CLAIMS

1. A biocompatible tissue filler comprising silk fibroin or silk fibroin fragments, hyaluronic acid (HA), and polyethylene glycol (PEG) and/or polypropylene glycol (PPG),

wherein a portion of the HA is modified or crosslinked by one or more linker moieties comprising one or more of polyethylene glycol (PEG), polypropylene glycol (PPG), and a secondary alcohol,

wherein the silk fibroin or silk fibroin fragments have an average weight average molecular weight selected from between ~~about~~ 1 kDa to ~~about~~ 250 kDa, from between ~~about~~ 5 kDa to ~~about~~ 150 kDa, from between ~~about~~ 6 kDa to ~~about~~ 17 kDa, from between ~~about~~ 17 kDa to ~~about~~ 39 kDa, or from between ~~about~~ 39 kDa to ~~about~~ 80 kDa, and

wherein the tissue filler has a light absorbance of at least 0.03 AU at any wavelength between 350 nm and 500 nm.

2. The tissue filler of claim 1, wherein a portion of silk fibroin or silk fibroin fragments have an average weight average molecular weight selected from about 12 kDa, about 13 kDa, about 14 kDa, about 15 kDa, about 16 kDa, about 48 kDa, and about 100 kDa.

3. The tissue filler of claim 1 or 2, wherein a portion of silk fibroin or silk fibroin fragments have an average weight average molecular weight lower than 28 kDa.

4. The tissue filler of any one of claims 1 to 3, wherein the silk fibroin or silk fibroin fragments have a polydispersity of between 1 and ~~about~~ 5.0, between ~~about~~ 1.5 and ~~about~~ 3.0, between 1 and ~~about~~ 1.5, between ~~about~~ 1.5 and ~~about~~ 2.0, between ~~about~~ 2.0 and ~~about~~ 2.5, between ~~about~~ 2.0 and ~~about~~ 3.0, or between 2.5 and ~~about~~ 3.0.

5. The tissue filler of any one of claims 1 to 4, wherein the tissue filler has a degree of modification (MoD) of about 5%, about 6%, about 7%, about 8%, about 9%, about 10%, about 11%, about 12%, about 13%, about 14%, or about 15%.

6. The tissue filler of any one of claims 1 to 5, wherein modification or cross-linking is obtained using as cross-linker a monoepoxy- or diepoxy-PEG, a monoglycidyl-, diglycidyl-, or polyglycidyl-PEG, a monoglycidyl- or diglycidyl-PEG, a monoepoxy- or diepoxy-PPG, a monoglycidyl-, diglycidyl-, or polyglycidyl-PPG, a monoglycidyl- or diglycidyl-PPG, or any combinations thereof.

7. The tissue filler of any one of claims 1 to 6, wherein modification or cross-linking is obtained using polyethylene glycol diglycidyl ether having a MW of about 200 Da, about 500 Da, about 1000 Da, about 2,000 Da, or about 6000 Da.

8. The tissue filler of any one of claims 1 to 6, wherein modification or cross-linking is obtained using polypropylene glycol diglycidyl ether having a MW of about 380 Da, or about 640 Da.

9. The tissue filler of any one of claims 1 to 8, further comprising lidocaine.

10. The tissue filler of claim 9, wherein the concentration of lidocaine in the tissue filler is about 0.3%.

11. The tissue filler of any one of claims 1 to 10, wherein the tissue filler is a gel or a hydrogel, wherein the hydrogel further comprises water.

12. The tissue filler of any one of claims 1 to 11, wherein the tissue filler is monophasic.

13. The tissue filler of any one of claims 1 to 12, wherein the total concentration of HA and silk fibroin or silk fibroin fragments in the tissue filler is about 15 mg/mL, about 16 mg/mL, about 17 mg/mL, about 18 mg/mL, about 19 mg/mL, about 20 mg/mL, about 21 mg/mL, about 22 mg/mL, about 23 mg/mL, about

24 mg/mL, about 25 mg/mL, about 26 mg/mL, about 27 mg/mL, about 28 mg/mL, about 29 mg/mL, about 30 mg/mL, about 31 mg/mL, about 32 mg/mL, about 33 mg/mL, about 34 mg/mL, about 35 mg/mL, about 36 mg/mL, about 37 mg/mL, about 38 mg/mL, about 39 mg/mL, or about 40 mg/mL.

14. The tissue filler of any one of claims 1 to 13, wherein the ratio of HA to silk fibroin or silk fibroin fragments in the tissue filler is about 91/9, about 92/8, about 93/7, about 94/6, about 95/5, about 96/4, about 97/3, about 18/12, about 27/3, about 29.4/0.6, about 99/1, about 92.5/7.5, or about 90/10.

15. The tissue filler of any one of claims 1 to 14, wherein the tissue filler is a dermal filler.

16. The tissue filler of any one of claims 1 to 15, wherein the tissue filler is biodegradable.

17. The tissue filler of any one of claims 1 to 16, wherein the tissue filler is injectable.

18. The tissue filler of claim 17, wherein the tissue filler is injectable through 30 G or 27 G needles.

19. The tissue filler of any one of claims 1 to 18, wherein the tissue filler has a storage modulus (*G'*) of from ~~about~~ 5 Pa to ~~about~~ 500 Pa, from ~~about~~ 15 Pa to ~~about~~ 50 Pa, from ~~about~~ 50 Pa to ~~about~~ 100 Pa, from ~~about~~ 100 Pa to ~~about~~ 200 Pa, or from ~~about~~ 200 Pa to ~~about~~ 300 Pa.

20. The tissue filler of any one of claims 1 to 19, wherein the tissue filler has a complex viscosity from ~~about~~ 1 Pa·s to ~~about~~ 10 Pa·s.

21. The tissue filler of any one of claims 1 to 20, wherein the tissue filler is a deep tissue filler, or a superficial tissue filler.

22. The tissue filler of any one of claims 1 to 21 for use in therapy.

23. ~~Use of t~~The tissue filler of any one of claims 1 to 21 for use in the ~~manufacture of a medicament for the~~ treatment of a skin condition, a facial disease, a facial disorder, a facial defect or a facial imperfection.

24. The use of claim 23, wherein the skin condition is selected from skin dehydration, lack of skin elasticity, skin roughness, lack of skin tautness, a skin stretch line, a skin stretch mark, skin paleness, a dermal divot, a sunken cheek, a thin lip, a retro-orbital defect, a facial fold, and a wrinkle.

25. A method of cosmetic treatment in a subject in need thereof, wherein the tissue filler of any one of claims 1 to 21~~comprising administering~~ is to be administered to the subject in a therapeutically effective amount ~~of the tissue filler of any one of claims 1 to 21~~.

26. The tissue filler for use of claim 22, the use of claim 23 or 24, or the method of claim 25, wherein the tissue filler is to be administered into a dermal region of the subject.

27. The method of claim 25 or 26, wherein the method is an augmentation, a reconstruction, correcting a defect or imperfection of a body part, region or area.

28. The method of claim 25 or 26, wherein the method is a facial augmentation or a facial reconstruction.

29. The method of any one of claims 25 to 28, wherein the method comprises deep subcutaneous and/or deep supraperiosteal administration.

30. The method of any one of claims 25 to 29, wherein the method comprises one or more of cheek augmentation, lip augmentation, dermal implantation, correction of perioral rhytids, and/or correction of nasolabial fold.

31. The tissue filler for use of claim 22, the use of claim 23 or 24, or the method of any one of claims 25 to 30, wherein the tissue filler to be administered to the subject results in one or more of:

the tissue filler resists biodegradation, bioerosion, bioabsorption, and/or bioresorption, for at least about 3 days, about 7 days, about 14 days, about 21 days, about 28 days, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, or about 6 months;

a reduced inflammatory response compared to the inflammatory response induced by a control tissue filler comprising a substantially similar HA, wherein the control tissue filler does not include silk fibroin or silk fibroin fragments;

a reduced inflammatory response compared to the inflammatory response induced by a control tissue filler comprising a substantially similar HA, wherein the control tissue filler does not include silk fibroin or silk fibroin fragments and/or PEG or PPG; and/or

an increased or decreased collagen production compared to the collagen production induced by a control tissue filler comprising a substantially similar HA, wherein the control tissue filler does not include silk fibroin or silk fibroin fragments, or wherein the control tissue filler does not include silk fibroin or silk fibroin fragments and/or PEG or PPG.