BRIEF DESCRIPTION OF THE DRAWINGS

[006] **FIG. 1** shows the mean lomitapide pediatric starting dose (mg) based on PBPK modeling and allometric scaling.

[007] **FIG. 2** shows the design of the clinical study in Example 2.

SUMMARY

[007a] In an aspect of the present disclosure, there is provided a use of lomitapide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating homozygous familial hypercholesterolemia (HoFH) in a pediatric patient in need thereof, wherein:
(a) an initial dose of 2 mg per day of lomitapide, or a pharmaceutically acceptable salt thereof is to be administered to a patient aged 5 to 10 years for about 1 to about 4 weeks;
(b) an initial dose of 2 mg per day of lomitapide, or a pharmaceutically acceptable salt thereof, is to be administered to a patient aged 11 to 15 years for about 1 to about 4 weeks; and
(c) an initial dose of 5 mg per day of lomitapide, or a pharmaceutically acceptable salt thereof, is to be administered to a patient aged 16 to 17 years for about 1 to about 4 weeks.

[008] In examples, the present disclosure provides, a method of safely administering lomitapide, or a pharmaceutically acceptable salt thereof, to a pediatric patient comprising:

(a) administering a first daily dose of about 0.5 mg to about 2.5 mg of lomitapide, or a pharmaceutically acceptable salt thereof to a patient aged 5 to 15 years; and

(b) administering a first daily dose of about 2.5 mg to about 7.5 mg of lomitapide, or a pharmaceutically acceptable salt thereof to a patient aged 16 to 17 years,

wherein the first daily dose is administered to the patient for about 1 to 4 weeks.

[009] In examples, the present disclosure provides a method of treating hyperlipidemia or hypercholesterolemia in a pediatric patient, comprising:

(a) administering a first daily dose of about 0.5 mg to about 2.5 mg of lomitapide, or a pharmaceutically acceptable salt thereof to a patient's age is 5 to 15 years;

(b) administering a first daily dose of about 2.5 mg to about 7.5 mg of lomitapide, or a pharmaceutically acceptable salt thereof to a patient's age is 16 to 17 years,

wherein the first daily dose is administered to the patient for about 1 to 4 weeks.

[0010] In examples, provided herein is a method of treating hyperlipidemia or hypercholesterolemia, comprising:

administering a first daily dose of about 0.5 mg to about 2.5 mg of lomitapide, or a pharmaceutically acceptable salt thereof to a pediatric patient age 5 to 10 years, wherein the first daily dose is administered to the patient for about 1 to 4 weeks.

[0011] In examples, provided herein is a method of treating hyperlipidemia or hypercholesterolemia, comprising:

administering a first daily dose of about 0.5 mg to about 2.5 mg of lomitapide, or a pharmaceutically acceptable salt thereof to a pediatric patient age 11 to 15 years, wherein the first daily dose is administered to the patient for about 1 to 4 weeks.

[0012] In examples, the present disclosure provides a method of treating hyperlipidemia or hypercholesterolemia, comprising:

administering a first daily dose of about 2.5 mg to about 7.5 mg of lomitapide, or a pharmaceutically acceptable salt thereof to a pediatric patient age 16 to 17 years, wherein the first daily dose is administered to the patient for about 1 to 4 weeks.

DEFINITIONS

[0013] The term "about" when immediately preceding a numerical value means a range (e.g., plus or minus 10% of that value). For example, "about 50" can mean 45 to 55, "about 25,000" can mean 22,500 to 27,500, etc., unless the context of the disclosure indicates otherwise, or is inconsistent with such an interpretation. For example in a list of numerical values such as "about 49, about 50, about 55, …", "about 50" means a range extending to less than half the interval(s) between the preceding and subsequent values, e.g., more than 49.5 to less than 50.5. Furthermore, the phrases "less than about" a value or "greater than about" a value should be understood in view of the definition of the term "about" provided herein. Similarly, the term "about" when preceding a series of numerical values or a range of values (e.g., "about 10, 20, 30" or "about 10-30") refers, respectively to all values in the series, or the endpoints of the range.

[0014] Throughout this disclosure, various patents, patent applications and publications are referenced. The disclosures of these patents, patent applications and publications in their entireties are incorporated into this disclosure by reference for all purposes in order to more fully describe the state of the art as known to those skilled therein as of the date of this disclosure. This disclosure will govern in the instance that there is any inconsistency between the patents, patent applications and publications cited and this disclosure.

[0015] For convenience, certain terms employed in the specification, examples and claims are collected here. Unless defined otherwise, all technical and scientific terms used in this disclosure have the same meanings as commonly understood by one of ordinary skill in the art to which this disclosure belongs.

[0016] The terms "administer," "administering" or "administration" as used herein refer to either directly administering a compound or pharmaceutically acceptable salt or ester of the

CLAIMS

What is claimed:

1. Use of lomitapide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating homozygous familial hypercholesterolemia (HoFH) in a pediatric patient in need thereof, wherein:

    (a) an initial dose of 2 mg per day of lomitapide, or a pharmaceutically acceptable salt thereof is to be administered to a patient aged 5 to 10 years for about 1 to about 4 weeks;

    (b) an initial dose of 2 mg per day of lomitapide, or a pharmaceutically acceptable salt thereof, is to be administered to a patient aged 11 to 15 years for about 1 to about 4 weeks; and

    (c) an initial dose of 5 mg per day of lomitapide, or a pharmaceutically acceptable salt thereof, is to be administered to a patient aged 16 to 17 years for about 1 to about 4 weeks.

2. The use of claim 1, wherein the administration provides a reduction in the patient's low-density lipoprotein (LDL-C):

    a) compared to prior to the administration; and/or

    b) to less than 135 mg/dL.

3. The use of claim 1 or 2, wherein the administration provides a reduction in the patient's total cholesterol (TC), apolipoprotein B (apo B), non-high-density lipoprotein cholesterol (non-HDL-C), very low-density lipoprotein cholesterol (VLDL-C), triglyceride, and high-density lipoprotein cholesterol (HDL-C) compared to prior to the administration.

4. The use of claim 1, wherein the initial dose is to be further titrated to a maximum daily dose of:

    a) 20 mg per day for the patient aged 5 to 10 years;

    b) 40 mg per day for the patient aged 11 to 15 years; and/or

    c) 60 mg per day for the patient aged 16 to 17 years.

5. The use of claim 1, wherein the initial dose is to be further titrated to a second dose, wherein the second dose is:

(a) 2 mg per day of lomitapide, or pharmaceutically acceptable salt thereof, for the patient aged 5 to 10 years,

(b) 5 mg per day of lomitapide, or pharmaceutically acceptable salt thereof, for the patient aged 11 to 15 years, and

(c) 10 mg per day of lomitapide, or pharmaceutically acceptable salt thereof, for the patient aged 16 to 17 years,

wherein the second dose is to be administered for about 1 to about 4 weeks;

optionally wherein the second dose is to be further titrated to a third dose, wherein the third dose is:

(a) 5 mg per day of lomitapide, or pharmaceutically acceptable salt thereof, for the patient aged 5 to 10 years,

(b) 10 mg per day of lomitapide, or pharmaceutically acceptable salt thereof, for the patient aged 11 to 15 years, and

(c) 20 mg per day of lomitapide, or pharmaceutically acceptable salt thereof, for the patient aged 16 to 17 years,

wherein the third dose is to be administered for about 1 to about 4 weeks;

optionally wherein the third dose is to be further titrated to a fourth dose, wherein the fourth dose is:

(a) 10 mg per day of lomitapide, or pharmaceutically acceptable salt thereof, for the patient aged 5 to 10 years,

(b) 20 mg per day of lomitapide, or pharmaceutically acceptable salt thereof, for the patient aged 11 to 15 years, and

(c) 40 mg per day of lomitapide, or pharmaceutically acceptable salt thereof, for the patient aged 16 to 17 years,

wherein the fourth dose is to be administered for about 1 to about 4 weeks.

6. The use of any one of claims 1 to 3, wherein the patient has hepatic impairment characterized by Child-Pugh A.
7. The use of claim 6, wherein the initial dose is to be further titrated to a maximum daily dose of:
    a) 10 mg per day for the patient aged 5 to 10 years;
    b) 20 mg per day for the patient aged 11 to 15 years;
    c) 40 mg per day for the patient aged 16 to 17 years.
8. The use of any one of claims 1 to 7, wherein the patient is on a stable lipid-lowering therapy.
9. The use of any one of claims 1 to 8, vitamin E, alpha-linolenic acid, linoleic acid, eicosapentaenoic acid, and docosahexaenoic acid are to be further administered to the patient.
10. The use of any one of claims 1 to 9, wherein the lomitapide or pharmaceutically acceptable salt thereof is a lomitapide mesylate; optionally wherein the lomitapide mesylate is encapsulated in a capsule.
11. The use of claim 1, wherein the patient has at least 2 mutant alleles at the LDLR, apo B, PCSK9, or LDLRAP1 gene locus.
12. The use of claim 1, wherein the patient has an untreated LDL-C level of greater than 500 mg/dL and cutaneous or tendon xanthoma before 10 years of age or untreated LDL-C level consistent with heterozygous familial hypercholesterolemia in both parents.
13. The use of claim 1, wherein the patient has a treated LDL-C level of at least 300 mg/dL and cutaneous or tendon xanthoma before 10 years of age or untreated LDL-C level consistent with heterozygous familial hypercholesterolemia in both parents.
14. The use of claim 1, wherein the patient has no documented cardiovascular disease and LDL-C level of greater than 160 mg/dL prior to the administration.
15. The use of claim 1, wherein the patient has established cardiovascular disease and LDL-C level of greater than 130 mg/dL prior to the administration.