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing heterotopic ossification in a subject with fibrodysplasia ossificans progressiva, wherein the subject weighs 60 kg or more, wherein: (i) during a period when the subject is not experiencing any flare-up symptom, an amount of 4 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject, and (ii) during a period when the subject is experiencing at least one flare-up symptom, an amount of 15 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for 28 days, and after the 28 days, an amount of 7.5 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for at least 56 days.

50. Use of palovarotene, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing heterotopic ossification in a subject with fibrodysplasia ossificans progressiva, wherein: (i) during a period when the subject is not experiencing any flare-up symptom,

an amount of 5 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject, and (ii) during a period when the subject is experiencing at least one flare-up symptom, an amount of 10 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for at least 56 days.

51. Use of palovarotene, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing heterotopic ossification in a subject with fibrodysplasia ossificans progressiva, wherein: (i) during a period when the subject is not experiencing any flare-up symptom, an amount of 5 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject, and (ii) during a period when the subject is experiencing at least one flare-up symptom, an amount of 15 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for 28 days, and after the 28 days, an amount of 10 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for at least 56 days.

52. Use of palovarotene, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing heterotopic ossification in a subject with fibrodysplasia ossificans progressiva, wherein: (i) during a period when the subject is not experiencing any flare-up symptom, an amount of 5 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject, and (ii) during a period when the subject is experiencing at least one flare-up symptom, 10 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for 28 days, and after the 28 days, an amount of 10 mg of palovarotene, or a pharmaceutically acceptable salt thereof, is to be orally administered daily to the subject for at least 56 days.

53. The use of any one of claims 1-10, 13-22, and 24-33, wherein the amount to be administered during the period of 14 to 112 days is to be administered daily for a period of 84 days.

54. The use of any one of claims 1-10, 13-22, and 24-33, wherein the amount to be administered during the period of 14 to 112 days is to be administered daily for a period of 56 days.

55. The use of any one of claims 1-10, 13-22, and 24-33, wherein the amount to be administered during the period of 14 to 112 days is to be administered daily for a period of 56 days, and is to be administered daily for an additional 28 days if the subject continues to experience at least one flare-up symptom.

56. The use of any one of claims 1-10, 13-22, and 24-33, wherein the amount to be administered during the period of 14 to 112 days is to be administered daily for a period of 112 days.

57. The use of any one of claims 1-11 and 13-39, wherein the amount to be administered during the period of 20 to 40 days is to be administered daily for a period of 28 ± 4 days.

58. The use of any one of claims 1-37, wherein the amount to be administered during the period of 20 to 40 days is to be administered daily for a period of 28 days.

59. The use of any one of claims 1-58, wherein the at least one flare-up symptom is chosen from swelling, pain, erythema, warmth, stiffness, and decreased range of motion.

60. The use of any one of claims 1-59, wherein the amount to be administered daily is of palovarotene.

61. The use of any one of claims 1-59, wherein the amount to be administered daily is of a pharmaceutically acceptable salt of palovarotene.