CLAIMS

1. A pharmaceutical composition, comprising:

one or more liposome suspended in an external medium, said liposome comprising:

(a) an external lipid bilayer, comprising at least one vesicle-forming phospholipid; and

(b) an internal aqueous medium, comprising treprostinil and a salt to provide a pH gradient between the internal aqueous medium and the external medium,

wherein the weight ratio of treprostinil to the at least one vesicle-forming phospholipid (i.e., T/P ratio) is equal to or higher than about 0.035 and about less than 60% of the treprostinil is released within 2 hours after the administration of the pharmaceutical composition and more than 80% of the treprostinil is released more than 2 hours to about 72 hours after the administration of the pharmaceutical composition.

2. The pharmaceutical composition of claim 1, wherein the T/P ratio is equal to or higher than about 0.041.

3. The pharmaceutical composition of claim 1, wherein the T/P ratio is equal to or higher than about 0.052.

4. The pharmaceutical composition of claim 1, wherein the T/P ratio is equal to or higher than about 0.056.

5. The pharmaceutical composition of claim 1, wherein the external lipid bilayer further comprising a sterol.

6. The pharmaceutical composition of claim 5, wherein said sterol is cholesterol, cholesterol hexasuccinate, ergosterol, lanosterol or any combination thereof.

7. The pharmaceutical composition of claim 1, wherein the salt to provide a pH gradient is a weak acid salt.

8. The pharmaceutical composition of claim 7, wherein the weak acid salt is carboxylic acid salt or bicarbonate salt.

9. The pharmaceutical composition of claim 8, wherein the carboxylic acid salt is formate, acetate, propionate, butyrate, isobutyrate, valerate, isovalerate, benzoate or any combination thereof.

10. The pharmaceutical composition of claim 9, wherein the acetate is sodium acetate, calcium acetate or any combination thereof.

11. The pharmaceutical composition of claim 1, wherein the salt to provide a pH gradient is an amino acid.

12. The pharmaceutical composition of claim 11, wherein the amino acid is a polar amino acid.

13. The pharmaceutical composition of claim 12, wherein the polar amino acid is a neutral polar amino acid.

14. The pharmaceutical composition of claim 12, wherein the polar amino acid is a basic polar amino acid.

15. The pharmaceutical composition of claim 1, wherein more than 80% of the treprostinil is released more than 2 hours to about 48 hours after the administration of the pharmaceutical composition.

16. The pharmaceutical composition of claim 1, wherein more than 80% of the treprostinil is released more than 2 hours to 24 hours after the administration of the pharmaceutical composition.

17. The pharmaceutical composition of claim 1, wherein the internal aqueous medium is substantially free of precipitation.

18. The pharmaceutical composition of claim 1, wherein the vesicle-forming lipid is a mixture of a first phospholipid and a second phospholipid or a mixture of a first phospholipid and a charged lipid.

19. The pharmaceutical composition of claim 18, wherein the first phospholipid is phosphatidylcholine (PC), phosphatidylglycerol (PG), phosphatidylinositol (PI), phosphatidic acid (PA), phosphatidyethanolamine (PE), phosphatidylserine (PS) or any combination thereof, the second phospholipid is a PEG modified phospholipid, a positively charged or a negatively charged phospholipid or any combination thereof, and the charged lipid is a positively charged or a negatively charged lipid.

20. The pharmaceutical composition of claim 18, wherein the first phospholipid is HSPC, DSPC, DPPC, DMPC or any combination thereof and the second phospholipid is DSPG, DPPG, DMPG, PEG-DSPE or any combination thereof.

21. The pharmaceutical composition of claim 18, wherein the first phospholipid is HSPC, DSPC, DPPC, DMPC or any combination thereof and the charged lipid is stearylamine, 1,2-dioleoyl-3-trimethylammonium-propane (DOTAP), 3ß-[N-(N',N'-dimethylaminoethane)-carbamoyl]cholesterol (DC-Cholesterol), N^4-Cholesteryl-Spermine (GL67), dimethyldioctadecylammonium (DDAB), 1,2-di-O-octadecenyl-3-trimethylammonium propane (DOTMA), ethylphosphocholine (ethyl PC) or any combination thereof.

22. A pharmaceutical composition of any one of the claims 1-21 for use in therapy.

23. Use of a pharmaceutical composition of any one of claims 1-21 in the manufacture of a medicament for treating a respiratory disease.

24. The use of claim 23, wherein the medicament is to be administered by inhalation and a side effect of the treprostinil is reduced in the upper respiratory tract.

25. Use of a pharmaceutical composition of any one of claims 1-21 in the manufacture of a medicament for reducing a side effect of treprostinil in the upper respiratory track.