

What is claimed is:

1. A method of producing an ECM valve conduit for regenerating a semi-lunar valve to replace a defective semi-lunar valve within a heart of a first subject, the defective semi-lunar valve being attached at an annular region between a ventricle of the heart of the first subject and an artery of the first subject, the method comprising:
 - providing a sheet of acellular extracellular matrix (ECM) material;
 - ~~removing the defective semi-lunar valve from the heart of the subject;~~
 - positioning a said sheet of ~~extracellular matrix~~ (ECM) material in a folded position, the said sheet having a top portion comprising a top edge of the said sheet and a bottom portion comprising a bottom edge of the said sheet; wherein, in the said folded position, the said bottom edge of the said sheet is folded toward the said top edge of the said sheet such that the said bottom edge of the said sheet is spaced a selected first distance from the said top edge of the said sheet;
 - securing the said sheet of ECM material in the said folded position, thereby forming a said folded ECM material valve construct having an upper portion, a lower portion, a first side edge, and a second side edge, the said lower portion comprising a first layer and a second layer, the said first layer of the said lower portion corresponding to the said folded bottom portion of the said sheet of said ECM material;
 - attaching said first layer to said second layer only at locations adjacent and along said bottom edge of said sheet, wherein the said first and second layers is are attached to the at first and second layer at a attachment points, said first attachment point and a second attachment point, and wherein the first attachment point is being spaced from the said second attachment point by a selected second distance, wherein a sinus-promoting portion is formed on said ECM valve construct upper portion and a commissure-promoting portion is formed on said ECM valve construct lower portion first layer;
 - positioning the folded said ECM material valve construct in an aligned position, in which the said first side edge of the folded said ECM material valve construct is in substantial alignment with the said second side edge of the folded said ECM material valve construct; and

~~with the folded said ECM material valve construct in the said aligned position, securing the said first side edge of the folded said ECM material valve construct to the said second side edge of the folded said ECM material valve construct at a securement location, thereby forming an said ECM material valve conduit comprising having a lumen and having a longitudinal axis, wherein the said lower portion of the folded said ECM material valve construct corresponds to an inlet portion of the said ECM material valve conduit, the said inlet portion of the said ECM material valve conduit defining an inlet in fluid communication with the said lumen of the said ECM material valve conduit, wherein the said first layer of the said lower portion of the folded said ECM material valve construct corresponds to an inner layer positioned within the said lumen of the said ECM material valve conduit, and wherein the said upper portion of said ECM construct corresponds to an outlet portion of said ECM valve conduit, and wherein said second layer of the said lower portion of the folded said ECM material valve construct cooperates with the said upper portion of the folded said ECM material valve construct to define an outer wall of the said ECM material valve conduit; and~~

~~attaching the ECM material valve conduit to the annular region of the, wherein said inner layer of said ECM valve conduit is continuous around its circumference except at said first and second attachment points and said securement location;~~

~~said ECM valve conduit being suitable for attachment to the annular region of said heart of the said first subject and the said artery of the said first subject such that the, whereby said inlet portion of the said ECM material valve conduit is positioned proximate the said annular region,~~

~~wherein the inner layer of the ECM material valve conduit comprises leaflet-promoting portions, wherein the outer layer of the ECM material valve conduit comprises sinus-promoting portions, and whereinwhereby, following attachment of the said ECM material valve conduit to the said annular region of the said first subject's heart of the subject and the said artery of the said first subject, the leaflet~~

~~(i) said commissure-promoting portions of the said ECM valve conduit inner layer regenerate three remodels and fuses with said upper portion of said ECM valve construct, wherein a regenerated valve leaflets of a replacement semi-lunar valve is formed in said ECM valve conduit lumen, and the~~

~~(ii) said sinus-promoting portions of the outer layer fuse with the remodels and fuses with said ECM valve conduit inner layer of the said ECM material valve~~

~~conduit to regenerate, wherein a regenerated sinus portions of the said replacement semi-lunar valve is formed,~~

~~(iii) said regenerated valve leaflet and said regenerated sinus portion of said ECM valve conduit comprising remodeled cardiovascular tissue.~~

2. ~~The method of Claim-claim 1, wherein the said first attachment point and the said second attachment point are positioned substantially within on a first common plane, the said first common plane being substantially perpendicular to the said longitudinal axis of the said ECM-material valve conduit.~~

3. ~~The method of Claim-claim 2, wherein the said first attachment point is spaced from the said first side edge by a first third distance, wherein the said second attachment point is spaced from the said second side edge by a second fourth distance, and wherein the first said third distance and the second said fourth distance are substantially equal to the selected said second distance by which the said first attachment point is spaced from the said second attachment point.~~

4. ~~The method of Claim 1, wherein the step of securing the first side edge of the folded ECM material construct to the second side edge of the folded ECM material construct comprises forming a seam with a plurality of sutures along the longitudinal axis of the ECM material valve conduit.~~

5. ~~The method of Claim 4, wherein the first layer of the lower portion of the folded ECM material construct is further attached to the second layer of the lower portion of the folded ECM material construct at a third attachment point intermediate the first side edge and the first attachment point, wherein the first, second, and third attachment point are positioned substantially within a common plane, the common plane being substantially perpendicular to the longitudinal axis of the ECM material valve conduit.~~

4. ~~The method of claim 1, wherein said first layer of said lower portion of said ECM valve construct is further attached to said second layer of said lower portion of said ECM valve construct at a third attachment point intermediate said first side edge and said first attachment point, wherein said first, second, and third attachment points are positioned on a second common plane, said second common plane being perpendicular to said longitudinal axis of said ECM valve conduit, and wherein an additional sinus-promoting portion is formed on said ECM valve construct upper~~

portion and an additional commissure-promoting portion is formed on said lower portion first layer,

whereby said additional sinus-promoting portion is suitable, following attachment of said ECM valve conduit to said annular region of said first subject's heart and said first subject's artery, to remodel and fuse with said inner layer of said ECM valve construct,

wherein an additional regenerated sinus portion of said replacement semi-lunar valve is formed, whereby said additional commissure-promoting portion is suitable to remodel and fuse with said upper portion of said ECM valve construct, and

wherein an additional regenerated valve leaflet is formed.

65. ~~The method of Claim-claim 54, wherein the distance by which the said third attachment point is spaced from the said first attachment point is substantially a fifth distance, and wherein said fifth distance equal to the selected said second distance by which the said first attachment point is spaced from the said second attachment point.~~

7. ~~—The method of Claim 5, wherein the third attachment point is positioned proximate the first side edge such that, after securing the first side edge of the folded ECM material construct to the second side edge of the folded ECM material construct, the third attachment point is positioned proximate the seam of the ECM material valve conduit.~~

86. ~~The method of Claim-claim 54, wherein the said first layer of the said lower portion of the folded said ECM material valve construct is further attached to the said second layer of the said lower portion of the folded said ECM material valve construct at a fourth attachment point intermediate the said second side edge and the said second attachment point, wherein the first, second, third, and fourth attachment points are positioned substantially within the on said second common plane.~~

97. ~~The method of Claim-claim 86, wherein the distance by which the said fourth attachment point is spaced from the said second attachment point is substantially a sixth distance, and wherein said sixth distance equal to the selected said second distance by which the said first attachment point is spaced from the said second attachment point.~~

10. ~~—The method of Claim 8, wherein the fourth attachment point is positioned proximate the second side edge such that, after securing the first side edge of the folded ECM material construct to the second side edge of the folded ECM material~~

construct, the fourth attachment point is positioned proximate the seam of the ECM material valve conduit.

~~11. The method of Claim 1, wherein the inner layer of the ECM material valve conduit further comprises commissure-promoting portions, and wherein, following attachment of the ECM material valve conduit to the annular region of the heart of the subject and the artery of the subject, the commissure-promoting portions of the inner layer fuse with at least a portion of the outer layer of the ECM material valve conduit.~~

~~12. An extracellular matrix (ECM) material valve conduit for regenerating a semi-lunar valve within a heart of a subject, the ECM material valve conduit formed according to the method of Claim 1.~~

8. The method of claim 1, wherein said sheet of acellular ECM material is decellularized by introducing said ECM material into a reactor pressure vessel, introducing at least a first liquid sterilant into said reactor pressure vessel at a first controlled pressurization rate, pressurizing said reactor pressure vessel at a pressure in the range of 1000-3500 psi, maintaining said ECM material in contact with said first liquid sterilant for a first time period in the range of 10 min. to 24 hours, and depressurizing said reactor pressure vessel at a first depressurizing rate, said first depressurizing rate being greater than 400 psi/min.

9. The method of claim 8, wherein said first liquid sterilant comprises supercritical carbon dioxide.

10. The method of claim 8, wherein said reactor pressure vessel is maintained at a temperature of at least 31.1° C. during said pressurization of said reactor pressure vessel.

~~1311. The ECM material valve conduit method of Claim-claim 11, wherein the said ECM material valve conduit comprises at least one tissue, each tissue of the at least one tissue being from a respective tissue source, wherein the tissue source of each tissue of the at least one tissue is extracellular matrix tissue from a mammalian tissue source, said mammalian tissue source being selected from the group consisting of small intestinal submucosa, stomach submucosa, small intestine submucosa, large intestinal-intestine tissue, urinary bladder submucosa tissue, liver basement membrane tissue, pericardium, epicardium, endocardium, myocardium heart tissue, lung tissue, kidney tissue, pancreatic tissue, prostate tissue, mesothelial tissue, fetal tissue, a placenta, a ureter, veins, arteriesartery, heart valves with or without their attached~~

vessels, and tissue surrounding the roots of developing teeth, and tissue surrounding growing bone.

14.——A method of regenerating a semi-lunar valve to replace a defective semi-lunar valve within a heart of a subject, the defective semi-lunar valve being attached at an annular region therebetween a ventricle of the heart of the subject and an artery of the subject, the method comprising:

removing the defective semi-lunar valve from the heart of the subject;

positioning an extracellular matrix (ECM) material conduit in a reflected position, the ECM material conduit defining a lumen and having a top portion comprising a top end of the ECM material conduit and a bottom portion comprising a bottom end of the ECM material conduit, wherein, in the reflected position, the bottom end of the ECM material conduit is inwardly reflected within the lumen of the ECM material conduit toward the top end of the ECM material conduit such that the bottom end is spaced a selected distance from the top end;

securing the ECM material conduit in the reflected position, thereby forming an ECM material valve conduit having a longitudinal axis and comprising a lumen, an inlet portion, and an outlet portion, the outlet portion defining an outlet in communication with the lumen of the ECM material valve conduit, the inlet portion defining an inlet in communication with the lumen of the ECM material valve conduit and comprising an outer layer and an inner layer positioned within the lumen of the ECM material valve conduit, the inner layer of the inlet portion corresponding to the reflected bottom end of the ECM material valve conduit, wherein the inner layer is attached to the outer layer at three attachment points, the three attachment points being substantially equally spaced along an outer circumference of the ECM material valve conduit, wherein the outer layer of the inlet portion of the ECM material valve conduit cooperates with the outlet portion of the ECM material valve conduit to define an outer wall of the ECM material valve conduit; and

attaching the ECM material valve conduit to the annular region of the heart of the subject and the artery of the subject such that the inlet portion of the ECM material valve conduit is positioned proximate the annular region;

wherein the inner layer of the ECM material valve conduit comprises leaflet-promoting portions, wherein the outer layer of the ECM material valve conduit comprises sinus-promoting portions, and wherein, after attaching the ECM material

valve conduit to the annular region of the heart of the subject and the artery of the subject, the leaflet-promoting portions of the inner layer regenerate three leaflets of a replacement semi-lunar valve and the sinus-promoting portions of the outer layer fuse with the inner layer of the ECM material valve conduit to regenerate sinus portions of the replacement semi-lunar valve.

15.—The method of Claim 14, wherein the three attachment points are positioned substantially within a common plane, the common plane being substantially perpendicular to the longitudinal axis of the ECM material valve conduit.

16.—The method of Claim 14, wherein the inner layer of the ECM material valve conduit further comprises commissure-promoting portions, and wherein, following attachment of the ECM material valve conduit to the annular region of the heart of the subject and the artery of the subject, the commissure-promoting portions of the inner layer fuse with at least a portion of the outer layer of the ECM material valve conduit.

17.—An extracellular matrix (ECM) material valve conduit for regenerating a semi-lunar valve within a heart of a subject, the ECM material valve conduit formed according to the method of Claim 14:

18.—The ECM material valve conduit of Claim 17, wherein the ECM material valve conduit comprises at least one tissue, each tissue of the at least one tissue being from a respective tissue source, wherein the tissue source of each tissue of the at least one tissue is selected from the group consisting of small intestinal submucosa, stomach submucosa, large intestinal tissue, urinary bladder submucosa, liver basement membrane, pericardium, epicardium, endocardium, myocardium, lung tissue, kidney tissue, pancreatic tissue, prostate tissue, mesothelial tissue, fetal tissue, a placenta, a ureter, veins, arteries, heart valves with or without their attached vessels, tissue surrounding the roots of developing teeth, and tissue surrounding growing bone.

19.—An extracellular matrix (ECM) material valve conduit for regenerating a semi-lunar valve within a heart of a subject, the ECM material valve conduit having a longitudinal axis and comprising a lumen, an inlet portion, and an outlet portion, the outlet portion defining an outlet in communication with the lumen of the ECM material valve conduit, the inlet portion defining an inlet in communication with the lumen of the ECM material valve conduit and comprising an outer layer and an inner layer positioned within the lumen of the ECM material valve conduit, the inner layer of the outlet portion being inwardly reflected within the lumen of the ECM material

~~valve conduit, wherein the inner layer is attached to the outer layer at three attachment points, the three attachment points being substantially equally spaced along an outer circumference of the ECM material valve conduit, wherein the outer layer of the inlet portion of the ECM material valve conduit cooperates with the outlet portion of the ECM material valve conduit to define an outer wall of the ECM material valve conduit, wherein the inner layer of the ECM material valve conduit comprises leaflet-promoting portions,~~

~~wherein the outer layer of the ECM material valve conduit comprises sinus-promoting portions, and~~

~~wherein, following attachment of the ECM material valve conduit to an annular region of the heart of the subject and an artery of the subject such that the inlet portion of the ECM material valve conduit is positioned proximate the annular region, the leaflet-promoting portions of the inner layer are configured to regenerate three leaflets of a replacement semilunar valve and the sinus-promoting portions of the outer layer are configured to fuse with the inner layer of the ECM material valve conduit to regenerate sinus portions of the replacement semi-lunar valve.~~

20. — ~~The ECM material valve conduit of Claim 19, wherein the three attachment points are positioned substantially within a common plane, the common plane being substantially perpendicular to the longitudinal axis of the ECM material valve conduit.~~

21. — ~~The ECM material valve conduit of Claim 19, wherein the ECM material valve conduit comprises at least one tissue, each tissue of the at least one tissue being from a respective tissue source, wherein the tissue source of each tissue of the at least one tissue is selected from the group consisting of small intestinal submucosa, stomach submucosa, large intestinal tissue, urinary bladder submucosa, liver basement membrane, pericardium, epicardium, endocardium, myocardium, lung tissue, kidney tissue, pancreatic tissue, prostate tissue, mesothelial tissue, fetal tissue, a placenta, a ureter, veins, arteries, heart valves with or without their attached vessels, tissue surrounding the roots of developing teeth, and tissue surrounding growing bone.~~

12. The method of claim 11, wherein said mammalian tissue source comprises mammalian tissue from a second subject.

13. The method of claim 11, wherein said ECM material includes an additional pharmacological agent.

14. The method of claim 13, wherein said pharmacological agent comprises an

anti-inflammatory.

15. The method of claim 13, wherein said pharmacological agent comprises a statin.

16. The method of claim 15, wherein said statin is selected from the group consisting of atorvastatin, cerivastatin, fluvastatin, lovastatin, mevastatin, pitavastatin, pravastatin, rosuvastatin and simvastatin.

17. The method of claim 13, wherein said pharmacological agent comprises a growth factor.

18. The method of claim 17, wherein said growth factor is selected from the group consisting of a platelet derived growth factor (PDGF), epidermal growth factor (EGF), transforming growth factor alpha (TGF-alpha), transforming growth factor beta (TGF-beta), fibroblast growth factor-2 (FGF-2), basic fibroblast growth factor (bFGF), vascular epithelial growth factor (VEGF), hepatocyte growth factor (HGF), insulin-like growth factor (IGF), platelet derived growth factor (PDGF), and placental growth factor (PLGF).

19. The method of claim 13, wherein said pharmacological agent comprises an anti-arrhythmic agent.