including patients with and without established CVD (Holman RR, et al., *Effects of Once-Weekly Exenatide on Cardiovascular Outcomes in Type 2 Diabetes*, 377 N. ENGL. J. MED. 1228-1239 (2017) ("EXCSEL")). On the other hand, albiglutide, liraglutide and semaglutide were found to reduce the risk of major adverse cardiovascular events in patient populations comprised entirely (albiglutide) or predominantly (liraglutide and semaglutide) of patients with established CVD. (Hernandez AF, et al., *Albiglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes and Cardiovascular Disease (Harmony Outcomes): a Double-blind, Randomized Placebo-controlled Trial*, 392 LANCET 1519-1529 (2018) ("Harmony Outcomes"); Marso SP, et al., *Liraglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes*, 375 N. ENGL. J. MED. 311-322 (2016) ("LEADER")); Marso SP, et al., *Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes* 375 N. ENGL. J. MED. 1834–1844 (2016) ("SUSTAIN-6")).

Despite the therapies described above, the need for new treatment options capable of reducing the risk of major adverse cardiovascular events in T2DM patients remains. In particular, the need remains for treatment options capable of reducing the risk of major adverse cardiovascular events in T2DM patients who do not already have established cardiovascular disease.

Summary

In an aspect of the present disclosure, there is provided a use of dulaglutide in the manufacture of a medicament for reducing the risk of non-fatal stroke in a patient with type 2 diabetes mellitus, wherein the patient has type 2 diabetes mellitus and multiple cardiovascular risk factors without established cardiovascular disease, and wherein a therapeutically effective amount of

dulaglutide is to be administered to the patient once weekly.

WE CLAIM:

1. Use of dulaglutide in the manufacture of a medicament for reducing the risk of non-fatal stroke in a patient with type 2 diabetes mellitus, wherein the patient has type 2 diabetes mellitus and multiple cardiovascular risk factors without established cardiovascular disease, and wherein a therapeutically effective amount of dulaglutide is to be administered to the patient once weekly.

2. The use of claim 1, wherein the medicament is for improving glycemic control and reducing the risk of first occurrence of a non-fatal stroke in a patient with type 2 diabetes mellitus, wherein a therapeutically effective amount of dulaglutide is to be administered to the patient once weekly.

3. The use of claim 1 or 2, wherein the cardiovascular risk factors are selected from the group consisting of (a), (b), (c), (d) and (e):

(a) tobacco use;

(b) at least 1 of:

i) use of at least 1 approved lipid modifying therapy to treat hypercholesterolemia; or

ii) a documented untreated low-density lipoprotein cholesterol (LDL-C) ≥3.4 mmol/L (130 mg/dL) within the past 6 months;

(c) at least 1 of:

i) high-density lipoprotein cholesterol (HDL-C) measurement within the past 6 months of: <1.0 mmol/L (40 mg/dL) for men; and <1.3 mmol/L (50 mg/dL) for women; or

ii) triglycerides ≥2.3 mmol/L (200 mg/dL) within the past 6 months;

(d) at least 1 of:

i) use of at least 1 blood pressure medication to treat hypertension; or

ii) untreated systolic blood pressure (SBP) ≥140 mm Hg or diastolic blood pressure (DBP) ≥95 mmHg; and

(e) measured waist-to-hip ratio >1.0 for men and >0.8 for women.

4. The use of any one of claims 1-3 wherein there is reduction of the risk of a non-fatal stroke by at least 10%.

5. The use of any one of claims 1-4 wherein the therapeutically effective amount of dulaglutide is 1.5 mg, 3.0 mg or 4.5 mg.

6. The use of any one of claims 1-5 wherein the therapeutically effective amount of dulaglutide is 1.5 mg.

7. The use of any one of claims 1-6 wherein the once weekly administration of dulaglutide is continued for approximately 5 years.

8. The use of any one of claims 1-7 wherein the dulaglutide is for use with one or more of: an ACE inhibitor; an ARB; a beta blocker; a calcium channel blocker; a diuretic; an antithrombotic agent; acetylsalicyclic acid (ASA) or a statin.