IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Manku et al.
Appl. No.:	13/614,111
Filed:	September 13, 2012
Title:	Stable Pharmaceutical Compositions and Methods of Using Same
Art Unit:	1629
Examiner:	Sasan
Docket No.:	3717958-00248

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SUPPLEMENTAL RESPONSE TO NON-FINAL OFFICE ACTION DATED NOVEMBER 8, 2012

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

1 – 30 (Cancelled)

31. (Currently Amended) A method of treating mixed dyslipidemia in a subject on statin therapy ~~and~~ comprising, administering to the subject ~~an effective amount of~~ 2500 mg to 5000 mg of ethyl eicosapentaenoate daily, wherein upon 12 weeks of said administration the subject exhibits a reduction in ~~for a period effective to reduce~~ triglycerides of at least 15% and a reduction in [[and]] LDL-C of at least 5% compared to placebo control ~~in the subject~~.

32. (Currently Amended) The method of claim 31 ~~comprising, administering to the subject an effective amount of ethyl eicosapentaenoate daily to reduce~~ wherein upon 12 weeks of said administration the subject exhibits a reduction in fasting triglycerides [[by]] of at least [[10%]] 20% compared to placebo control ~~in the subject~~.

33. (Cancelled).

34. (Currently Amended) The method of claim 31 ~~comprising, administering to the subject an effective amount of ethyl eicosapentaenoate daily to reduce~~ wherein upon 12 weeks of said administration the subject exhibits a reduction in fasting apolipoprotein B compared to placebo control ~~in the subject~~.

35. (Currently Amended) The method of claim 31 ~~comprising, administering to the subject an effective amount of ethyl eicosapentaenoate daily to reduce~~ wherein upon 12 weeks of said administration the subject exhibits a reduction in fasting VLDL-C compared to placebo control ~~in the subject~~.

36. (Currently Amended) The method of claim 31 ~~comprising, administering to the subject an effective amount of ethyl eicosapentaenoate daily to reduce~~ wherein upon 12 weeks of said administration the subject exhibits a reduction in fasting VLDL-C [[by]] of at least 10% compared to placebo control ~~in the subject~~..

37. (Currently amended) The method of claim 36 where the ~~effective amount of~~ ethyl eicosapentaenoate is administered to the subject in ~~compositions~~ capsules each comprising about 900 mg to about 1 g of ethyl eicosapentaenoate.

38. (Currently Amended) The method of claim [[37]] 36 where the ~~effective amount of~~ ethyl eicosapentaenoate is administered to the subject in ~~compositions~~ capsules each comprising about 1 g of ethyl eicosapentaenoate.

REMARKS/ARGUMENTS

Claims 31, 32 and 34 - 38 are amended. Claim 33 is cancelled. No new matter is added.

Support for amended claim 31 can be found in the specification as filed at least at paragraphs 0018, 0109, 0112 and 0138.

With respect to the range of 2500 mg to 5000 mg, Applicants respectfully direct the Examiner's attention to *In re Wertheim*, 541 F.2d 257 (CCPA 1976) which states:

> In the context of this invention, in light of the description of the invention as employing solids contents within the range of 25-60% along with specific embodiments of 36% and 50%, we are of the opinion that, as a factual matter, persons skilled in the art would consider processes employing a 35-60% solids content range to be part of appellants' invention...

Applicants' specification discloses, *inter alia*, a daily dose of ethyl-EPA of 50 mg to about 5000 mg per day as well as a specific amount of 2500 mg per day at least at paragraph [0020]. In view of *Wertheim*, wherein disclosure of a range of 25-60% and a specific value of 36% properly supported a claim to the range of 35-60%, the presently claimed range of 2500 mg to 5000 mg is also properly supported by disclosure of a range of 50 mg – 5000 mg and disclosure of a specific embodiment of 2500 mg per day as discussed in paragraph [0018].

Support for amended claim 32 can be found in the specification as filed at least at paragraphs 0107 and 0109.

Support for amended claim 34 can be found in the specification as filed at least at paragraphs 0107 and 0113.

Support for amended claims 35 and 36 can be found in the specification as filed at least at paragraphs 0107 and 0114.

Support for amended claims 37 and 38 can be found in the specification as filed at least at paragraphs 0028 and 0018.

Attached herewith is a copy of Ballantyne et al., American Journal of Cardiology Volume 110, Issue 7, Pages 984-992, October 1, 2012 ("Ballantyne") setting forth details and results of the ANCHOR trial. ANCHOR was a multicenter, placebo-controlled, randomized, double-blind, 12-week clinical trial evaluating the efficacy and safety of Vascepa® (also referred to as AMR101 and icosapent ethyl) in patients at high risk for coronary heart disease (CHD). These

patients had residual high triglyceride (TG) levels in the range of 200 mg/dl to 499 mg/dl despite being on stable statin therapy for control of low density lipoprotein cholesterol (LDL-C in the range of 40-100 mg/dL). Patients in the ANCHOR study are said to have mixed dyslipidemia (as presently claimed), where the primary goal is to control LDL-C. As set forth in Ballantyne, in the Anchor study 4 g per day of Vascepa® unexpectedly reduced LDL-C compared to placebo control. By contrast with mixed dyslipidemic subjects in ANCHOR, subjects with triglyceride levels $\geq$ 500 mg/dL are characterized as having "very high triglycerides." For these patients the primary treatment goal is to lower the elevated triglyceride levels in order to prevent pancreatitis.

Applicants respectfully note that it is settled law that unexpected results, no matter when generated (even after a patent issues), can be relied on to support patentability of a claimed invention. In *Knoll Pharmaceutical Company, Inc. et al., v. Teva Pharmaceuticals USA, Inc.*, 367 F.3d 1381 (Fed. Cir. 2004), the Federal Circuit held that it was error for the district court to refuse to consider unexpected results evidence because "the unexpected benefits or results were discovered after the '252 patent had been issued." The Federal Circuit stated that " [t]here is no requirement that an inventions's properties and advantages were fully known before the patent application was filed , or that the patent application contains all of the work done in studying the invention, in order for that work to be introduce into evidence in response to litigation attack." *Id* at 1385. See also *Genetics Institute, LLC, v. Novartis Vaccines and Diagnostics, Inc.* No. 2010-1264 (Fed. Cir. 2011) ("evidence of unexpected results may be used to rebut a case of *prima facie* obviousness even if that evidence was obtained after the patent's filing or issue date.").

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