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**Stone**

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- (54) **XENOGRAFT HEART VALVES**
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- (\* ) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 84 days.  
  
This patent is subject to a terminal disclaimer.

5,171,660 A	12/1992	Carpenter et al.	435/1
5,192,312 A	3/1993	Orton	623/2
5,206,023 A	4/1993	Hunziker	424/423
5,216,126 A	6/1993	Cox et al.	530/350
5,263,984 A	11/1993	Li et al.	623/15
5,306,304 A	4/1994	Gendler	623/16
5,306,311 A	4/1994	Stone et al.	623/18
5,333,626 A	8/1994	Morse et al.	128/898
5,352,463 A	10/1994	Badylak et al.	424/551
5,358,525 A	10/1994	Fox et al.	623/18
5,507,810 A	4/1996	Prewett et al.	623/11
5,516,532 A	5/1996	Atala et al.	424/548
5,521,087 A	5/1996	Lee et al.	435/240.2
5,587,442 A	12/1996	Kiesling et al.	
5,613,982 A	3/1997	Goldstein	623/11
5,632,778 A	5/1997	Goldstein	623/11

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**A01N 1/02** (2006.01)  
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(52) **U.S. Cl.** ..... **435/1.1; 623/2.1; 623/2.42; 435/325**

(58) **Field of Classification Search** ..... 435/1.1, 435/325; 623/2.1, 2.42  
See application file for complete search history.

(56) **References Cited**

**U.S. PATENT DOCUMENTS**

4,034,418 A	7/1977	Jackson et al.	3/1.911
4,344,193 A	8/1982	Kenny	3/1.911
4,361,586 A	11/1982	Meinke et al.	
4,400,833 A	8/1983	Kurland	3/1
4,502,161 A	3/1985	Wall	3/1.91
4,597,266 A	7/1986	Entrekin	62/46
4,609,627 A	9/1986	Goldstein	435/269
4,627,853 A	12/1986	Campbell et al.	623/16
4,642,120 A	2/1987	Nevo et al.	623/16
4,678,470 A	7/1987	Nashef et al.	623/16
4,755,593 A	7/1988	Lauren	530/356
4,776,853 A	10/1988	Klement et al.	8/94.11
4,789,663 A	12/1988	Wallace et al.	514/21
4,801,299 A	1/1989	Brendel et al.	
4,846,835 A	7/1989	Grande	623/11
4,880,429 A	11/1989	Stone	623/18
4,902,295 A	2/1990	Walthall et al.	623/23.72
4,932,973 A	6/1990	Gendler	623/16
5,007,934 A	4/1991	Stone	623/20
5,067,962 A	11/1991	Campbell et al.	623/13
5,071,741 A	12/1991	Brockbank	435/1
5,078,744 A	1/1992	Chvapil	623/13
5,092,894 A	3/1992	Kenny	623/18
5,116,374 A	5/1992	Stone	623/16
5,131,850 A	7/1992	Brockbank	435/1
5,158,574 A	10/1992	Stone	623/66
5,160,313 A	11/1992	Carpenter et al.	600/36
5,171,273 A	12/1992	Silver et al.	623/13
5,171,322 A	12/1992	Kenny	623/18

(Continued)

**FOREIGN PATENT DOCUMENTS**

EP	347496	12/1989
WO	WO 84/03036	8/1984
WO	WO 95/26740	10/1995
WO	WO 95/28412	10/1995
WO	WO 95/33828	12/1995

**OTHER PUBLICATIONS**

Hicks et al. Cell Tiss. Res. 1977, 175:467-481.\*

(Continued)

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(57) **ABSTRACT**

The invention provides an article of manufacture comprising a substantially non-immunogenic heart valve xenograft for implantation into humans. The invention further provides methods for preparing a heart valve xenograft by removing at least a portion of a soft tissue from a non-human animal to provide a xenograft; washing the xenograft in saline and alcohol; subjecting the xenograft to cellular disruption treatment; treating the xenograft with crosslinking agents, and digesting the xenograft with a proteoglycan-depleting factor and/or glycosidase. The invention also provides an article of manufacture produced by the above-identified method of the invention. The invention further provides a heart valve xenograft for implantation into a human including a portion of a heart valve from a non-human animal, wherein the portion has extracellular components and substantially only dead cells. The extracellular components have reduced proteoglycan molecules. Each of the xenografts of the invention are substantially non-immunogenic and have substantially the same mechanical properties as a corresponding native heart valve.

**7 Claims, No Drawings**