

CLAIMS

1. Use of a BTK inhibitor, e.g. an irreversible BTK inhibitor, e.g. LOU064 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prevention of an IgE driven allergic reaction to one or more allergens, e.g. food, drug, or venom allergic reaction, e.g. treatment or prevention of an anaphylactic reaction.

2. The use according to claim 1 wherein one or more allergens comprises or is food allergen.

3. The use according to claim 2 wherein food allergen is selected from peanut, tree nut, milk, wheat, egg, soy, sesame, fish and shellfish, particularly peanut.

4. The use according to claim 1, 2 or 3 wherein LOU064 is to be administered at a dose from about 20mg to about 200mg daily.

5. The use according to claim 4 wherein LOU064 is to be administered at a dose from about 10mg twice daily to about 100mg twice daily.

6. The use according to claim 5 wherein LOU064 is to be administered at a dose of about 10mg twice daily.

7. The use according to claim 5 wherein LOU064 is to be administered at a dose of about 25mg twice daily.

8. The use according to claim 5 wherein LOU064 is to be administered at a dose of about 100mg twice daily.

9. The use according to any one of claims 1 to 8 wherein LOU064 is to be administered for a short term, e.g. less than 6 months, preferably less than 3 months or less than 1 month.

10. The use according to claim 9 wherein LOU064 is to be administered during up to 18 weeks, e.g. during 4, 10, 12, 16 or 18 weeks.

11. The use according to any one of claims 1 to 8 wherein LOU064 is to be administered for a long term, e.g. more than 6 months, preferably one year or more than a year.

12. The use according to claim 10 or 11 wherein LOU064 is to be administered as a monotherapy.

13. The use according to any one of claims 1 to 12, wherein LOU064 is not to be administered concomitantly with a strong inhibitor of CYP3A, e.g. a strong inhibitor of CYP3A4.

14. The use according to any one of claims 1 to 11 and 13, wherein LOU064 is to be co-administered with a therapeutic agent.

15. The use according to claim 14, wherein LOU064 is to be co-administered with corticosteroid and/or an immunosuppressor (e.g. inhaled corticosteroid), a leukotriene receptor antagonist (LTRA), a short-acting beta agonist (SABA) or a long-acting beta agonist (LABA).

16. The use according to any one of claims 1 to 11 and 13, wherein LOU064 is to be co-administered with an oral immunotherapy (OIT), sublingual immunotherapy (SLIT), epicutaneous immunotherapy (EPIT), preferably an OIT.

17. The use according to claim 16 wherein LOU064 is an adjunct to oral immunotherapy (OIT), sublingual immunotherapy (SLIT), epicutaneous immunotherapy (EPIT), preferably an OIT .

18. The use according to claim 16 or 17 wherein the oral immunotherapy is a peanut protein (e.g. Palforzia™).

19. The use according to any one of claims 16 to 18, wherein LOU064 is to be administered starting at least 2 days (e.g. at least 2-14 days) prior to administration of the oral immunotherapy.

20. The use according to claim 19 wherein the BTK inhibitor, e.g. LOU064, is to be administered during the escalation phase of the immunotherapy treatment.

21. The use according to any one of claims 1 to 20 wherein the use is prevention of an IgE driven allergic reaction.

22. The use according to any one of claims 1 to 21 for preventing anaphylaxis after accidental exposure to any allergens (e.g. food allergen).

23. The use according to claim 21 or 22 wherein LOU064 achieves maximal prevention after a minimum of 2 days (e.g. after 2-14 days, preferably after 2-7 days) of treatment.

24. The use according to any one of claims 1 to 23 wherein the patient is selected according to one or more of the following criteria:

- (a) Male and female patients, 6 years of age or older (e.g. 6 to 11 years of age, 12-17 years of age or 18-55 years of age);
- (b) Documented medical history of allergy to foods, including but not limited to peanuts, tree nuts, wheat, egg, milk, soy, fish and shellfish;

- (c) Positive allergen-specific IgE (e.g. peanut sIgE ≥ 6 kUA/L at Screening); and
- (d) Skin prick test positive for allergen to which patient is allergic (e.g. defined as the average diameter (longest diameter and mid-point orthogonal diameter) ≥ 4 mm wheal compared to the negative control).

25. The use according to any one of claims 1 to 24 wherein the patient is an adult patient (18 years of age and above) or an adolescent (12-17 years of age).

26. The use according to any one of claims 1 to 24 wherein the patient is a child of age 2 to 11, e.g. age 2-5 or age 6-11.

27. The use according to any one of claims 1 to 26 wherein at least one of the following applies:

- a. At least 90% of the treated patients do not exhibit an allergic reaction upon food challenge with 600mg of peanut protein
- b. At least 90% of the treated patients do not exhibit an allergic reaction upon food challenge with 1000mg of peanut protein
- c. At least 80% of the treated patients do not exhibit an allergic reaction upon food challenge with 3000mg of peanut protein;

after up to 4 weeks of treatment with LOU064 (e.g. after 1 week, or after 2 weeks, or after 3 weeks or after 4 weeks).

28. The use according to any one of claims 1 to 27 wherein the patient achieves a reduction from baseline in the total domain score FAQLQ of 0.45-0.5.

29. The use according to any one of claims 1 to 28 wherein the patient achieves a reduction from baseline in the total domain score FAIM.

30. The use according to any one of claims 1 to 29 wherein in a double-blind placebo-controlled food challenge with 600mg of an allergen (e.g peanut allergen), the observed difference in the responder rate between the treated and non-treated patients is superior to 35%, wherein the responder rate is defined as no more than a mild response to 600mg oral food challenge.

31. The use according to any one of claims 1 to 30 wherein by week 12 or by week 24 of treatment the levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and lipase do not change by more than 10% as compared to the baseline level at the start of therapy.

32. The use according to any one of claims 1 to 31, wherein LOU064 is to be administered in the form of a suitable oral pharmaceutical formulation comprising nanosized particles of LOU064.

33. The use according to any one of claims 1 to 32, wherein LOU064 is to be administered in the form of a suitable oral pharmaceutical formulation comprising nanosized particles of LOU064 having a mean particle size as measured by PCS of between about 50 nm to about 750 nm.

34. The use according to any one of claims 1 to 33, wherein LOU064 is to be administered in the form of a suitable oral pharmaceutical formulation comprising LOU064 and binder at a weight ratio of about 2 : 1.

35. The use according to any one of claims 1 to 34, wherein LOU064 is to be administered in the form of a suitable oral pharmaceutical formulation comprising LOU064, binder and surfactant at a weight ratio of about 2 : 1 : 0.08.

36. The use according to any one of claims 1 to 33, wherein LOU064 is to be administered in the form of a suitable oral pharmaceutical formulation comprising LOU064 and binder at a weight ratio of about 1 : 1.

37. The use according to any one claims 1 to 34 and 36, wherein LOU064 is to be administered in the form of a suitable oral pharmaceutical formulation comprising LOU064, binder and surfactant at a weight ratio of about 1 : 1 : 0.05.

38. The use according to any one of claims 1 to 37, wherein LOU064 is to be administered in the form of a suitable oral pharmaceutical formulation comprising LOU064, polyvinylpyrrolidone-vinyl acetate copolymer as a binder and sodium lauryl sulfate as a surfactant.

39. The use according to any one of claims 1 to 38 wherein LOU064 is a crystalline form of the anhydrous free base characterized by an x-ray powder diffraction pattern comprising one or more representative peaks in terms of 2θ selected from the group consisting of $7.8 \pm 0.2^\circ 2\theta$, $9.2 \pm 0.2^\circ 2\theta$, $12.0 \pm 0.2^\circ 2\theta$, $13.6 \pm 0.2^\circ 2\theta$, $15.6 \pm 0.2^\circ 2\theta$, $16.0 \pm 0.2^\circ 2\theta$, $17.8 \pm 0.2^\circ 2\theta$, $18.3 \pm 0.2^\circ 2\theta$, $18.7 \pm 0.2^\circ 2\theta$, $19.2 \pm 0.2^\circ 2\theta$, $19.9 \pm 0.2^\circ 2\theta$, $22.1 \pm 0.2^\circ 2\theta$, $23.4 \pm 0.2^\circ 2\theta$, $23.9 \pm 0.2^\circ 2\theta$, $24.8 \pm 0.2^\circ 2\theta$, $25.2 \pm 0.2^\circ 2\theta$, $25.5 \pm 0.2^\circ 2\theta$, $27.2 \pm 0.2^\circ 2\theta$, and $29.6 \pm 0.2^\circ 2\theta$, when measured at a temperature of about 25°C and an x-ray wavelength, λ , of 1.5405 Å.

40. Use of LOU064 or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment or prevention of IgE driven allergic reaction, wherein preferably LOU064 is to be administered at a dose of about 10 mg twice daily to about 100 mg twice daily.