

SUMMARY

[0004a] In one aspect, the present disclosure refers to the use of a PCSK9 inhibitor in the manufacture of a pharmaceutical for treating coronary atherosclerosis, wherein the treatment comprises a first and a second therapy, wherein the second therapy is to be conducted on a subject that is on the first therapy, wherein the first therapy comprises a non-PCSK9 LDL-C lowering therapy, wherein the second therapy comprises the treatment with the PCSK9 inhibitor, wherein both the first and second therapies are to be conducted on the subject with an amount of the PCSK9 inhibitor and time sufficient to reverse coronary atherosclerosis in the subject, and wherein the first therapy is not the same as the second therapy.

[0004b] In another aspect, the present disclosure refers to the use of an anti-PCSK9 neutralizing antibody in the manufacture of a pharmaceutical for decreasing percent atheroma volume (PAV) in a subject, wherein the anti-PCSK9 neutralizing antibody is to be administered to a subject that has received at least a moderate level of treatment by a statin, in an amount sufficient and time sufficient to lower the LDL-C level to less than 90 mg/dL, thereby decreasing a percent atheroma volume (PAV) in the subject.

[0004c] In another aspect, the present disclosure refers to the use of an anti-PCSK9 neutralizing antibody in the manufacture of a pharmaceutical for

decreasing total atheroma volume (TAV) in a subject, wherein the anti-PCSK9 neutralizing antibody is to be administered to a subject that has received at least a moderate level of treatment by a statin, in an amount sufficient and time sufficient to lower the LDL-C level to less than 90 mg/dL, thereby decreasing a total atheroma volume in the subject.

[0004d] In another aspect, the present disclosure refers to the use of an anti-PCSK9 neutralizing antibody in the manufacture of a pharmaceutical for combination therapy for treating coronary atherosclerosis, wherein treating coronary atherosclerosis comprises regression of coronary atherosclerosis, wherein the treatment comprises: a. that at least the low dose statin treatment is to be conducted on a statin-intolerant subject; and b. that the amount of an anti-PCSK9 neutralizing antibody is to be administered to the subject, thereby treating coronary atherosclerosis; wherein the low dose statin treatment and administration of the anti-PCSK9 neutralizing antibody are to be conducted together or separately.

[0004e] In yet another aspect, the present disclosure refers to the use of a monoclonal antibody to human PCSK9 in the manufacture of a pharmaceutical for reducing an amount of atherosclerotic plaque in a subject, wherein the monoclonal antibody to human PCSK9 is to be administered to the subject having atherosclerotic plaque, wherein the subject is receiving optimized statin therapy, thereby reducing the amount of atherosclerotic plaque in the subject.

[0004f] In yet another aspect, the present disclosure refers to the use of evolocumab in the manufacture of a pharmaceutical for producing LDL-C lowering and regression of coronary atherosclerosis at a dose that is well tolerated, wherein at least a moderate intensity of a statin therapy is to be administered to a subject; an adequate amount of evolocumab is to be administered to the subject such that the subject's LDL-C levels drop to no more than 40 mg/dL; and the subject's LDL-C levels is to be maintained at no more than 40 mg/dL for at least one year; wherein evolocumab and the statin therapy are to be conducted together or separately.

[0004g] In yet another aspect, the present disclosure refers to the use of a PCSK9 inhibitor in the manufacture of a pharmaceutical for decreasing percent atheroma volume (PAV) in a subject, wherein the PCSK9 inhibitor is to be administered to a subject that has received at least a moderate level of treatment by a non-PCSK9 LDL-C lowering agent, in an amount sufficient and time sufficient to lower the LDL-C level to less than 90 mg/dL, thereby decreasing a percent atheroma volume (PAV) in the subject.

[0004h] In yet another aspect, the present disclosure refers to the use of a PCSK9 inhibitor in the manufacture of a pharmaceutical for decreasing total atheroma volume (TAV) in a subject, wherein the PCSK9 inhibitor is to be administered to a subject that has received at least a moderate level of treatment

by a non-PCSK9 LDL-C lowering agent, in an amount sufficient and time sufficient to lower the LDL-C level to less than 90 mg/dL, thereby decreasing a total atheroma volume in the subject.

[0004i] In yet another aspect, the present disclosure refers to the use of a PCSK9 inhibitor in the manufacture of a pharmaceutical for combination therapy for producing LDL-C lowering and regression of coronary atherosclerosis at a dose that is well tolerated, wherein at least a moderate intensity of a non-PCSK9 LDL-C lowering therapy is to be conducted on a subject; an adequate amount of the PCSK9 inhibitor is to be administered to the subject such that the subject's LDL-C levels drop to no more than 40 mg/dL; and the subject's LDL-C levels is to be maintained at no more than 40 mg/dL for at least one year; wherein administration of the PCSK9 inhibitor and the non-PCSK9 LDL-C lowering therapy are to be conducted together or separately.

[0005] In some examples, a method of treating coronary atherosclerosis is provided. The method comprises a) identifying a subject that is on a first therapy, wherein the first therapy comprises a non-PCSK9 LDL-C lowering therapy, and b) administering a second therapy to the subject. The second therapy comprises a PCSK9 inhibitor therapy. Both the first and second

WHAT IS CLAIMED IS:

1. Use of a PCSK9 inhibitor in the manufacture of a pharmaceutical for treating coronary atherosclerosis, wherein
the treatment comprises a first and second therapy, wherein the second therapy is to be conducted on a subject that is on the first therapy, wherein the first therapy comprises a non-PCSK9 LDL-C lowering therapy, wherein the second therapy comprises the treatment with the PCSK9 inhibitor, wherein both the first and second therapies are to be conducted on the subject with an amount of the PCSK9 inhibitor and time sufficient to reverse coronary atherosclerosis in the subject, and wherein the first therapy is not the same as the second therapy.
2. Use of an anti-PCSK9 neutralizing antibody in the manufacture of a pharmaceutical for decreasing percent atheroma volume (PAV) in a subject, wherein
the anti-PCSK9 neutralizing antibody is to be administered to a subject that has received at least a moderate level of treatment by a statin, in an amount sufficient and time sufficient to lower the LDL-C level to less than 90 mg/dL, thereby decreasing a percent atheroma volume (PAV) in the subject.
3. Use of an anti-PCSK9 neutralizing antibody in the manufacture of a pharmaceutical for decreasing total atheroma volume (TAV) in a subject, wherein
the anti-PCSK9 neutralizing antibody is to be administered to a subject that has received at least a moderate level of treatment by a statin, in an amount sufficient and time sufficient to lower the LDL-C level to less than 90 mg/dL, thereby decreasing a total atheroma volume in the subject.
4. Use of an anti-PCSK9 neutralizing antibody in the manufacture of a pharmaceutical for combination therapy for treating coronary atherosclerosis, wherein treating coronary atherosclerosis comprises regression of coronary atherosclerosis, wherein the treatment comprises:
 - a. that at least a low dose statin treatment is to be conducted on a statin-intolerant subject; and

- b. that the amount of an anti-PCSK9 neutralizing antibody is to be administered to the subject, thereby treating coronary atherosclerosis; wherein the low dose statin treatment and administration of the anti-PCSK9 neutralizing antibody are to be conducted together or separately.
- 5. Use of a monoclonal antibody to human PCSK9 in the manufacture of a pharmaceutical for reducing an amount of atherosclerotic plaque in a subject, wherein the monoclonal antibody to human PCSK9 is to be administered to the subject having atherosclerotic plaque, wherein the subject is receiving optimized statin therapy, thereby reducing the amount of atherosclerotic plaque in the subject.
- 6. Use of evolocumab in the manufacture of a pharmaceutical for combination therapy for producing LDL-C lowering and regression of coronary atherosclerosis at a dose that is well tolerated, wherein
 - at least a moderate intensity of a statin therapy is to be administered to a subject;
 - an adequate amount of evolocumab is to be administered to the subject such that the subject's LDL-C levels drop to no more than 40 mg/dL; and
 - the subject's LDL-C levels is to be maintained at no more than 40 mg/dL for at least one year; wherein administration of evolocumab and the statin therapy are to be conducted together or separately.
- 7. Use of a PCSK9 inhibitor in the manufacture of a pharmaceutical for decreasing percent atheroma volume (PAV) in a subject, wherein
 - the PCSK9 inhibitor is to be administered to a subject that has received at least a moderate level of treatment by a non-PCSK9 LDL-C lowering agent, in an amount sufficient and time sufficient to lower the LDL-C level to less than 90 mg/dL, thereby decreasing a percent atheroma volume (PAV) in the subject.
- 8. Use of a PCSK9 inhibitor in the manufacture of a pharmaceutical for decreasing total atheroma volume (TAV) in a subject, wherein
 - the PCSK9 inhibitor is to be administered to a subject that has received at least a moderate level of treatment by a non-PCSK9 LDL-C lowering agent, in an

amount sufficient and time sufficient to lower the LDL-C level to less than 90 mg/dL, thereby decreasing a total atheroma volume in the subject.

9. Use of a PCSK9 inhibitor in the manufacture of a pharmaceutical for combination therapy for producing LDL-C lowering and regression of coronary atherosclerosis at a dose that is well tolerated, wherein:

at least a moderate intensity of a non-PCSK9 LDL-C lowering therapy is to be conducted on a subject;

an adequate amount of the PCSK9 inhibitor is to be administered to the subject such that the subject's LDL-C levels drop to no more than 40 mg/dL; and

the subject's LDL-C levels is to be maintained at no more than 40 mg/dL for at least one year; wherein administration of the PCSK9 inhibitor and the non-PCSK9 LDL-C lowering therapy are to be conducted together or separately.

10. The use of any one of claims 1 or 7-9 wherein the PCSK9 inhibitor is selected from the group consisting of neutralizing antibodies to PCSK9 and RNAi to PCSK9.
11. The use of claim 10, wherein the neutralizing antibody to PCSK9 comprises evolocumab, alirocumab, bococizumab, REGN728, RG7652, LY3015014, LGT209, 1D05, or 1B20, or wherein the RNAi to PCSK9 comprises ALN-PCSc.
12. The use of any one of claims 1-5 or 7-9, wherein the PCSK9 inhibitor, or the anti-PCSK9 neutralizing antibody, or the monoclonal antibody to human PCSK9, or the neutralizing antibody to PCSK9 comprises evolocumab, alirocumab, bococizumab, REGN728, RG7652, LY3015014, LGT209, 1D05, or 1B20.
13. The use of any of claims 1 or 7-12, wherein the non-PCSK9 LDL-C lowering therapy or agent is selected from the group consisting of a statin, a selective cholesterol absorption inhibitor, a lipid lowering therapy fibrate or fibric acid derivative, a resin, cholestyramine, cholestipol, cholesevelan HCl, or a combination thereof.