TRI™ Valves: A Superior Alternative to Glutaraldehyde

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Technology: 300,000 valve transplantations occur annually due to infection, congenital defects, degenerative heart valve disease, etc.[1] TRI™ is a novel fabrication method to chemically treat porcine aortic heart valve leaflets or bovine pericardium to produce superior bioprosthetic heart valves (BHVs). TRI™ utilizes irreversible carbodiimide chemistry, neomycin trisulfate, and pentagalloyl glucose in a proprietary treatment method in lieu of traditional glutaraldehyde fixation (GLUT), the current market gold standard. The patent protecting this IP belongs to Clemson University and both inventors are currently at Clemson University. GLUT fixation results in implant failure through calcification and/or structural degradation within 10 – 15 years.[1] TRI™ fabrication yields a durable, compliant biomaterial (Figure 1 right) that is resistant to calcification (Figure 1 left) and structural degradation.

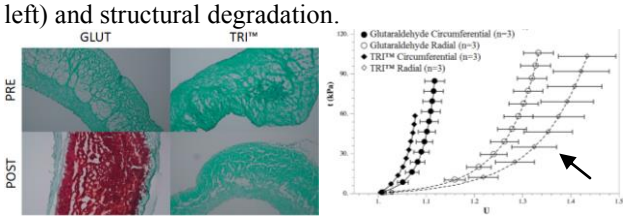

Figure 1. (Left) Alazarin red staining for glutaraldehyde or TRI™ treated leaflets pre or post subcutaneous implantation in juvenile rat calcification models for 90 days. Calcium deposits stained red. (Right) Biaxial tension testing of glutaraldehyde or TRI™ treated leaflets.

Market: The heart valve market is valued at ~$1.26B as of 2011 with ~7% CAGR.[1,2] Edward Life Sciences (ELS), St. Jude Medical (SJ), and Medtronic are the major players in this space making up over 70% of the market.[2] BHVs make up 60% of the market and this segment is dominated by ELS.[2] BHVs are preferred over mechanical heart valves for advanced durability and optimal flow dynamics with no anticoagulant therapy. However, current BHVs fail prematurely in younger patients (~5-7 years) thus mechanical heart valves are used in this segment (SJ leads this customer segment[2]). Innovation in better BHVs threaten to phase out mechanical valves. The market is also shifting towards the trans luminal valves because it allows for minimally invasive implantation.[2]

TRI™ has the potential to outperform all other BHV fabrication techniques within this space. TRI™ processing could quickly eliminate the demand for mechanical heart valves (2^o competitors) because they resist calcification and structural degradation enabling them to last in younger patients without anticoagulant therapy. TRI™ processing can capture market share from GLUT BHVs (1^o competitors) because of increased functionality and biocompatibility. TRI™ processing could also be better suited for trans luminal valves because of their increased compliance and durability over GLUT valves (cooperative opportunity with adjacent competitor). Surgery procedures, liability, and reimbursement plans with insurance companies already exist for BHVs and would remain the same. Costs incurred to producers that switch to TRI™ from GLUT are negligible because existing tooling, facilities, distribution, labeling, and packaging can be used.

Commercialization Strategy: Leaflets treated with TRI™ are currently being studied for long term accelerated wear stability and resistance to calcification. This endeavor is funded by an NIH R01 research grant at Clemson University. Once these basic proof of concept goals are met, TRI™ processing will be licensed out to TRI Heart LLC which will actively seek funding for development of an industry-standard heart valve biomaterial, consistent fabrication technique, and completion of a preclinical trial. Angel investment will cover initial licensing fees and push product development during early stages. This consists of developing (1) a reproducible process for large scale production that yields consistent material properties, (2) accelerated *in vitro* wear testing, (3) *in vitro* toxicity testing, and (4) feasibility studies, risk assessment, pro forma, costumer discovery through surgeon and end user focus groups, and opening of marketing/advertising channels (~$500k, 3 years). Larger federal and state grants such as SBIRs will go towards a large animal study (~$3M – 5M, 2 years). This study will be done in a sheep model to demonstrate TRI™ valve's long term ability to (1) resist calcification, (2) retain key material composite components, (3) not elicit a sustained immunogenic or inflammatory response, and (4) not generate an adverse systemic reaction in a clinically relevant model. Rigorous accelerated wear testing will accompany this study and animal toxicity studies to gather ASTM, ISO, and AAMI data. Exclusive licensing or acquisition by one of the key players (i.e., ELS) or key raw producers of biomaterials is likely to occur once robust proof of concept is demonstrated in a large animal. They will carry the product to market using their own commercialization channels (i.e., advertising, marketing, branding, etc.)

TRI™ BHVs will be classified as Class III medical devices by the FDA under 21 CFR 830.7925 and must undergo premarket approval. This entails costly human clinical studies, therefore, after acquisition, it is advantageous for the acquirer to further develop this product then conduct clinical studies and release in the EU first where obtaining regulatory approval (CE mark) is more streamlined and cost effective. Revenue streams for TRI Heart LLC will begin during FY4 or FY5 through licensing acquisition fees upon completion of the preclinical. Royalties will start to come in at FY8 or FY9. During FY3, we must also start to build out a customer service department and develop a relationship with our licensees. Revenue streams will be poured back into R&D to apply the TRI™ process in other applications.

References: 1) Manji R. Am Heart J 2012; 164:177-85. 2) Research and Markets; Worldwide Heart Valve Market 2012. **Acknowledgements:** NIH R01HL108330