CLAIMS

WHAT IS CLAIMED IS:

1. Use of plinabulin, or a pharmaceutically acceptable salt thereof, in preparation of a medicament for treating, preventing, reducing, or shortening a duration of an immunotherapy related adverse event in a subject, wherein the subject is to be administered one or more immune checkpoint inhibitor.

2. The use according to claim 1, wherein the one or more immune checkpoint inhibitor is selected from the group consisting of a PD-1 inhibitor, a PD-L1 inhibitor, a PD-L2 inhibitor, a PD-L3 inhibitor, a PD-L4 inhibitor, a CTLA-4 inhibitor, a LAG3 inhibitor, a B7-H3 inhibitor, a B7-H4 inhibitor, a KIR inhibitor and a TIM3 inhibitor.

3. The use according to claim 1 or 2, wherein the one or more immune checkpoint inhibitor is a PD-1 inhibitor.

4. The use according to claim 1 or 2, wherein the one or more immune checkpoint inhibitor is a PD-L1 inhibitor.

5. The use according to claim 1 or 2, wherein the one or more immune checkpoint inhibitor is a CTLA-4 inhibitor.

6. The use according to claim 1, wherein the subject is to be administered a first immune checkpoint inhibitor and a second immune checkpoint inhibitor, and wherein the first immune checkpoint inhibitor is different from the second immune checkpoint inhibitor.

7. The use according to claim 6, wherein the first and the second immune checkpoint inhibitor is independently an inhibitor selected from the group consisting of a PD-1 inhibitor, a PD-L1 inhibitor, a PD-L2 inhibitor, a PD-L3 inhibitor, a PD-L4 inhibitor, a CTLA-4 inhibitor, a LAG3 inhibitor, a B7-H3 inhibitor, a B7-H4 inhibitor, a KIR inhibitor and a TIM3 inhibitor.

8. The use according to claim 7, wherein the first immune checkpoint inhibitor is a PD-1 inhibitor or a PD-L1 inhibitor, and the second immune checkpoint inhibitor is a CTLA-4 inhibitor.

9. The use according to claim 1, wherein the immunotherapy is a monotherapy that comprises administering a single immune checkpoint inhibitor selected from the group consisting of a PD-1 inhibitor, a PD-L1 inhibitor, a PD-L2 inhibitor, a PD-L3 inhibitor, a PD-L4 inhibitor, a CTLA-4 inhibitor, a LAG3 inhibitor, a B7-H3 inhibitor, a B7-H4 inhibitor, a KIR inhibitor and a TIM3 inhibitor.

10. The use according to claim 9, wherein the immune checkpoint inhibitor is a PD-1 inhibitor.

11. The use according to claim 9, wherein the immune checkpoint inhibitor is a PDL1 inhibitor.

12. The use according to claim 9, wherein the immune checkpoint inhibitor is a CTLA-4 inhibitor.

13. The use according to claim 1, wherein the immunotherapy is a combination therapy, and wherein the combination therapy comprises administering two or more immune checkpoint inhibitors selected from the group consisting of a PD-1 inhibitor, a PD-L1 inhibitor, a PD-L2 inhibitor, a PD-L3 inhibitor, a PD-L4 inhibitor, a CTLA-4 inhibitor, a LAG3 inhibitor, a B7-H3 inhibitor, a B7-H4 inhibitor, a KIR inhibitor and a TIM3 inhibitor.

14. The use according to claim 13, wherein the combination therapy comprises administering a PD-1 inhibitor and a CTLA-4 inhibitor.

15. The use according to claim 13, wherein the combination therapy comprises administering a PD-L1 inhibitor and a CTLA-4 inhibitor.

16. The use according to any one of claims 13 to 15, wherein the amount of plinabulin is in the range of about 1 mg to about 100 mg.

17. The use according to any one of claims 1 to 16, wherein the immunotherapy related adverse event is a grade 3/4 adverse event.

18. The use according to any one of claims 1 to 17, comprising identifying a subject at risk of developing a grade 3/4 immunotherapy related adverse event.

19. The use according to any one of claims 1 to 18, wherein the immunotherapy related adverse event is selected from the group consisting of Pneumonitis, Colitis, Hepatitis, Endocrinopathies, Nephritis and Renal Dysfunction, Skin Adverse Reactions, and Encephalitis

20. The use according to claim 20, wherein the immunotherapy related adverse event is pancreatitis, and wherein the one or more immune checkpoint inhibitor to be administered is a PD-1 inhibitor and a CTLA-4 inhibitor.

21. The use according to any one of claims 1 to 19, wherein the immunotherapy related adverse event is the immunotherapy induced inflammation.

22. The use according to claim 21, wherein the immunotherapy induced inflammation is selected from the group consisting of pancreatitis, pneumonitis, colitis, hepatitis, nephritis and

renal dysfunction, hypothyroidism and hyperthyroidism, uveitis, demyelination, autoimmune neuropathy, adrenal insufficiency, facial and abducens nerve paresis, hypophysitis, diabetic ketoacidosis, hypopituitarism, Guillain-Barré syndrome, myasthenic syndrome, hypothysitis, thyroiditis, type 1 diabetes mellitus, arthritis, exfoliative dermatitis, bullous pemphigoid, myositis, myasthenia gravis, vasculitis, hemolytic anemia, partial seizures arising in a patient with inflammatory foci in brain parenchyma, dermatitis, rash, pruritus, meningitis, sarcoidosis, pericarditis, fatal myocarditis, angiopathy, temporal arteritis, vasculitis, polymyalgia rheumatica, conjunctivitis, blepharitis, episcleritis, scleritis, iritis, leukocytoclastic vasculitis, erythema multiforme, psoriasis, arthritis, autoimmune thyroiditis, neurosensory hypoacusis, autoimmune central neuropathy, myositis, polymyositis, and ocular myositis, and hemolytic anemia.

23. The use according to any one of claims 1 to 22, further comprising identifying a subject having the immunotherapy related adverse event prior to administering an effective amount of plinabulin to the subject.

24. The use according to any one of claims 1 to 23, further comprising identifying a subject having a grade 3/4 immunotherapy related adverse event prior to administering an effective amount of plinabulin to the subject

25. The use according to any one of claims 1 to 24, wherein the incidence of immunotherapy related adverse event is reduced by at least 10%.

26. The use according to any one of claims 1 to 25, wherein the severity of immunotherapy related adverse event is reduced by at least 10%.

27. The use according to any one of claims 1-26, wherein the subject also receives a radiation therapy.