articles in 2004 and 2005 strong evidence showed that fish-oil supplements had a substantial and beneficial effect on triglycerides that was greater with larger intakes of fish oil; most studies reported a net decrease of about 10-33%. Increasing the consumption of O3FA is considered a standard part of treatment of hypertriglyceridemia. In addition to over-the-counter supplements containing O3FA, there are three prescription products in the US: EPANOVA (a mixture of concentrated O3FA purified from crude fish oil containing EPA and DHA in their free fatty acid form at a total concentration of 50 - 60% EPA and 15 - 25% DHA in a gel capsule designed to release them in the ileum), LOVAZA (a gel capsule containing ethyl esters of O3FA sourced from fish oils, approximately 52% EPA ethyl ester and 42% DHA ethyl ester), and VASCEPA (a gel capsule containing EPA ethyl ester derived from fish oil). The term "an omega-3 fatty acid" or "O3FA" is used here to include both the free acids, particularly EPA or DHA, or a combination of omega-3 fatty acids, such as are derived from fish oils (as in EPANOVA and over-the-counter supplements), and also their esters (e.g. ethyl esters, as in LOVAZA and VASCEPA).

[0012] No drugs have been shown to be effective in the treatment of Type I hyperlipoproteinemia (LPL deficiency); and, despite the available therapies described above, including an appropriate (low-fat) diet, some patients with SHTG, including especially those with Type I or Type V hyperlipoproteinemia, remain refractory (that is, they fail to reach a TG level less than 1000 mg/dL, such as less than 10 mM, despite dietary changes and one or more of the therapies mentioned above).

[0013] A gene-replacement therapy for LPL deficiency, alipogene tiparvovec (GLYBERA), has been developed and was approved in Europe in 2012 (as an orphan drug), but has not yet been approved in the US. It is administered as a single treatment consisting of multiple injections into the leg muscles of 10^{12} genome copies of the gene in a virus protein shell – 47 injections for a 70 Kg patient: spinal or regional anesthesia (or deep sedation), is recommended for the procedure, and methylprednisolone pretreatment is required; and an immunosuppressive regimen is required for 3 days before and 12 weeks after the treatment. Pradigastat, an oral diacylglycerol acyltransferase-1 inhibitor, is currently in Phase 3 trials for FCS. CAT-2003, a conjugate of niacin with EPA, has completed three pilot Phase 2 trials in patients with HTG, including Type I hyperlipoproteinemia.

[0014] Apheresis is the removal of TGs and TG-rich lipoproteins from blood by therapeutic plasma exchange (TPE) or filtration. In TPE, blood is removed from the patient and the plasma

What is claimed is:

1. The use of a compound that is *(R)*-2-(4-((2-ethoxy-3-(4-(trifluoromethyl)phenoxy-propyl)thio)-2-methylphenoxy)acetic acid or a salt thereof in the manufacture of a medicament for treating severe hypertriglyceridemia in a subject.

2. The use of claim 1 where the MBX-8025 or an MBX-8025 salt is MBX-8025 L-lysine dihydrate salt.

3. The use of claim 1 or 2 where the medicament is intended for oral administration.

4. The use of any one of claims 1 to 3 where the dose of the compound is 20 – 200 mg/day when the dose is calculated as *(R)*-2-(4-((2-ethoxy-3-(4-(trifluoromethyl)phenoxypropyl)thio)-2-methylphenoxy)acetic acid.

5. The use of claim 4 where the dose of the compound is 50 – 200 mg/day when the dose is calculated as *(R)*-2-(4-((2-ethoxy-3-(4-(trifluoromethyl)phenoxypropyl)thio)-2-methylphenoxy)acetic acid.

6. The use of any one of the previous claims where the medicament is intended to be administered once/day.

7. The use of any one of claims 1 to 6 where the subject is also administered a fibrate.

8. The use of claim 7 where the fibrate is gemfibrozil, fenofibrate, choline fenofibrate, bezafibrate, or ciprofibrate.

9. The use of any one of claims 1 to 6 where the subject is also administered niacin.

10. The use of any one of claims 1 to 6 where the subject is also administered an omega-3 fatty acid.

11. The use of any one of claims 1 to 6 where the subject is also administered two or more of a fibrate, niacin, and an omega-3 fatty acid.

12. The use of claim 11 where the subject is also administered three of a fibrate, niacin, and an omega-3 fatty acid.

13. The use of any one of the previous claims where the subject is also treated by apheresis.

14. The use of any one of claims 1 to 13 where severe hypertriglyceridemia refers to a serum triglyceride level of at least 500 mg/dL.

15. The use of any one of claims 1 to 13 where severe hypertriglyceridemia refers to a serum triglyceride level of at least 750 mg/dL.

16. The use of any one of claims 1 to 13 where severe hypertriglyceridemia refers to a serum triglyceride level of at least 1000 mg/dL.

17. The use of any one of the previous claims where the severe hypertriglyceridemia is Type I or Type V hyperlipoproteinemia.

18. The use of claim 17 where the severe hypertriglyceridemia is Type I hyperlipoproteinemia.

19. The use of claim 17 where the severe hypertriglyceridemia is Type V hyperlipoproteinemia.

20. The useof any one of the previous claims where the severe hypertriglyceridemia is refractory.