[0048] Articles of manufacture, which include packaging material, a compound described herein, or a pharmaceutically acceptable salt thereof, within the packaging material, and a label that indicates that a PPARδ agonist (e.g. Compound 1, or a pharmaceutically acceptable salt thereof), is used for modulating the activity of PPARδ, or for the treatment, prevention or amelioration of one or more symptoms of a fatty acid oxidation disorder (FAOD) that would benefit from modulation of PPARδ activity, are provided.

[0048a] In one aspect, provided herein is a use of a peroxisome proliferator-activated receptor delta (PPARδ) agonist compound in the manufacture of a medicament for the treatment of a fatty acid oxidation disorder (FAOD) in a mammal, wherein the PPARδ agonist compound is *(E)*-[4-[3-(4-fluorophenyl)-3-[4-[3-(morpholin-4-yl)propynyl]phenyl]allyloxy]-2-methyl-phenoxy]acetic acid, or a pharmaceutically acceptable salt thereof, and wherein the mammal is a human, and wherein the FAOD comprises one or more mutations in one or more of the enzymes or proteins of the mitochondrial fatty acid beta-oxidation pathway; wherein the one or more enzymes or proteins of the mitochondrial fatty acid beta-oxidation pathway are selected from the group consisting of short-chain acyl-CoA dehydrogenase (SCAD), medium-chain acyl-CoA dehydrogenase (MCAD), long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD), very long-chain acyl-CoA dehydrogenase (VLCAD), mitochondrial trifunctional protein (TFP), carnitine transporter (CT), Carnitine palmitoyltransferase I (CPT I), carnitine-acylcarnitine translocase (CACT), carnitine palmitoyltransferase II (CPT II), isolated long-chain L3-hydroxyl-CoA dehydrogenase, medium-chain L3-hydroxyl-CoA dehydrogenase, short-chain L3-hydroxyl-CoA dehydrogenase, medium-chain 3-ketoacylCoA thiolase, and long-chain 3-ketoacylCoA thiolase (LCKAT).

[0048b] In one aspect, provided herein is a use of *(E)*-[4-[3-(4-Fluorophenyl)-3-[4-[3-(morpholin-4-yl)propynyl]phenyl]allyloxy]-2-methyl-phenoxy]acetic acid or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a fatty acid oxidation disorder (FAOD) in a mammal; wherein the fatty acid oxidation disorder comprises

carnitine palmitoyltransferase II (CPT2) deficiency, very long-chain Acyl-CoA dehydrogenase (VLCAD) deficiency, long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency, Trifunctional Protein (TFP) Deficiency; or a combination thereof; wherein *(E)*-[4-[3-(4-Fluorophenyl)-3-[4-[3-(morpholin-4-yl)propynyl]phenyl]allyloxy]-2-methyl-phenoxy]acetic acid or a pharmaceutically acceptable salt thereof, is to be administered to the mammal at a dose of 50 mg to 200 mg; and wherein the mammal is a human.

[0049] Other objects, features and advantages of the compounds, methods and compositions described herein will become apparent from the following detailed description. It should be understood, however, that the detailed description and the specific examples, while indicating specific examples, are given by way of illustration only, since various changes and modifications within the spirit and scope of the instant disclosure will become apparent to those skilled in the art from this detailed description.

BRIEF DESCRIPTION OF THE FIGURES

[0050] **Figure 1** shows the effect of Compound 1 (50 mg once a day for 12 weeks) on the 12-minute walk test in patients with genetically diagnosed long chain FAOD with symptoms of myopathy.

DETAILED DESCRIPTION

[0051] Mitochondria are the main site for the oxidation of fatty acids and triglycerides through a series of four enzyme reactions called β-oxidation. The β-oxidation pathway is a cyclic process in which two carboxy-terminal carbon atoms are released from fatty acids as acetyl-CoA units each time a cycle is fully completed. The acetyl-CoA can enter the citric acid cycle and the electron carriers deliver the electrons to the electron transport chain. Fatty acid oxidation (FAO) both produces acetyl-CoA to fuel the tricarboxylic acid (TCA) cycle and ketogenesis, and reduces flavin adenine dinucleotide (to FADH2) and nicotinamide adenine dinucleotide (to NADH); these reduced products directly feed into the respiratory chain. As the acyl-CoA gets shorter, its physicochemical properties change. To be able to fully degrade fatty acids, the β-oxidation machinery harbors different chain length–specific enzymes. Inherited defects for most

CLAIMS

WHAT IS CLAIMED IS:

1. Use of a peroxisome proliferator-activated receptor delta (PPARδ) agonist compound in the manufacture of a medicament for the treatment of a fatty acid oxidation disorder (FAOD) in a mammal, wherein the PPARδ agonist compound is *(E)*-[4-[3-(4-fluorophenyl)-3-[4-[3-(morpholin-4-yl)propynyl]phenyl]allyloxy]-2-methyl-phenoxy]acetic acid, or a pharmaceutically acceptable salt thereof, and wherein the mammal is a human, and
   wherein the FAOD comprises one or more mutations in one or more of the enzymes or proteins of the mitochondrial fatty acid beta-oxidation pathway;
   wherein the one or more enzymes or proteins of the mitochondrial fatty acid beta-oxidation pathway are selected from the group consisting of short-chain acyl-CoA dehydrogenase (SCAD), medium-chain acyl-CoA dehydrogenase (MCAD), long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD), very long-chain acyl-CoA dehydrogenase (VLCAD), mitochondrial trifunctional protein (TFP), carnitine transporter (CT), Carnitine palmitoyltransferase I (CPT I), carnitine-acylcarnitine translocase (CACT), carnitine palmitoyltransferase II (CPT II), isolated long-chain L3-hydroxyl-CoA dehydrogenase, medium-chain L3-hydroxyl-CoA dehydrogenase, short-chain L3-hydroxyl-CoA dehydrogenase, medium-chain 3-ketoacylCoA thiolase, and long-chain 3-ketoacylCoA thiolase (LCKAT).
2. The use of claim 1, wherein:
   treatment of the FAOD comprises improving whole-body fatty acid oxidation (FAO) in the mammal, improving the mammal's exercise tolerance, decreasing pain, decreasing fatigue, or a combination thereof.
3. The use of claim 2, wherein:
   administration of the PPARδ agonist compound to the mammal increases FAO capacities in the mammal, normalizes FAO capacities in the mammal, up-regulates gene expression of any one of the enzymes or proteins involved in FAO, increases the activity of an enzyme or protein involved in FAO, or a combination thereof.
4. The use of any one of claims 1-3, wherein:
   the fatty acid oxidation disorder comprises one or more defects in one or more of the enzymes or proteins involved in the entry of long-chain fatty acids into mitochondria, intramitochondrial β-oxidation defects of long-chain fatty acids affecting membrane bound enzymes, β-oxidation defects of short- and medium-chain fatty acids affecting enzymes of the mitochondrial matrix, defects in the enzymes or proteins involved with

electron transfer to the respiratory chain from mitochondrial β-oxidation, or a combination thereof.

5. The use of any one of claims 1-4, wherein:
the fatty acid oxidation disorder (FAOD) comprises carnitine transporter deficiency, carnitine/acylcarnitine translocase deficiency, carnitine palmitoyl transferase deficiency Type 1, carnitine palmitoyl transferase deficiency Type 2, long-chain 3-hydroxyacyl CoA dehydrogenase deficiency, medium-chain acyl CoA dehydrogenase deficiency, short-chain acyl CoA dehydrogenase deficiency, short-chain 3-hydroxyacyl CoA dehydrogenase deficiency, trifunctional protein deficiency, or very long-chain acyl CoA dehydrogenase deficiency, or a combination thereof.

6. The use of any one of claims 1-5, wherein:
the fatty acid oxidation disorder comprises carnitine palmitoyltransferase II (CPT2) deficiency, very long-chain Acyl-CoA dehydrogenase (VLCAD) deficiency, long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency, Trifunctional Protein (TFP) Deficiency; or a combination thereof.

7. The use of any one of claims 1-4, wherein:
the one or more enzymes or proteins of the mitochondrial fatty acid beta-oxidation pathway are selected from the group consisting of long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD), very long-chain acyl-CoA dehydrogenase (VLCAD), mitochondrial trifunctional protein (TFP), carnitine palmitoyltransferase II (CPT II), and long-chain 3-ketoacylCoA thiolase (LCKAT).

8. The use of any one of claims 1-7, wherein:
the mammal has elevated creatine kinase (CPK) levels, hepatic dysfunction, cardiomyopathy, hypoglycemia, rhabdomyolysis, acidosis, decreased muscle tone (hypotonia), muscle weakness, exercise intolerance, or combinations thereof.

9. The use of any one of claims 1-8, wherein:
the PPARδ agonist compound is *(E)*-[4-[3-(4-fluorophenyl)-3-[4-[3-(morpholin-4-yl)propynyl]phenyl]allyloxy]-2-methyl-phenoxy]acetic acid, or a pharmaceutically acceptable salt thereof, and is to be administered to the mammal at a dose of 10mg to 500mg.

10. The use of any one of claims 1-8, wherein:
the PPARδ agonist compound is *(E)*-[4-[3-(4-Fluorophenyl)-3-[4-[3-(morpholin-4-yl)propynyl]phenyl]allyloxy]-2-methyl-phenoxy]acetic acid or a pharmaceutically acceptable salt thereof, and is to be administered to the mammal at a dose of 50mg to 200mg.

11. The use of any one of claims 1-8, wherein:
the PPARδ agonist compound is *(E)*-[4-[3-(4-Fluorophenyl)-3-[4-[3-(morpholin-4-yl)propynyl]phenyl]allyloxy]-2-methyl-phenoxy]acetic acid or a pharmaceutically acceptable salt thereof, and is to be administered to the mammal at a dose of 50mg.

12. The use of any one of claims 1-8, wherein:
the PPARδ agonist compound is *(E)*-[4-[3-(4-Fluorophenyl)-3-[4-[3-(morpholin-4-yl)propynyl]phenyl]allyloxy]-2-methyl-phenoxy]acetic acid or a pharmaceutically acceptable salt thereof, and is to be administered to the mammal at a dose of 100mg.

13. The use of any one of claims 1-12, wherein:
the PPARδ agonist compound is to be systemically administered to the mammal in the form of an oral solution, oral suspension, powder, pill, tablet or capsule; and the PPARδ agonist compound is to be administered to the mammal once daily.

14. The use of any one of claims 1-13, wherein at least one additional therapeutic is to be further administered to the mammal, wherein:
the at least one additional therapeutic is ubiquinol, ubiquinone, niacin, riboflavin, creatine , L-carnitine, acetyl-L-carnitine, biotin, thiamine, pantothenic acid, pyridoxine, alpha-lipoic acid, n-heptanoic acid, CoQ10, vitamin E, vitamin C, methylcobalamin, folinic acid, resveratrol, N-acetyl-L-cysteine (NAC), zinc, folinic acid/leucovorin calcium, or a combination thereof;
or the at least one additional therapeutic is an odd-chain fatty acid, odd-chain fatty ketone, L-carnitine, or combinations thereof;
or the at least one additional therapeutic is an odd-chain fatty acid, odd-chain fatty ketone, L-carnitine, or combinations thereof;
or the at least one additional therapeutic is triheptanoin, n-heptanoic acid, a triglyceride, or a salt or thereof, or combinations thereof;
or the at least one additional therapeutic is an antioxidant;
or the at least one additional therapeutic is bezafibrate.

15. Use of *(E)*-[4-[3-(4-Fluorophenyl)-3-[4-[3-(morpholin-4-yl)propynyl]phenyl]allyloxy]-2-methyl-phenoxy]acetic acid or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a fatty acid oxidation disorder (FAOD) in a mammal;
wherein the fatty acid oxidation disorder comprises carnitine palmitoyltransferase II (CPT2) deficiency, very long-chain Acyl-CoA dehydrogenase (VLCAD) deficiency, long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency, Trifunctional Protein (TFP) Deficiency; or a combination thereof;

wherein *(E)*-[4-[3-(4-Fluorophenyl)-3-[4-[3-(morpholin-4-yl)propynyl]phenyl]allyloxy]-2-methyl-phenoxy]acetic acid or a pharmaceutically acceptable salt thereof, is to be administered to the mammal at a dose of 50 mg to 200 mg; and
wherein the mammal is a human.

16. The use of claim 15, wherein treatment of the FAOD comprises improving whole-body fatty acid oxidation (FAO) in the mammal, improving the mammal's exercise tolerance, decreasing pain, decreasing fatigue, or a combination thereof.