Administration in Healthy Subjects." 2390-PUB, A624, ADA-2017; Portron, A. *et al*. "Pharmacodynamics, pharmacokinetics, safety and tolerability of the novel dual glucose-dependent insulinotropic polypeptide/glucagon-like peptide-1 agonist RG7697 after single subcutaneous administration in healthy subjects." *Diabetes Obes. Metab*. 2017;19:14446-1453. The dose limitation associated with gastrointestinal adverse events may prevent dosing to the desired effective dose, may compromise patient compliance with treatment, and may limit the effectiveness of the treatment regimen.

There is a need for novel doses of tirzepatide to provide desired glycemic control, as evidenced for example, by further reductions of HbA1c, and/or weight loss, while maintaining an acceptable profile of safety and adverse events. There is also a need for a novel dosing regimen of tirzepatide to provide desired glycemic control, as evidenced for example, by further reductions of HbA1c, and/or weight loss, while maintaining an acceptable profile of safety and adverse events. Also, there is a need for a GIP/GLP1 dual agonist treatment option for a condition selected from chronic kidney disease, atherosclerosis, NAFLD, and NASH. Furthermore, there is a desire for a treatment to cure diabetes by preventing, reducing severity of, or inducing remission of diabetes. There is a desire for a treatment to reduce or delay progression of diabetes.

Summary

In one aspect of the present disclosure, there is provided a use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating type 2 diabetes in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

In another aspect of the present disclosure, there is provided a use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for inducing remission or regression of diabetes in a patient in need thereof, wherein: an

escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

In a further aspect of the present disclosure, there is provided a use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for preventing diabetes in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

In another aspect of the present disclosure, there is provided a use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for improving weight management in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

In a further aspect of the present disclosure, there is provided a use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating chronic kidney disease, wherein an effective amount of tirzepatide or a pharmaceutically acceptable salt thereof, is to be administered to a patient in need of such treatment.

In another aspect of the present disclosure, there is provided a use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating atherosclerosis, wherein an effective amount of tirzepatide or a pharmaceutically acceptable salt thereof, is to be administered to a patient in need of such treatment.

In a further aspect of the present disclosure, there is provided a use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating nonalcohol fatty liver disease, wherein an effective amount of tirzepatide or a pharmaceutically acceptable salt thereof, is to be administered to a patient in need of such treatment.

In another aspect of the present disclosure, there is provided a use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating nonalcohol steatohepatitis, wherein an effective amount of tirzepatide or a pharmaceutically acceptable salt thereof is to be administered to a patient in need of such treatment.

In a further aspect of the present disclosure, there is provided a use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating obesity in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

In another aspect of the present disclosure, there is provided a use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating diabetic kidney disease in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected

WE CLAIM:

1. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating type 2 diabetes in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

2. The use of claim 1 for treating type 2 diabetes in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

3. The use as claimed by claim 1 or 2, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

4. The use of claim 1 or 2, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

5. The use of claim 1 or 2, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.

6. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for inducing remission or regression of diabetes in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance

dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

7. The use of claim 6 to induce remission or regression of diabetes in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

8. The use of claim 6 or 7, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

9. The use of claim 6 or 7, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

10. The use of claim 6 or 7, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.

11. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for preventing diabetes in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

12. The use of claim 11 to prevent diabetes in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is

selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

13. The use of claim 11 or 12, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

14. The use of claim 11 or 12, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

15. The use of claim 11 or 12, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.

16. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for improving weight management in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

17. The use of claim 16 to improve weight management in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

18. The use of claim 16 or 17, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

19. The use of claim 16 or 17, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

20. The use of claim 16 or 17, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.

21. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating chronic kidney disease, wherein an effective amount of tirzepatide or a pharmaceutically acceptable salt thereof, is to be administered to a patient in need of such treatment.

22. The use of claim 21, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

23. The use of claim 21 for treating chronic kidney disease in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

24. The use of claim 22 or 23, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

25. The use of claim 22 or 23, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

26. The use of claim 22 or 23, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.

27. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating atherosclerosis, wherein an effective amount of tirzepatide or a pharmaceutically acceptable salt thereof, is to be administered to a patient in need of such treatment.

28. The use of claim 27, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

29. The use of claim 27 for treating atherosclerosis in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

30. The use of claim 28 or 29, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

31. The use of claim 28 or 29, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

32. The use of claim 28 or 29, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.

33. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating nonalcohol fatty liver disease, wherein an effective amount of tirzepatide or a pharmaceutically acceptable salt thereof, is to be administered to a patient in need of such treatment.

34. The use of claim 33, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the

maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

35. The use of claim 33 for treating nonalcohol fatty liver disease in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

36. The use of claim 34 or 35, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

37. The use of claim 34 or 35, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

38. The use of claim 34 or 35, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.

39. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating nonalcohol steatohepatitis, wherein an effective amount of tirzepatide or a pharmaceutically acceptable salt thereof is to be administered to a patient in need of such treatment.

40. The use of claim 39, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

41. The use of claim 39 for treating nonalcohol steatohepatitis in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the

escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

42. The use of claim 40 or 41, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

43. The use of claim 40 or 41, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

44. The use of claim 40 or 41, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.

45. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating obesity in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

46. The use of claim 45 for treating obesity in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

47. The use of claim 45 or 46, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

48. The use of claim 45 or 46, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

49. The use of claim 45 or 46, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.

50. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating diabetic kidney disease in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

51. The use of claim 50 for treating diabetic kidney disease in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

52. The use of claim 50 or 51, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

53. The use of claim 50 or 51, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

54. The use of claim 50 or 51, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.