METHODS FOR TREATING FAMILIAL CHYLOMICRONEMIA SYNDROME

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of priority to U.S. Application Serial No. 63/165,457 filed on March 24, 2021, and U.S. Application Serial No. 63/155,960 filed on March 3, 2021, the contents of each of which are hereby incorporated by reference in their entireties for all purposes.

BACKGROUND

[0002] Familial chylomicronemia Syndrome (FCS) is a rare, genetic condition characterized by extremely high levels of plasma triglycerides and is estimated to occur in approximately 1 in 1,000,000 individuals worldwide.

[0003] The extreme triglyceride elevations in FCS lead to periodic abdominal pain, which is often seen in childhood. As the disease progresses later in life, it can result in multiple and recurrent episodes of acute pancreatitis, associated abdominal pain, xantomatosis (plain, eruptive and tuberous), lipemia retinalis, and renal failure. Occasionally, pancytopenia (due to the presence of lipid-laden macrophages in the bone marrow) and neurological symptoms such as depression and cognitive impairment have also been reported. The major cause of morbidity in FCS patients is recurrent pancreatitis leading to pancreatic insufficiency and, ultimately, pancreatic failure.

[0004] Patients with FCS fail to respond to currently available lipid-lowering agents (e.g., fibrates and omega-3 fatty acids) so dietary management with an extremely low-fat diet and supplementation with Medium Chain Tryglicerides (MCT)-remains the cornerstone of therapy. However, TG levels remain significantly elevated in most FCS patients despite severe dietary restrictions and FCS patients are exposed to acute pancreatitis.

[0005] Thus, there is an unmet need for safe and effective treatments for patients with FCS.

SUMMARY

[0005a] 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 familial chylomicronemia syndrome (FCS) in a patient in need thereof, wherein:

a) a first daily dose of about 5 mg of lomitapide, or a pharmaceutically acceptable salt thereof, is to be orally administered to the patient for a first dosing period;

b) the fasting triglyceride levels of the patient after the first dosing period is measured, wherein if the patient's fasting triglyceride levels are ≤ 1000 mg/dL while adhering to a low-fat diet, the patient is maintained at a daily dose of lomitapide, or a pharmaceutically acceptable salt thereof, of about 5 mg;

c) if the patient's measured fasting triglyceride levels are > 1000 mg/dL while adhering to a low-fat diet after the first dosing period, the patient is to be orally administered a second daily dose of about 10 mg of lomitapide, or a pharmaceutically acceptable salt thereof, for a second dosing period;

d) the fasting triglyceride levels of the patient after the second dosing period is measured, wherein if the patient's fasting triglyceride levels are ≤ 1000 mg/dL while adhering to a low-fat diet, the patient is maintained at a daily dose of lomitapide, or a pharmaceutically acceptable salt thereof, of about 10 mg;

e) if the patient's measured fasting triglyceride levels are > 1000 mg/dL while adhering to a low-fat diet after the second dosing period, the patient is to be orally administered a third daily dose of about 15 mg to about 20 mg of lomitapide, or a pharmaceutically acceptable salt thereof, for a third dosing period.

[0005b] In another 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 familial chylomicronemia syndrome (FCS) in a pediatric patient in need thereof, wherein:

a) a first daily dose of about 2 mg to about 5 mg of lomitapide, or a pharmaceutically acceptable salt thereof, is to be administered to the patient for a first dosing period;

b) the fasting triglyceride levels of the patient after the first dosing period is measured, wherein if the patient's fasting triglyceride levels are ≤ 1000 mg/dL, the patient is maintained at a daily dose of lomitapide, or a pharmaceutically acceptable salt thereof, of about 2 mg to about 5 mg;

c) if the patient's measured fasting triglyceride levels are > 1000 mg/dL after the first dosing period, the patient is to be orally administered a second daily dose of about 5 mg to about 10 mg of lomitapide, or a pharmaceutically acceptable salt thereof, for a second dosing period;

d) the fasting triglyceride levels of the patient after the second dosing period is measured, wherein if the patient's fasting triglyceride levels are ≤ 1000 mg/dL, the patient is maintained at a daily dose of lomitapide, or a pharmaceutically acceptable salt thereof, of about 5 mg to about 10 mg;

e) if the patient's measured fasting triglyceride levels are > 1000 mg/dL after the second dosing period, the patient is to be orally administered a third daily dose of about 10 mg to about 20 mg of lomitapide, or a pharmaceutically acceptable salt thereof, for a third dosing period.

[0006] The present disclosure provides, among other things, methods of treating familial chylomicronemia syndrome (FCS) in a patient in need thereof, the method comprising:

adhering to a low-fat diet, the patient is maintained at a daily dose of lomitapide, or a pharmaceutically acceptable salt thereof, of about 10 mg;

e) if the patient's measured fasting triglyceride levels are > about 750 mg/dL while adhering to a low-fat diet after the second dosing period, the patient is orally administered a third daily dose of about 20 mg of lomitapide, or a pharmaceutically acceptable salt thereof, for a third dosing period.

[0008] In some ~~embodiment~~examples, the patient in need of FCS treatment is confirmed homozygote, compound heterozygote or double heterozygote for one or more loss-of-function mutations in genes causing FCS.

[0009] In some ~~embodiment~~examples, the patient in need of FCS treatment has a history of pancreatitis.

[0010] In some ~~embodiment~~examples, when the patient's liver aminotransferase (ALT/AST) levels are ≥5 times the upper limit of normal (ULN) after the first dosing period, the second dosing period or the third dosing period, the patient is withdrawn from lomitapide treatment. In some ~~embodiment~~examples, the patient is withdrawn from treatment until ALT/AST levels are < 3 times the ULN. In some ~~embodiment~~examples, the method further comprises reducing the patient's dose to the last dose that provided patient ALT/AST levels of < 3 times the ULN.

[0011] In some ~~embodiment~~examples, when the patient's ALT/AST levels are from 3-5 times the ULN, the method comprises confirming the patient's ALT/AST levels are 3-5 times the ULN within one week of the elevated ALT/AST test result. In some ~~embodiment~~examples, the method further comprises reducing the patient's dose to the last dose that provided patient ALT/AST levels of < 3 times the ULN.

[0012] In some ~~embodiment~~examples, methods of the present disclosure comprise adjusting the patient's daily lomitapide dose to provide fasting triglyceride levels ≤ 1000 mg/dL and ALT/AST levels ≤ 3 times the ULN.

[0013] In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 1000 mg/dL and ALT/AST levels ≤ 3 times the ULN is selected from the group consisting of 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, 50 mg, 55 mg, and 60 mg of lomitapide or a pharmaceutically acceptable salt thereof.

[0014] In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 1000 mg/dL and ALT/AST levels ≤ 3 times the ULN is selected from the group consisting of 5 mg,

10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg, and 60 mg of lomitapide or a pharmaceutically acceptable salt thereof.

[0015] In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 1000 mg/dL and ALT/AST levels ≤ 3 times the ULN is selected from the group consisting of 5 mg, 10 mg, 20 mg, 30 mg, and 60 mg of lomitapide or a pharmaceutically acceptable salt thereof.

[0016] In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 1000 mg/dL and ALT/AST levels ≤ 3 times the ULN is selected from the group consisting of 5 mg, 10 mg, 20 mg, 40 mg, and 60 mg of lomitapide or a pharmaceutically acceptable salt thereof.

[0017] In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 1000 mg/dL and ALT/AST levels ≤ 3 times the ULN is selected from the group consisting of 5 mg, 10 mg, 15 mg, and 20 mg of lomitapide or a pharmaceutically acceptable salt thereof.

[0018] In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 1000 mg/dL and ALT/AST levels ≤ 3 times the ULN is 5 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 1000 mg/dL and ALT/AST levels ≤ 3 times the ULN is 10 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 1000 mg/dL and ALT/AST levels ≤ 3 times the ULN is 15 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 1000 mg/dL and ALT/AST levels ≤ 3 times the ULN is 20 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 1000 mg/dL and ALT/AST levels ≤ 3 times the ULN is 30 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 1000 mg/dL and ALT/AST levels ≤ 3 times the ULN is 40 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 1000 mg/dL and ALT/AST levels ≤ 3 times the ULN is 50 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 1000 mg/dL and ALT/AST levels ≤ 3 times the ULN is 60 mg of lomitapide or a pharmaceutically acceptable salt thereof.

[0019] In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 750 mg/dL and ALT/AST levels ≤ 3 times the ULN is selected from the group consisting of 5 mg,

10 mg, 15 mg, 20 mg, 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, 50 mg, 55 mg, and 60 mg of lomitapide or a pharmaceutically acceptable salt thereof.

[0020] In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 750 mg/dL and ALT/AST levels ≤ 3 times the ULN is selected from the group consisting of 5 mg, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg, and 60 mg of lomitapide or a pharmaceutically acceptable salt thereof.

[0021] In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 750 mg/dL and ALT/AST levels ≤ 3 times the ULN is 5 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 750 mg/dL and ALT/AST levels ≤ 3 times the ULN is 10 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 750 mg/dL and ALT/AST levels ≤ 3 times the ULN is 15 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 750 mg/dL and ALT/AST levels ≤ 3 times the ULN is 20 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 750 mg/dL and ALT/AST levels ≤ 3 times the ULN is 30 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 750 mg/dL and ALT/AST levels ≤ 3 times the ULN is 40 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 750 mg/dL and ALT/AST levels ≤ 3 times the ULN is 50 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 750 mg/dL and ALT/AST levels ≤ 3 times the ULN is 60 mg of lomitapide or a pharmaceutically acceptable salt thereof.

[0022] In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 500 mg/dL and ALT/AST levels ≤ 3 times the ULN is selected from the group consisting of 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, 50 mg, 55 mg, and 60 mg of lomitapide or a pharmaceutically acceptable salt thereof.

[0023] In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 500 mg/dL and ALT/AST levels ≤ 3 times the ULN is selected from the group consisting of 5 mg,

10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg, and 60 mg of lomitapide or a pharmaceutically acceptable salt thereof.

[0024] In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 500 mg/dL and ALT/AST levels ≤ 3 times the ULN is 5 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 500 mg/dL and ALT/AST levels ≤ 3 times the ULN is 10 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 500 mg/dL and ALT/AST levels ≤ 3 times the ULN is 15 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 500 mg/dL and ALT/AST levels ≤ 3 times the ULN is 20 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 500 mg/dL and ALT/AST levels ≤ 3 times the ULN is 30 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 500 mg/dL and ALT/AST levels ≤ 3 times the ULN is 40 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤ 500 mg/dL and ALT/AST levels ≤ 3 times the ULN is 50 mg of lomitapide or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the daily dose that provides fasting triglyceride levels ≤500 mg/dL and ALT/AST levels ≤ 3 times the ULN is 60 mg of lomitapide or a pharmaceutically acceptable salt thereof.

[0025] In some ~~embodiment~~examples of the methods provided herein, the lomitapide administration does not provide a clinically significant increase in hepatic fat liver during the treatment period.

[0026] In some ~~embodiment~~examples of the methods provided herein, the lomitapide administration substantially decreases the episodes of pancreatitis compared to prior to said treatment.

[0027] In some ~~embodiment~~examples the present disclosure provides methods of treating familial chylomicronemia syndrome (FCS) in a pediatric patient in need thereof, the method comprising:

a) orally administering a first daily dose of about 2 mg to about 5 mg of lomitapide, or a pharmaceutically acceptable salt thereof, to the patient for a first dosing period;

b) measuring the fasting triglyceride levels of the patient after the first dosing period, wherein if the patient's fasting triglyceride levels are ≤ 1000 mg/dL, the patient is

maintained at a daily dose of lomitapide, or a pharmaceutically acceptable salt thereof, of about 2 mg to about 5 mg;

c) if the patient's measured fasting triglyceride levels are > 1000 mg/dL after the first dosing period, the patient is orally administered a second daily dose of about 5 mg to about 10 mg of lomitapide, or a pharmaceutically acceptable salt thereof, for a second dosing period;

d) measuring the fasting triglyceride levels of the patient after the second dosing period, wherein if the patient's fasting triglyceride levels are ≤ 1000 mg/dL, the patient is maintained at a daily dose of lomitapide, or a pharmaceutically acceptable salt thereof, of about 5 mg to about 10 mg;

e) if the patient's measured fasting triglyceride levels are > 1000 mg/dL after the second dosing period, the patient is orally administered a third daily dose of about 10 mg to about 20 mg of lomitapide, or a pharmaceutically acceptable salt thereof, for a third dosing period.

[0028] In some ~~embodiment~~example~~s~~ the present disclosure provides methods of treating familial chylomicronemia syndrome (FCS) in a pediatric patient in need thereof, the method comprising:

a) orally administering a first daily dose of about 2 mg to about 5 mg of lomitapide, or a pharmaceutically acceptable salt thereof, to the patient for a first dosing period;

b) measuring the fasting triglyceride levels of the patient after the first dosing period, wherein if the patient's fasting triglyceride levels are ≤ 750 mg/dL, the patient is maintained at a daily dose of lomitapide, or a pharmaceutically acceptable salt thereof, of about 2 mg to about 5 mg;

c) if the patient's measured fasting triglyceride levels are > 750 mg/dL after the first dosing period, the patient is orally administered a second daily dose of about 5 mg to about 10 mg of lomitapide, or a pharmaceutically acceptable salt thereof, for a second dosing period;

d) measuring the fasting triglyceride levels of the patient after the second dosing period, wherein if the patient's fasting triglyceride levels are ≤ 750 mg/dL, the patient is maintained at a daily dose of lomitapide, or a pharmaceutically acceptable salt thereof, of about 5 mg to about 10 mg;

e) if the patient's measured fasting triglyceride levels are > 750 mg/dL after the second dosing period, the patient is orally administered a third daily dose of about 10 mg to about 20 mg of lomitapide, or a pharmaceutically acceptable salt thereof, for a third dosing period.

[0029] In some ~~embodiment~~examples, the pediatric patient in need of FCS treatment is administered a daily dose of 2 mg of lomitapide or a pharmaceutically acceptable salt thereof in the first dosing period, a daily dose of 5 mg of lomitapide or a pharmaceutically acceptable salt thereof in the second dosing period, and a daily dose of 10 mg of lomitapide or a pharmaceutically acceptable salt thereof in the third dosing period.

[0030] In some ~~embodiment~~examples, the pediatric patient in need of FCS treatment is administered a daily dose of 5 mg of lomitapide, or a pharmaceutically acceptable salt thereof in the first dosing period, a daily dose of 10 mg of lomitapide, or a pharmaceutically acceptable salt thereof in the second dosing period, and a daily dose of 20 mg of lomitapide, or a pharmaceutically acceptable salt thereof in the third dosing period.

BRIEF DESCRIPTION OF THE DRAWINGS

[0031] FIG. 1 shows mean triglyceride (TG) levels (mg/dL) in FCS patients (n=18) treated with lomitapide over 26 weeks from the study described in Example 1.

[0032] FIG. 2 shows mean total cholesterol (TC) levels (mg/dL) in FCS patients (n=18) treated with lomitapide over 26 weeks from the study described in Example 1. Terms TC or CT are used interchangeably.

[0033] FIG. 3 shows mean HDL-C levels (mg/dL) in FCS patients (n=18) treated with lomitapide over 26 weeks from the study described in Example 1.

[0034] FIG. 4 shows the mean lomitapide dose (mg) administered to FCS patients (n=18) over the course of the 26-week study described in Example 1

[0035] FIG. 5 shows mean liver ALT levels (ul/L) in FCS patients (n=18) treated with lomitapide over the course of the 26-week study described in Example 1.

[0036] FIG. 6 shows mean liver AST levels (ul/L) in FCS patients (n=18) treated with lomitapide over the course of the 26-week study described in Example 1.

CLAIMS

What is claimed:

1. Use of lomitapide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for ~~A method of~~ treating familial chylomicronemia syndrome (FCS) in a patient in need thereof, ~~the method comprising~~wherein:

   a) ~~orally administering~~ a first daily dose of about 5 mg of lomitapide, or a pharmaceutically acceptable salt thereof, is to be orally administered to the patient for a first dosing period;

   b) ~~measuring~~ the fasting triglyceride levels of the patient after the first dosing period is measured, wherein if the patient's fasting triglyceride levels are ≤ 1000 mg/dL while adhering to a low-fat diet, the patient is maintained at a daily dose of lomitapide, or a pharmaceutically acceptable salt thereof, of about 5 mg;

   c) if the patient's measured fasting triglyceride levels are > 1000 mg/dL while adhering to a low-fat diet after the first dosing period, the patient is to be orally administered a second daily dose of about 10 mg of lomitapide, or a pharmaceutically acceptable salt thereof, for a second dosing period;

   d) ~~measuring~~ the fasting triglyceride levels of the patient after the second dosing period is measured, wherein if the patient's fasting triglyceride levels are ≤ 1000 mg/dL while adhering to a low-fat diet, the patient is maintained at a daily dose of lomitapide, or a pharmaceutically acceptable salt thereof, of about 10 mg;

   e) if the patient's measured fasting triglyceride levels are > 1000 mg/dL while adhering to a low-fat diet after the second dosing period, the patient is to be orally administered a third daily dose of about 15 mg to about 20 mg of lomitapide, or a pharmaceutically acceptable salt thereof, for a third dosing period.

2. The ~~method~~use of claim 1, wherein the patient is a confirmed homozygote, compound heterozygote or double heterozygote for one or more loss-of-function mutations in genes causing FCS.

3. The ~~method~~use of any one of claims 1-2, wherein the patient has a history of pancreatitis.

4. The ~~method~~use of any one of claim 1-3, wherein the patient's post-heparin plasma lipoprotein lipase (LpL) activity is ≤ 20% of normal.

5. The ~~method~~use of any one of claim 1-4, wherein the patient has confirmed presence of LpL inactivating antibodies.

6. The ~~method~~use of any one of claim 1-5, wherein the patient's FCS is refractory to plasma LDL apheresis.

7. The ~~method~~use of any one of claim 1-6, wherein the lomitapide is to be administered as an adjunct to a low-fat diet and other lipid-lowering treatments (such as, statin, ezetimibe, nicotinic acid, bile acid sequestrant, fibrate or LDL apheresis).

8. The ~~method~~use of any one of claims 1-7, wherein the low-fat diet comprises a diet wherein less than 10% of patient's total calories are from fat.

9. The ~~method~~use of any one of claim 1-8, wherein the patient expresses a microsomal triglyceride transport protein gene (*MTP*) variant that improves the patient's response to lomitapide treatment compared to patients that do not express the *MTP* variant.

10. The ~~method~~use of any one of claims 1-9, wherein the first dosing period is at least two weeks.

11. The ~~method~~use of any one of claims 1-10, wherein the second dosing period is at least four weeks.

12. The ~~method~~use of any one of claims 1-11, wherein the third dosing period is at least four weeks.

13. The ~~method~~use of any one of claims 1-12, wherein if the patient's liver aminotransferase (ALT/AST) levels are ≥5 times the upper limit of normal (ULN) after the first dosing period, the second dosing period or the third dosing period, the patient is withdrawn from lomitapide treatment.

14. The ~~method~~use of claim 13, ~~further comprising determining~~wherein the patient's alkaline phosphatase, total bilirubin and INR are further determined.

15. The ~~method~~use of claim 14, ~~further comprising reducing~~ wherein the patient's dose is further reduced to the last dose that provided patient ALT/AST levels of < 3 times the ULN.

16. The ~~method~~use of claim 15, wherein the patient's dose is reduced from 10 mg to 5 mg.

17. The ~~method~~use of claim 15, wherein the patient's dose is reduced from 20 mg to 10 mg.

18. The ~~method~~use of claim 15, wherein the patient's dose is reduced from 20 mg to 5 mg.

19. The ~~method~~use of any one of claims 1-12, wherein if the patient's ALT/AST levels are from 3-5 times the ULN, ~~confirming~~ the patient's ALT/AST levels are confirmed to be 3-5 times the ULN within one week of the elevated ALT/AST test result.

20. The ~~method~~use of claim 19, wherein if the elevated ALT/AST test result is confirmed, ~~determining~~ the patient's alkaline phosphatase, total bilirubin and INR are determined.

21. The ~~method~~use of claim 20, ~~further comprising weekly testing~~ wherein the patient's ALT/AST levels, alkaline phosphatase, total bilirubin and INR are further tested weekly.

22. The ~~method~~use of claim 21, wherein if the patient's total bilirubin and INR increase, ALT/AST levels increase to > 5 times ULN or the patient's ALT/AST levels do not fall below < 3 times ULN within about 4 weeks, ~~withdrawing~~ the patient is withdrawn from lomitapide treatment.

23. The ~~method~~use of claim 22, ~~further comprising reducing~~ wherein the patient's dose is further reduced to the last dose that provided patient ALT/AST levels of < 3 times the ULN.

24. The ~~method~~use of claim 23, wherein the patient's dose is reduced from 10 mg to 5 mg.

25. The ~~method~~use of claim 23, wherein the patient's dose is reduced from 20 mg to 10 mg.

26. The ~~method~~use of claim 23, wherein the patient's dose is reduced from 20 mg to 5 mg.

27. The ~~method~~use any one of claims 1-26, ~~further comprising adjusting~~ wherein the patient's daily lomitapide dose is adjusted to provide fasting triglyceride levels ≤ 1000 mg/dL and ALT/AST levels ≤ 3 times the ULN.

28. The ~~method~~use of claim 27, wherein the patient's daily lomitapide dose is increased or decreased from every 2-4 weeks to provide fasting triglyceride levels ≤ 1000 mg/dL and ALT/AST levels ≤ 3 times the ULN.

29. The ~~method~~use of claim 28, wherein the daily dose that provides fasting triglyceride levels ≤ 1000 mg/dL and ALT/AST levels ≤ 3 times the ULN is selected from the group consisting of 5 mg, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg, and 60 mg.

30. The ~~method~~use of any one of claims 27-29, wherein the daily dose that provides fasting triglyceride levels ≤ 1000 mg/dL and ALT/AST levels ≤ 3 times the ULN is to be administered for at least 8 weeks.

31. The ~~method~~use of any one of claims 1-30, wherein the patient's change in hepatic fat liver is measured during the treatment period.

32. The ~~method~~use of any one of claims 1-31, wherein the lomitapide administration does not provide a clinically significant increase in hepatic fat liver during the treatment period.

33. The ~~method~~use of any one of claims 1-32, wherein the lomitapide administration substantially decreases the episodes of pancreatitis compared to prior to said treatment.

34. Use of lomitapide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for ~~A method of~~ treating familial chylomicronemia syndrome (FCS) in a pediatric patient in need thereof, ~~the method comprising~~wherein:

a) ~~orally administering~~ a first daily dose of about 2 mg to about 5 mg of lomitapide, or a pharmaceutically acceptable salt thereof, is to be administered to the patient for a first dosing period;

b) ~~measuring~~ the fasting triglyceride levels of the patient after the first dosing period is measured, wherein if the patient's fasting triglyceride levels are ≤ 1000 mg/dL, the patient is maintained at a daily dose of lomitapide, or a pharmaceutically acceptable salt thereof, of about 2 mg to about 5 mg;

c) if the patient's measured fasting triglyceride levels are > 1000 mg/dL after the first dosing period, the patient is to be orally administered a second daily dose of about 5 mg to about 10 mg of lomitapide, or a pharmaceutically acceptable salt thereof, for a second dosing period;

d) ~~measuring~~ the fasting triglyceride levels of the patient after the second dosing period is measured, wherein if the patient's fasting triglyceride levels are ≤ 1000 mg/dL, the patient is maintained at a daily dose of lomitapide, or a pharmaceutically acceptable salt thereof, of about 5 mg to about 10 mg;

e) if the patient's measured fasting triglyceride levels are > 1000 mg/dL after the second dosing period, the patient is to be orally administered a third daily dose of about 10 mg to about 20 mg of lomitapide, or a pharmaceutically acceptable salt thereof, for a third dosing period.

35. The ~~method~~use of claim 34, wherein the patient's age is from 5 to 10 years.

36. The ~~method~~use of claim 35, wherein the daily dose of lomitapide in the first dosing period is 2 mg, the daily dose of lomitapide in the second dosing period is 5 mg, and the daily dose of lomitapide in the third dosing period is 10 mg.

37. The ~~method~~use of claim 36, wherein the first dosing period is about 8 weeks, the second dosing period is about 4 weeks, and the third dosing period is about 4 weeks.

38. The ~~method~~use of claim 34, wherein the patient's age is from 11 to 15 years.

39. The ~~method~~use of claim 38, wherein the daily dose of lomitapide in the first dosing period is 2 mg, the daily dose of lomitapide in the second dosing period is 5 mg, and the daily dose of lomitapide in the third dosing period is 10 mg.

40. The ~~method~~use of claim 39, wherein the first dosing period is about 4 weeks, the second dosing period is about 4 weeks, and the third dosing period is about 4 weeks.

41. The ~~method~~use of claim 34, wherein the patient's age is 16 to 17 years.

42. The ~~method~~use of claim 41, wherein the daily dose of lomitapide in the first dosing period is 5 mg, the daily dose of lomitapide in the second dosing period is 10 mg, and the daily dose of lomitapide in the third dosing period is 20 mg.

43. The ~~method~~use of claim 42, wherein the first dosing period is about 4 weeks, the second dosing period is about 4 weeks, and the third dosing period is about 4 weeks.