CRYOLIFE INC
Form 10-K
February 15, 2013

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2012

OR

¨ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission file number 1-13165

CRYOLIFE, INC.

(Exact name of registrant as specified in its charter)

Florida	**59-2417093**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

1655 Roberts Boulevard N.W., Kennesaw, GA 30144

(Address of principal executive offices) (zip code)
Registrant s telephone number, including area code (770) 419-3355

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Name of each exchange on which registered**
Common Stock, $.01 par value	**New York Stock Exchange**
Preferred Share Purchase Rights	**New York Stock Exchange**

Securities registered pursuant to Section 12(g) of the Act:

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ¨ No x

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K Section 229.405 of this chapter is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No ¨

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a nonaccelerated filer, or a smaller reporting company. See definitions of large accelerated filer , accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one).

Large accelerated filer ¨	Accelerated filer x
Non-accelerated filer ¨	Smaller reporting company ¨

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ¨ No x

As of June 30, 2012 the aggregate market value of the voting stock of the Registrant held by non-affiliates of the registrant was $130,523,457 computed using the closing price of $5.23 per share of Common Stock on June 30, 2012, the last trading day of the registrant s most recently completed second fiscal quarter, as reported by the New York Stock Exchange, based on management s belief that Registrant has no affiliates other than its directors and executive officers.

As of February 12, 2013 the number of outstanding shares of Common Stock of the registrant was 27,483,499.

Documents Incorporated By Reference

Document	Parts Into Which Incorporated
Proxy Statement for the Annual Meeting of Stockholders to be filed within 120 days after December 31, 2012.	Part III

PART I

Item 1. Business.

Overview

CryoLife, Inc. (CryoLife, the Company, we, or us), incorporated in 1984 in Florida, preserves and distributes human tissues for transplantation and develops, manufactures, and commercializes medical devices for cardiac and vascular applications. The cardiac and vascular human tissues distributed by CryoLife include the CryoValve® SG pulmonary heart valve (CryoValve SGPV) and the CryoPatch® SG pulmonary cardiac patch tissue (CryoPatch SG), both processed using CryoLife s proprietary SynerGraft® technology. CryoLife s surgical sealants and hemostats include BioGlue® Surgical Adhesive (BioGlue), BioFoam® Surgical Matrix (BioFoam), and PerClot®, an absorbable powdered hemostat, which the Company distributes for Starch Medical, Inc. (SMI) in the European Community and other select international markets. CryoLife s subsidiary, Cardiogenesis Corporation (Cardiogenesis), specializes in the treatment of coronary artery disease using a laser console system and single use, fiber-optic handpieces to treat patients with severe angina. CryoLife and its subsidiary, Hemosphere, Inc. (Hemosphere), market the Hemodialysis Reliable Outflow Graft (HeRO® Graft), which is a solution for end-stage renal disease (ESRD) in certain hemodialysis patients.

Preservation Services and Products

Tissue Preservation Services. CryoLife distributes preserved human cardiac and vascular tissues to implanting institutions throughout the U.S., Canada, and Europe. CryoLife processes and preserves cardiac and vascular tissues using proprietary processing and freezing techniques, or cryopreservation. Management believes the human tissues it distributes offer specific advantages over mechanical, synthetic, and animal-derived alternatives. Depending on the alternative, the advantages of the Company s heart valves include more natural blood flow properties, the ability to use with patients who have endocarditis, the elimination of a need for long-term drug therapy to prevent excessive blood clotting, and a reduced risk of catastrophic failure, thromboembolism (stroke), or calcification. The Company s cardiac tissues include the CryoValve SGPV and the CryoPatch SG, both processed with the Company s proprietary SynerGraft decellularization technology. CryoLife uses the SynerGraft technology for a portion of its pulmonary valve and pulmonary cardiac patch tissue processing. The Company s vascular tissues, including the CryoVein and CryoArtery, have been used to treat a variety of vascular reconstructions such as peripheral bypass, hemodialysis access, and aortic infections which have saved the lives and limbs of patients.

Surgical Sealants and Hemostats. CryoLife s proprietary product, BioGlue, designed for cardiac, vascular, pulmonary, and general surgical applications, is a polymer based on bovine blood protein and an agent for cross-linking proteins. CryoLife distributes BioGlue throughout the U.S. and in more than 80 other countries for designated applications. In the U.S., BioGlue is U.S. Food and Drug Administration (FDA) approved as an adjunct to sutures and staples for use in adult patients in open surgical repair of large vessels. CryoLife distributes BioGlue for repair of soft tissues (which include cardiac, vascular, pulmonary, and additional soft tissues) in the European Economic Area (EEA) under Conformité Européene Mark product certification (CE Mark). CryoLife distributes BioGlue in Japan for use in the repair of aortic dissections. Additional marketing approvals have been granted for specified applications in several other countries throughout the world, including Canada, Brazil, and Australia.

CryoLife s proprietary product, BioFoam, is a protein hydrogel biomaterial with an expansion agent, which generates a mixed-cell foam. The foam creates a mechanical barrier to decrease blood flow and develops pores for the blood to enter, leading to cellular aggregation and enhanced hemostasis. Due to its foaming characteristic, BioFoam has the potential to rapidly seal organs, such as the liver, and may provide hemostasis in penetrating wounds and trauma. CryoLife distributes BioFoam under CE Mark certification for use as an adjunct in the sealing of the liver and spleen and as an adjunct to hemostasis in cardiovascular surgery when cessation of bleeding by ligature or conventional methods is ineffective or impractical.

CryoLife has a worldwide distribution agreement (except in China and certain related territories and governing areas) and a license and manufacturing agreement with SMI of San Jose, California for PerClot, a polysaccharide hemostatic agent used in surgery. PerClot is an absorbable powdered hemostat that has CE Mark designation allowing commercial distribution into the European Community and other markets. It is indicated for use in surgical procedures, including cardiac, vascular, orthopaedic, neurological, gynecological, ENT, and trauma surgery as an adjunct hemostat when control of bleeding from capillary, venous, or arteriolar vessels by pressure, ligature, and other conventional means is either ineffective or impractical.

CryoLife refiled an investigational device exemption (IDE) in November 2012 with the FDA to begin clinical trials for the purpose of obtaining Premarket Approval (PMA) to distribute PerClot in the U.S. CryoLife has received questions from the FDA related to this filing and is currently working to address the questions and expects to respond to the FDA in the first quarter of 2013.

Revascularization Technologies. In May 2011 CryoLife completed its acquisition of Cardiogenesis. Cardiogenesis is a leading developer of surgical products used in the treatment of patients with severe angina resulting from diffuse coronary artery disease. Cardiogenesis markets the FDA approved Holmium: YAG laser console, single use and fiber-optic handpieces, and the servicing and maintenance of the console for performing a surgical procedure known as transmyocardial revascularization (TMR), used for treating patients with severe angina that is not responsive to conventional therapy. Patients undergoing TMR treatment with Cardiogenesis products have been shown to have angina reduction, longer event-free survival, reduction in cardiac related hospitalizations, and increased exercise tolerance. Cardiogenesis has also developed the Phoenix System, which is designed to combine the delivery of biologic materials with TMR. The synergy of injecting biologics, such as stem cells or growth factors, with TMR may provide greater angina reduction, and improve cardiac function in patients with diffuse coronary artery disease who are not candidates for surgical bypass or intervention. The Phoenix System has received CE Mark designation allowing commercial distribution into the European Community. CryoLife intends to continue to investigate requirements to obtain an IDE for clinical evaluation of the Phoenix System in the U.S.

HeRO Grafts. In May 2012 CryoLife completed its acquisition of Hemosphere. Hemosphere developed and markets the HeRO Graft, a proprietary graft-based solution for ESRD hemodialysis patients with limited access options. The HeRO Graft is the only fully subcutaneous arteriovenous (AV) access solution clinically proven to maintain long-term access for hemodialysis patients with central venous stenosis. The HeRO Graft is indicated for ESRD patients who are either catheter dependent or approaching catheter dependency, on long-term hemodialysis, and have exhausted all other access options, as well as for patients with failing fistulas and grafts due to central venous stenosis.

Research and Business Development

Through its continuing research and development activities, CryoLife uses its expertise in chemistry (protein, material, organic, and bio); biomaterials; molecular biology; and engineering, and its understanding of the cardiac and vascular surgery medical specialties to develop useful technologies, services, and products. In addition, CryoLife uses this expertise to acquire and license supplemental and complimentary products and technologies. CryoLife seeks to identify market areas that can benefit from medical devices, preserved tissues, and other related technologies, to develop innovative products and techniques within these areas, to secure their commercial protection, to establish their efficacy, and then to market these products and techniques. In order to expand CryoLife s service and product offerings, CryoLife is in the process of developing or investigating several products and technologies. Some of the products in development and under investigation have not been subject to completed clinical trials and have not received FDA or other regulatory approval, so CryoLife may not derive any revenues from them. CryoLife performs significant research and development work before offering its services and products, building on either existing proprietary and non-proprietary knowledge or acquired technology and know-how. CryoLife s current tissue preservation services were developed internally. CryoLife developed its BioGlue and BioFoam products from a technology originally developed by a third-party and acquired by CryoLife. CryoLife purchased the rights to distribute and manufacture PerClot from a third-party and is working towards obtaining FDA approval to distribute PerClot in the U.S. CryoLife acquired Cardiogenesis and its revascularization technologies and intends to continue to investigate requirements to obtain an IDE approval for clinical evaluation of the Phoenix System in the U.S. CryoLife also acquired Hemosphere, and its HeRO Graft, and is working on product enhancements.

Risk Factors

CryoLife s business is subject to a number of risks. See Part I, Item 1A, Risk Factors below for a discussion of these and other risk factors.

Strategy

The key elements of the Company s strategy relate to growing its business and leveraging its strengths and expertise in its core marketplaces in order to generate revenue and earnings growth. These key elements are described below:

Identify and Evaluate Acquisition and Investment Opportunities of Complementary Product Lines and Companies. Leverage the Company s current distribution channel and its expertise in the cardiac and vascular medical specialties by selectively pursuing the potential acquisition, licensing, or distribution rights of additional technologies that complement existing services and products. Identify potential investment opportunities in companies that have complementary products that could, in the future, enhance the Company s current distribution channel and expertise in the cardiac and vascular specialties.

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Expand Core Business. Expand the Company s core business in cardiac and vascular medical specialties by expanding the market penetration of heart valves, cardiac patch tissues, vascular tissues, BioGlue, BioFoam, PerClot, revascularization technologies, and the HeRO Graft.

Develop the Company s Pipeline of Services and Products. Develop the Company s technologies and intellectual property for additional service and product offerings and commercialization of new services and products.

License Company Technology to Third-parties for Non-Competing Uses. Leverage the Company s current technology platforms, including its protein hydrogel technology (PHT) platform and SynerGraft technology, in medical specialties other than cardiac and vascular surgery through strategic alliances, licenses, or distribution arrangements for additional indications or product line extensions. The Company considers licensing or distribution opportunities for existing products or for products in its research and development pipeline if the Company determines that licensing or distribution opportunities could enhance shareholder value.

Analyze and Identify Underperforming Assets for Potential Sale or Disposal. Continue to analyze and identify underperforming assets not complementary to the strategies identified above for potential sale or disposal.

As a result of the above strategies, the Company has pursued several opportunities in the past few years that resulted in the acquisition of PerClot technologies in September 2010 and 2011, the acquisition of Cardiogenesis and its revascularization technologies in May 2011, and the acquisition of Hemosphere and its HeRO Graft in May 2012, as discussed above. Additionally, in July 2011 the Company purchased approximately 2.4 million shares of Series A Preferred Stock of ValveXchange, Inc. (ValveXchange) for approximately $3.5 million and in 2012 advanced $2 million to ValveXchange through a revolving credit facility. ValveXchange is a private medical device company that was spun off from Cleveland Clinic to develop a lifetime heart valve replacement technology platform featuring exchangeable bioprosthetic leaflets. CryoLife s investment represents an approximate 19% equity ownership in ValveXchange.

Services and Products

Preservation Services

The Company s proprietary preservation process involves the recovery of tissue from deceased human donors by tissue banks and organ procurement organizations (OTPOs), the timely and controlled delivery of such tissue to the Company, the screening, dissection, disinfection, processing, and preservation of the tissue by the Company, and the storage and shipment of the preserved tissue. In the operating room, the tissue undergoes a controlled thawing process under the supervision of the medical staff. Thereafter, the tissue is surgically implanted by a surgeon into a human recipient.

The transplant of human tissue that has not been preserved must be accomplished within extremely short time limits. Prior to the advent of human tissue cryopreservation, these time constraints resulted in the inability to use much of the tissue donated for transplantation. The application of the Company s cryopreservation technologies to donated tissue expands the amount of human cardiac and vascular tissues available to physicians for transplantation. Cryopreservation also expands the treatment options available to physicians and their patients by offering alternatives to implantable mechanical, synthetic, and animal-derived devices. The tissues currently preserved by the Company include heart valves, cardiac patch tissues, and vascular tissues.

CryoLife collects and maintains clinical data on the use and effectiveness of implanted human tissues that it has preserved and shares this data with implanting physicians and the OTPOs from which it receives tissue. The Company also uses this data to help direct its continuing efforts to improve its preservation services through ongoing research and development. Its physician relations and education staff, clinical research staff, and field representatives assist physicians by providing educational materials, seminars, and clinics on methods for handling and implanting the tissue preserved by the Company and the clinical advantages, indications, and applications for those tissues. The Company has ongoing efforts to train and educate physicians on the indications for, and uses of, the human tissues preserved by the Company. In addition, the Company sponsors programs where surgeons train other surgeons in best-demonstrated techniques. The Company also assists OTPOs through training and development of protocols and provides materials to improve their tissue recovery techniques and, thereby, increase the yield of usable tissue.

Cardiac Tissue. The human heart valves and cardiac patch tissues preserved by the Company are used in cardiac reconstruction and heart valve replacement surgeries. The Company currently preserves human aortic and pulmonary heart valves for implantation by cardiac surgeons. In addition, the Company preserves human cardiac patches for surgeons who wish to perform certain specialized cardiac repair procedures. The Company currently preserves human cardiac patches in three primarily anatomic configurations: pulmonary hemi-artery, pulmonary trunk, and pulmonary branch. Each of these preserved cardiac tissues maintains a structure which more closely resembles and simulates the performance of the patient s own tissue compared to non-human tissue alternatives.

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In 2008 CryoLife received 510(k) clearance from the FDA for its CryoValve SGPV, and in 2009 CryoLife received 510(k) clearance from the FDA for its CryoPatch SG, both processed with the Company s proprietary SynerGraft technology. The SynerGraft process reduces the presence of allogeneic donor cells, while maintaining the structural integrity of the tissue. CryoLife uses the SynerGraft technology for a portion of its pulmonary valve and cardiac patch processing. In 2012 71% of pulmonary valves and 46% of cardiac patch tissues shipped by CryoLife were processed with the SynerGraft technology.

Based on CryoLife s records of documented implants, management believes that the acceptance of the Company s heart valves is due in part to physicians recognition of the longevity and natural functionality of the Company s cardiac tissues, the Company s documented clinical data, and the support of the Company s physician relations and education staff, clinical research staff, customer service department, and field representatives. Management believes the Company offers advantages in the areas of clinical data and field services as compared to other human tissue processors and that the Company s tissues offer advantages in certain areas over mechanical, porcine, and bovine heart valve alternatives. Management believes preserved human heart valves and cardiac patch tissues have characteristics that make them the preferred replacement option for many patients. Specifically, human heart valves, such as those preserved by the Company, allow for more normal blood flow and provide higher cardiac output than stented porcine, bovine, and mechanical heart valves. Human heart valves are not as susceptible to progressive calcification, or hardening, as are traditional glutaraldehyde-fixed porcine and bovine heart valves, and do not require anti-coagulation drug therapy, as do mechanical valves. The synthetic sewing rings contained in mechanical and stented porcine and bovine valves may harbor bacteria and lead to endocarditis. Furthermore, prosthetic valve endocarditis can be difficult to treat with antibiotics, and this usually necessitates the surgical removal of these valves at considerable cost, morbidity, and risk of mortality. Consequently, for many physicians, human heart valves are the preferred alternative to mechanical and animal-derived tissue valves for patients who have or are at risk to contract endocarditis.

CryoLife shipped approximately 80,800 heart valves and cardiac patch tissues from 1984 through 2012, including approximately 3,200 shipments in 2012. Revenues from cardiac tissue preservation services accounted for 23%, 22%, and 24% of total Company revenues in 2012, 2011, and 2010, respectively. The Company estimates that in 2012 the total annual heart valve replacement and cardiac patch market in the U.S. was approximately $850 million. Management believes that of the $850 million, approximately $640 million or 75% of the procedures were for aortic, pulmonary, and tricuspid valve replacements for which the Company s tissues can be used. The Company believes that approximately 97,000 aortic, pulmonary, and tricuspid valve replacement surgeries were conducted in the U.S. in 2012.

Vascular Tissue. The human vascular tissues preserved by the Company, including the CryoVein and CryoArtery, are used to treat a variety of vascular reconstructions such as peripheral bypass, hemodialysis access, and aortic infections which have saved the lives and limbs of patients. The Company preserves human saphenous vein conduits (3mm to 6mm) for use in peripheral vascular reconstructions. Failure to achieve revascularization of an obstructed vessel may result in the loss of a limb or even death of the patient. When patients require peripheral bypass surgery, the surgeon s first choice generally is the patient s own vein tissue. However, in cases of advanced vascular disease, as many as 30% of patients have unsuitable vein tissue for transplantation, and the surgeon must consider using synthetic grafts or preserved human vascular tissue. Synthetic vascular grafts are generally not optimal for below-the-knee surgeries because they have a tendency to obstruct over time. Preserved human vascular tissues tend to remain open longer and, as such, are used in indications where synthetics typically fail. In addition, synthetic grafts are not suitable for use in infected areas since they may harbor bacteria and are difficult to treat with antibiotics. Preserved human vascular tissues have advantages for patients with previously infected graft sites. The Company also preserves femoral veins and arteries and aortoiliac arteries for bypass, hemodialysis access, or reconstruction within infected surgical areas.

The Company shipped approximately 70,700 vascular tissues from 1986 through 2012, including approximately 4,600 shipments in 2012. Revenues from vascular preservation services accounted for 26%, 28%, and 27% of total Company revenues in 2012, 2011, and 2010, respectively. The Company estimates the aggregate U.S. vascular surgical graft market was approximately $120 million in 2012.

Medical Devices

PHT Platform

The effective closure of internal wounds following surgical procedures is critical to the restoration of the function of tissue and to the ultimate success of the surgical procedure. Failure to effectively seal surgical wounds can result in leakage of blood in cardiac surgeries, air in lung surgeries, cerebral spinal fluid in neurosurgeries, and gastrointestinal contents in abdominal surgeries. Air and fluid leaks resulting from surgical procedures can lead to significant post-operative morbidity resulting in prolonged hospitalization, higher levels of post-operative pain, higher costs, and a higher mortality rate.

Sutures and staples facilitate healing by joining wound edges and allowing the body to heal naturally. However, because sutures and staples do not have inherent sealing capabilities, they cannot consistently eliminate air and fluid leakage at the wound site. This is particularly the case when sutures and staples are used to close tissues containing air or fluids under pressure, such as in blood vessels, the lobes of the lung, the dural membrane surrounding the brain and spinal cord, and the gastrointestinal tract. In some cases, the tissues may be friable, which complicates the ability to achieve closure. In addition, in minimally invasive surgical procedures where the physician must operate through small access devices, it can be difficult and time consuming for the physician to apply sutures and staples. The Company believes that the use of surgical adhesives and sealants with or without sutures and staples could enhance the efficacy of these procedures through more effective and rapid wound closure. In order to address the inherent limitations of sutures and staples, the Company developed and commercialized its PHT. PHT is based on a bovine protein that mirrors an array of amino acids that perform complex functions in the human body. Together with a cross-linker, the protein forms a hydrogel, a water-based biomaterial in some ways similar to human tissue. Materials and implantable replacement devices created with PHT may have the potential to provide structure, form, and function similar to certain human tissues.

BioGlue. BioGlue is the first product to be developed from the Company s PHT platform. BioGlue is a polymeric surgical adhesive based on bovine blood protein and an agent for cross-linking proteins. BioGlue has a tensile strength that is four to five times that of fibrin sealants. BioGlue begins to polymerize within 20 to 30 seconds and reaches its bonding strength within two minutes. BioGlue is pre-filled in 2ml, 5ml, and 10ml volumes. BioGlue is dispensed by a controlled delivery system that consists of either a reusable delivery device and disposable syringe or a disposable syringe alone. Both systems use an assortment of applicator tips (standard size tips, 12mm and 16mm spreader tips, 10cm and 27cm flexible extender tips, and a 10cm, 27cm, and 35cm delivery tip extender).

CryoLife is authorized to distribute BioGlue throughout the U.S. and in more than 80 other countries for designated applications. In the U.S., BioGlue is FDA approved as an adjunct to sutures and staples for use in adult patients in open surgical repair of large vessels. The Company estimates that aggregate U.S. sales for surgical internal tissue sealants were approximately $335 million in 2012.

CryoLife distributes BioGlue under CE Mark product certification in the EEA for repair of soft tissues (which include cardiac, vascular, pulmonary, and additional soft tissues). CryoLife has also received approval and distributes BioGlue for soft tissue repairs in Canada, Brazil, and Australia and for the repair of aortic dissections in Japan. Additional marketing approvals have been granted for specified applications in several other countries throughout the world.

Revenues from BioGlue represented 40%, 41%, and 41% of total Company revenues in 2012, 2011, and 2010, respectively.

BioFoam. BioFoam is the second product to be developed from the Company s PHT platform. BioFoam is a protein hydrogel biomaterial with an expansion agent which generates a mixed-cell foam. The foam creates a mechanical barrier to decrease blood flow and develops pores for the blood to enter, leading to cellular aggregation and enhanced hemostasis. It is easily applied and could potentially be used intraoperatively to control internal organ hemorrhage, limit blood loss, and reduce the need for future re-operations in liver resections.

BioFoam received CE Mark certification in August 2009 for use as an adjunct in the sealing of abdominal parenchymal tissues (liver and spleen) when cessation of bleeding by ligature or conventional methods is ineffective or impractical. CryoLife began a controlled launch of BioFoam at three clinical centers in Europe in 2009 and in 2010 began distribution of BioFoam in Europe. In November 2012 CryoLife received approval for an additional indication in Europe, allowing it to market BioFoam as an adjunct to hemostasis in cardiovascular surgery when cessation of bleeding by ligature or other conventional methods is ineffective or impractical. CryoLife plans to begin distribution of BioFoam in other international markets as required regulatory approvals are obtained.

Revenues from BioFoam represented less than 1% of total Company revenues in 2012, 2011, and 2010. CryoLife estimates the annual European market opportunity for cardiovascular and parenchymal tissue sealing, for which BioFoam can be used, is more than $100 million.

Hemostatic Agents

Hemostatic agents are frequently utilized as an adjunct to sutures and staples to control inter-operative bleeding. Hemostatic agents prevent excess blood loss and can help maintain good visibility of the operative site. These products can, in many instances, reduce operating room time and decrease the number of blood transfusions required in surgical procedures. Hemostatic agents are available in various forms including pads, sponges, liquids, and powders.

Revenues from hemostatic agents represented 2%, 4%, and 8% of total Company revenues in 2012, 2011, and 2010, respectively. The Company estimates that aggregate U.S. sales for hemostatic agents were approximately $890 million in 2012.

PerClot. PerClot is an absorbable, powdered hemostatic agent used in surgery. The PerClot technology modifies plant starch into ultra-hydrophilic adhesive forming hemostatic polymers. PerClot granules are biocompatible, absorbable polysaccharides containing no animal or human components. Utilizing this purified plant source material aids in minimizing the risks of infection and bleeding-related complications during surgery. PerClot granules have a molecular structure that rapidly absorbs water, forming a gelled adhesive matrix that provides a mechanical barrier to further bleeding and results in the accumulation of platelets, red blood cells, and coagulation proteins (thrombin, fibrinogen, etc.) at the site of application. The gelled adhesive matrix thus promotes the normal physiological clotting cascade. Easy to apply, PerClot does not require additional operating room preparation or special storage conditions. PerClot is readily dissolved by saline irrigation and is totally absorbed within several days. PerClot is currently available in 1 gram, 3 gram, and 5 gram configurations with a 100mm or 200mm applicator tip. PerClot Laparoscopic is available in 1 gram and 3 gram configurations with a 380mm applicator tip.

In September 2010 CryoLife entered into a worldwide distribution agreement and a license and manufacturing agreement with SMI for PerClot, which has CE Mark designation allowing commercial distribution into the European Community and other markets. It is indicated for use in surgical procedures, including cardiac, vascular, orthopaedic, neurological, gynecological, ENT, and trauma surgery as an adjunct hemostat when control of bleeding from capillary, venular, or arteriolar vessels by pressure, ligature, and other conventional means is either ineffective or impractical.

CryoLife filed an IDE with the FDA in March 2011 seeking approval to begin clinical trials for the purpose of obtaining a PMA to distribute PerClot in the U.S. In April 2011 the FDA disapproved CryoLife s IDE filing. In March 2012 CryoLife refiled its IDE and the FDA responded with comments in the second quarter of 2012. CryoLife filed a revised IDE in November 2012 and received questions from the FDA in December 2012 related to this filing. CryoLife is currently working to address the questions and expects to respond to the FDA in the first quarter of 2013.

CryoLife began distributing PerClot in Europe in the fourth quarter of 2010. Revenues for PerClot represented approximately 2% of total Company revenues in 2012 and 2011. CryoLife plans to begin distribution of PerClot in other international markets as required regulatory approvals are obtained.

HemoStase. CryoLife distributed HemoStase under a private label exclusive distribution agreement with Medafor, Inc. (Medafor) from May 2008 to March 2011. Medafor fully, finally, and effectively terminated the agreement in 2010. The parties litigated the agreement and termination and settled the litigation in 2012. Revenues for HemoStase represented 0%, 2%, and 8% of total Company revenues in 2012, 2011, and 2010, respectively.

Revascularization Technologies

CryoLife s subsidiary, Cardiogenesis, markets its Holmium: YAG laser console and single use, fiber-optic handpieces. These products are FDA approved for performing a surgical procedure known as TMR for treating patients with stable angina that is not responsive to conventional therapy. Patients undergoing TMR treatment with Cardiogenesis products have been shown to have angina reduction, longer event-free survival, reduction in cardiac related hospitalizations, and increased exercise tolerance.

During TMR, the surgeon uses one of the flexible, fiber-optic handpieces to deliver precise bursts of Holmium: YAG laser energy directly to an area of heart muscle that is suffering from ischemic heart disease. This condition can manifest itself with severe persistent chest pain, or chronic angina. The surgical procedure is performed through a small incision or

small ports with the patient under general anesthesia. The surgeon can position the laser fiber on the surface of the beating heart. It takes approximately 6 to 10 pulses of the laser to transverse the myocardium and create channels one millimeter in diameter. During a typical procedure, approximately 20 to 40 channels are made in the heart muscle.

The outside punctures seal over with little blood loss. Published research shows evidence that these channels promote the growth of new blood vessels or angiogenesis over time. That, in turn, provides the damaged heart tissue a better supply of blood and oxygen. Angina usually subsides with improved oxygen supply to the targeted areas of the damaged heart muscle.

SolarGen 2100s Console. The SolarGen 2100s Console implements advanced electronic and cooling system technology to greatly reduce the size and weight of the unit, while providing 115V power capability. The SolarGen 2100s Console was approved by the FDA in 2004 and received a CE Mark in 2005. The Company provides service plan options to ensure that the laser console is operating within the critical factory specifications and to protect the customer s investment.

SoloGrip® III. The SoloGrip III handpiece contains multiple, fine fiber-optic strands in a one millimeter diameter bundle. The flexible fiber-optic delivery system combined with the ergonomic handpiece provides access for treating all regions of the left ventricle. The SoloGrip III handpiece fiber-optic delivery system has an easy to install connector that screws into the laser base unit, and the device is pre-calibrated in the factory so it requires no special preparation. The SoloGrip III handpiece received FDA approval in 1999 and received a CE Mark in 1997.

PEARL 5.0. The minimally invasive Port Enabled Angina Relief with Laser (PEARL) 5.0 handpiece is compatible for use with Intuitive Surgical s da Vinci Surgical System. The PEARL 5.0 handpiece received FDA approval in 2007 and received a CE Mark in 2005.

PEARL 8.0. The PEARL 8.0 has been designed for use in a minimally invasive thoracoscopic procedure. The PEARL 8.0 handpiece received FDA approval in 2012 and CE Mark in 2005. The Company anticipates launching the PEARL 8.0 in 2013.

CryoLife began distributing the TMR product line in May 2011 when it completed the acquisition of Cardiogenesis. Revenues from revascularization technologies represented 6% and 5% of total Company revenues in 2012 and 2011, respectively. The Company estimates that the addressable market opportunity for TMR is approximately $175 million.

HeRO Grafts

CryoLife and its subsidiary Hemosphere market the HeRO Graft, a proprietary graft-based solution for ESRD hemodialysis patients with limited access options and central venous obstruction. The HeRO Graft received its initial FDA 510(k) clearance in 2008, and a CE Mark application for the HeRO Graft is currently under review by the Company s Notified Body. It is indicated for ESRD patients who are catheter dependent or approaching catheter dependency, on long-term hemodialysis, and have exhausted all other access options, as well as for patients with failing fistulas and grafts due to central venous stenosis. Prior to the introduction of the HeRO Graft, the only option for these patients was access through percutaneous tunneled dialysis catheters, which are higher cost, have high infection rates, limit a patient s lifestyle, and foster central venous stenosis, or narrowing of the venous system. The HeRO Graft overcomes the limitations of catheters by providing a completely subcutaneous graft that functions like a regular access graft during dialysis, providing superior blood flow, and achieving a 69% reduction in bacteremia (bacteria in the blood) compared with catheters. HeRO is the only fully subcutaneous AV access solution clinically proven to maintain long-term access for hemodialysis patients with central venous stenosis. The HeRO Graft traverses the central venous stenosis allowing for long-term hemodialysis access.

CryoLife began distributing the HeRO Graft in May 2012 when it completed the acquisition of Hemosphere. The Company estimates that the addressable market opportunity for the HeRO Graft in the U.S. is approximately $125 million worldwide. More than 6,000 HeRO Grafts were shipped from 2008 to 2012. Revenues from the HeRO Graft represented 2% of total Company revenues in 2012. CryoLife intends to introduce the HeRO graft into the European Union (EU) in mid-2013, upon receipt of its CE Mark, which it anticipates receiving in early 2013.

Other Medical Devices

ProPatch Soft Tissue Repair Matrix (ProPatch). ProPatch, manufactured from bovine pericardial tissue and treated with the SynerGraft process, is used to reinforce weakened soft tissues and provides a resorbable scaffold that is replaced by the patient s own soft tissue. ProPatch is intended to be used for implantation to reinforce defects of the abdominal and

thoracic wall, muscle flap reinforcement, hernias, suture-line reinforcement, and reconstructive procedures. ProPatch can also be used to reinforce tissues repaired by sutures or by suture anchors during tendon repair surgeries, including reinforcement of the rotator cuff, patellar, Achilles, biceps, quadriceps, or other tendons. Available in multiple size and shape configurations, ProPatch comes fully hydrated and ready to implant.

In late 2006 CryoLife received 510(k) clearance from the FDA for ProPatch. In 2011 CryoLife implemented modifications to streamline the manufacturing process. These modifications resulted in the submission of a new 510(k), which was cleared by the FDA in January 2012. CryoLife intends to commercialize ProPatch, which may include partnering with one or more third-parties as well as obtaining clinical data to support indications for direct distribution.

Seasonality and Segment Information

See Part II, Item 7, Management s Discussion and Analysis of Financial Condition and Results of Operations Seasonality, regarding seasonality of the Company s preservation services and products.

See Part II, Item 8, Note 19 of the Notes to Consolidated Financial Statements regarding segment and geographic information.

Distribution and Marketing

Preservation Services

CryoLife markets its preservation services to OTPOs, implanting physicians, and prospective tissue recipients. The Company works with OTPOs to ensure consistent and continued availability of donated human tissue for transplant and educates physicians and prospective tissue recipients with respect to the benefits of preserved human tissues.

Procurement of Tissue. Donated human tissue is procured from deceased human donors by OTPOs. After procurement, the tissue is packed and shipped, together with certain information about the tissue and its donor, to the Company in accordance with the Company s protocols. The tissue is transported to the Company s laboratory facilities via commercial airlines pursuant to arrangements with qualified courier services. Timely receipt of procured tissue is important, as tissue that is not received promptly cannot be cryopreserved successfully. The OTPOs are reimbursed by the Company for costs associated with these procurement services. The procurement fee, together with the charges for the preservation services of the Company, is ultimately paid to the Company by the hospital or healthcare facility with which the implanting physician is associated.

Since 1984 the Company has received tissue from over 120,000 donors. The Company has active relationships with approximately 40 OTPOs throughout the U.S. Management believes these relationships are critical in the preservation services industry and that the breadth of these existing relationships provides the Company with a significant advantage over potential new entrants to this market. The Company employs approximately 35 individuals in donor services and donor quality assurance to work with OTPOs. This includes three account managers who are stationed throughout the country to work directly with the OTPOs. The Company s central office for procurement relations is staffed 24 hours per day, 365 days per year.

Preservation of Tissue. Upon receiving tissue, a Company technician completes the documentation control for the tissue prepared by the OTPO and gives it a control number. The documentation identifies, among other things, donor age, and cause of death. A trained technician then removes the portion or portions of the delivered tissue that will be processed. The Company s cardiac and vascular tissues are preserved in a proprietary freezing process conducted according to Company protocols. After the preservation process, the tissues are transferred to liquid nitrogen freezers, initially under quarantine status, for long-term storage at temperatures at or below -135º C. The entire preservation process is controlled by guidelines established by the Company and are conducted under aseptic conditions in clean rooms.

At the same time the tissue is processed, samples are taken from the donated tissue and subjected to the Company s quality assurance program. This program, which includes review of the donor and tissue charts by CryoLife s tissue quality assurance department and its medical directors, may identify characteristics which would disqualify the tissue for preservation or implantation. Once the tissue is approved, it is moved from quarantine to an implantable status. Tissue that does not pass testing is discarded as appropriate or used for research or other purposes if the donor s family has consented.

Distribution of Tissue to Implanting Physicians. After the tissue has cleared quality control assurance and is moved to an implantable status, the tissue is stored by the Company until it is delivered to hospitals at the implanting physician s request. Cryopreserved tissue must be transported under stringent handling conditions and maintained within specific temperature tolerances at all times. Cryopreserved tissue is packaged for shipment using the Company s proprietary processes. After the Company transports the tissue to the hospital, the Company invoices the institution for its services, which include procurement, preservation, and transportation. At the hospital, the tissue is thawed and implanted immediately or is held in a liquid nitrogen freezer in accordance with Company protocols pending implantation. The Company provides a detailed protocol for thawing the cryopreserved tissue. The Company also makes its field personnel available by phone or in person to answer questions.

The Company provides Company-owned liquid nitrogen freezers to certain client hospitals. The Company currently has approximately 260 of these freezers installed at hospitals throughout the U.S. Participating hospitals generally pay the cost of liquid nitrogen. The availability of on-site freezers makes it easier for a hospital s physicians to utilize the Company s tissues by making the tissue more readily available.

Medical Devices

In the U.S. the Company markets its products to physicians and distributes its products through its field service representatives and cardiac specialists. The Company markets and distributes its products in international markets through independent distributors in Canada, Asia Pacific, and the Americas and through the Company s wholly owned European subsidiary, CryoLife Europa, Ltd. (Europa), which employs direct field representatives and manages relationships with other independent distributors in Europe, the Middle East, and Africa. Through its field representatives and distributors, the Company conducts field training for implanting surgeons regarding the application of its products.

Marketing, Educational, and Technical Support

The Company works to maintain relationships with, and market to, surgeons within the cardiac and vascular medical specialties. The Company has records of over 1,400 cardiac and vascular surgeons who implanted tissues preserved by the Company during 2012. In the U.S., the Company has 20 cardiac specialists who focus primarily on cardiac surgeons, approximately 28 cardiovascular representatives who focus primarily on vascular surgeons, eight dialysis therapy representatives who focus primarily on nephrologists and dialysis clinics, and eight region managers. A small number of these positions are open, and the Company is actively recruiting for these positions.

Because the Company markets its preservation services and products directly to physicians, an important aspect of increasing the distribution of the Company s preservation services and products is educating physicians on the use of the Company s preserved human tissues and medical device products and on proper implantation and surgical techniques. The Company s trained medical relations and education staff and field support personnel provide support to implanting institutions and surgeons. The Company sponsors training seminars where physicians teach other physicians the proper technique for handling and implanting preserved human tissue. The Company also produces educational videos for physicians and coordinates peer-to-peer training at various medical institutions. In addition, the Company hosts several workshops throughout the year including the Ross Summit, Aortic Allograft Workshops, TMR Workshops, and beginning in 2013, the Central Venous Pathology Summit. These workshops aim to provide didactic and hands-on training to surgeons. Management believes that these activities improve the medical community s acceptance of the tissues and products offered by the Company and help to differentiate the Company from other allograft processors and medical device companies.

In September 2012 CryoLife hosted the fourth annual Ross Summit at CryoLife s Corporate Headquarters with 48 cardiac surgeons and cardiologists from 17 countries in attendance. The primary goal of the meeting was to facilitate and encourage the use of the Ross Procedure. The Ross Procedure is an operation in which a patient s defective aortic valve is removed and replaced with his own pulmonary valve, and then a replacement pulmonary valve (typically a valve from a human donor) is surgically implanted to replace the removed native pulmonary valve.

To assist OTPOs, the Company provides educational materials and training on procurement, dissection, packaging, and shipping techniques. The Company also produces educational videos and coordinates laboratory sessions on procurement techniques for OTPO personnel. To supplement its educational activities, the Company employs a full-time technical trainer, who provides technical information and assistance and maintains a staff 24 hours per day, 365 days per year for OTPO support.

European Operations

The Company markets its tissue services and products in the EEA, the Middle East, and Africa (EMEA) region through its European subsidiary, Europa, based in Guildford, England. Europa, with its team of approximately 26 employees, provides customer service, logistics, marketing, and clinical support to cardiac, vascular, thoracic, and general surgeons throughout the EMEA region. Europa markets and distributes the Company s complete range of services and products, in both of its reportable segments, through its direct sales representatives in the U.K., Germany, Austria, and Ireland and through a network of independent distributors in the rest of the EMEA region. Europa also distributes tissue to certain hospitals in the EMEA region, primarily in Germany, Austria, and the U.K.

Backlog

The limited supply of certain types or sizes of preserved tissue, primarily for use in pediatric surgeries, can result in a backlog of orders for these tissues. The amount of backlog fluctuates based on the tissues available for shipment and varies based on the surgical needs of specific cases. The Company s backlog is generally not considered firm and must be confirmed with the customer before shipment. The Company currently does not have a backlog of orders related to BioGlue, BioFoam, PerClot, revascularization technologies, or HeRO Grafts.

Competition

Preservation Services

The Company currently faces competition from at least two non-profit tissue banks that preserve and distribute human cardiac heart valves, cardiac patch tissues, and vascular tissues, as well as from several companies that market mechanical, porcine, and bovine heart valves, and synthetic vascular grafts for implantation. Many established companies, some with financial and personnel resources greater than those of the Company, are engaged in manufacturing, marketing, and selling alternatives to preserved human tissue. These competitors may also have greater experience in developing products, conducting clinical trials, and obtaining regulatory approvals. Certain of these competitors may obtain patent protection, approval, or clearance by the FDA or foreign countries earlier than the Company. The Company may also compete with companies that have superior manufacturing efficiency and marketing capabilities. Any of these competitive disadvantages could materially, adversely impact the Company. Companies offering mechanical, synthetic, bovine, porcine, or allograft products may enter this market in the future. Any newly developed treatments may also compete with the use of tissues preserved by the Company. Management believes that it competes with other entities that preserve human tissue on the basis of technology, customer service, and quality assurance.

Heart Valves. Alternatives to human heart valves preserved by the Company include valve repair and valve replacement with mechanical valves, porcine valves, or valves constructed from bovine pericardium. St. Jude Medical, Inc. is the leading supplier of mechanical heart valves. Medtronic, Inc. is the leading supplier of porcine heart valves. Edwards Life Sciences, Inc. is the leading supplier of bovine pericardial heart valves. The Company is aware of at least six companies that offer porcine, bovine, and mechanical heart valves. In addition, management believes that at least one domestic tissue bank offers preserved human heart valves in competition with the Company.

Management believes that the human heart valves preserved by the Company, as compared to mechanical, porcine, and bovine heart valves, compete on the factors set forth above, as well as by providing a tissue that is the preferred replacement alternative with respect to certain medical conditions, such as pediatric cardiac reconstruction, valve replacements for women in their child-bearing years, and valve replacements for patients with endocarditis. The Company believes the CryoValve SGPV enables the Company to compete with other valves by providing a valve processed with a technology designed to remove donor cells and cellular remnants from the valve without compromising the integrity of the underlying collagen matrix. The Company also believes that the CryoValve SGPV and the CryoValve SG aortic heart valve (CryoValve SGAV) are important to patient management issues for potential whole organ transplant recipients. Implantation of the SynerGraft treated cardiac tissue reduces the risk for induction of HLA class I and class II alloantibodies, based on Panel Reactive Antibody (PRA) measured at up to one year, compared to standard processed cardiac tissues. While the link between immune response and allograft tissue performance is still being debated, there is evidence that an elevated PRA poses a significant risk to future organ transplant patients. Avoiding elevated PRA is important for patients receiving cardiac tissues as some of these patients may ultimately require a heart transplant. In these patients, an increased PRA can decrease the number of possible donors for subsequent organ transplants, and increase time on transplant waiting lists.

Cardiac Patches. Alternatives to human cardiac patches preserved by the Company include cardiac repair and reconstruction with small intestine submucosa (SIS) or patches constructed from bovine pericardium. CorMatrix Cardiovascular, Inc. is the leading supplier of SIS for cardiac repair and reconstruction with its CorMatrix ECM technology. There are several suppliers of bovine pericardial patches targeted for cardiac repair and reconstruction, including Edwards Life Sciences, Inc., Neovasc, Inc., and St. Jude Medical, Inc. Management believes that at least one domestic tissue bank offers preserved human cardiac patches in competition with the Company, including LifeNet Health, Inc. which processes allograft patches using its Matracell technology.

Management believes that the human cardiac patches preserved by the Company, as compared to SIS, bovine, or other allograft patches, compete on the factors set forth above with respect to heart valves, and that these human cardiac tissues are the preferred repair and reconstruction alternative for use for defect repair including Tetralogy of Fallot, Truncus Arteriosis, and Pulmonary Atresia. The Company believes the CryoPatch SG enables the Company to compete with other patches by providing a patch processed with a technology designed to remove donor cells and cellular remnants from the patch without compromising the integrity of the underlying collagen matrix. As discussed above for the CryoValve SGPV and CryoValve SGAV, the Company also believes that the CryoPatch SG is important to patient management issues for potential whole organ transplant recipients.

Vascular Tissue. There are a number of providers of synthetic alternatives to veins preserved by the Company and those alternatives are available primarily in medium and large diameters. Two primary synthetic grafts that compete with the Company s vascular tissue for below-the-knee surgery are W.L. Gore & Associates Propaten and C.R. Bard, Inc. s Distaflo. Artegraft s bovine carotid artery graft and Hancock Jaffe Laboratories, Inc. s Procol can be used for hemodialysis access, and Maquet, Inc. s Hemashield woven grafts can be used for aortoiliac aneurysm surgery. Currently, management believes there are at least two other non-profit tissue banks that preserve and distribute human vascular tissue in competition with the Company.

Generally, for each procedure that may utilize vascular human tissue that the Company preserves, there are alternative treatments. Often, in the case of veins, these alternatives include the repair, partial removal, or complete removal of the damaged tissue and may utilize other tissues from the patients themselves or synthetic products. The attending physician, in consultation with the patient, makes the selection of treatment choices. Any newly developed treatments may also compete with the use of vascular tissue preserved by the Company.

Medical Devices

The Company faces competition from several domestic and international medical device, pharmaceutical, and biopharmaceutical companies in its surgical sealants and hemostats product lines. Many of the Company s current and potential surgical adhesives, sealants, and hemostats competitors have substantially greater financial and personnel resources than the Company. These competitors may also have greater experience in developing products, conducting clinical trials, and obtaining regulatory approvals and may have large contracts with hospitals under which they can impose purchase requirements that place our products at a disadvantage. Certain of these competitors may obtain patent protection or approval or clearance by the FDA or foreign countries earlier than the Company. The Company may also compete with companies that have superior manufacturing efficiency and marketing capabilities. Any of these competitive disadvantages could materially, adversely impact the Company.

BioGlue. The Company s BioGlue products compete primarily with Baxter International, Inc. s Tisseel, CoSeal, and TachoSil; Ethicon, Inc. s (a Johnson & Johnson Company) Evicel and Omnex; Covidien Ltd. s U.S. Surgical Division s Duraseal product; NeoMend, Inc. s ProGEL; and Tenaxis, Inc. s (Tenaxis) ArterX. The Company currently competes with these products based on BioGlue s benefits and features, such as strength and ease of use. Additional competitive products may be under development by other large medical device, pharmaceutical, and biopharmaceutical companies.

BioFoam. The Company s BioFoam product competes with other surgical hemostatic agents that include Pfizer, Inc. s Gelfoam; Baxter International, Inc. s FloSeal; Ethicon, Inc. s Spongostan, Instat, Surgicel, and Surgicel Nu-Knit; C.R. Bard, Inc. s Avitene; Baxter International s TachoSil; and Orthovita, Inc. s Vitagel. Other medical device, pharmaceutical, and biopharmaceutical companies may also develop competitive products. The Company s BioFoam product competes on the basis of its clinical efficacy and ease of use.

PerClot. The Company s PerClot product competes with thrombin products, including King Pharmaceuticals, Inc. s Thrombin JMI; ZymoGenetics, Inc. s Recothrom; and Omrix Biopharmaceuticals, Inc. s (a Johnson & Johnson Company) Evithrom; and surgical hemostats, including Pfizer, Inc. s Gelfoam; C.R. Bard, Inc. s Avitene; Baxter International, Inc. s FloSeal; Ethicon, Inc. s Surgicel, Surgiflo, and Surgifoam products; Medafor s Arista; and BioCer s HaemoCer. Other competitive products may include argon beam coagulators, which provide an electrical source of hemostasis. A number of companies have surgical hemostat products under development. Other medical device, pharmaceutical, and biopharmaceutical companies may also develop competitive products. The Company s PerClot products compete on the basis of safety profile, clinical efficacy, absorption rates, and ease of use.

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Revascularization Technologies. The Company s revascularization technologies compete with other methods for the treatment of coronary artery disease, including drug therapy, percutaneous coronary intervention, coronary artery bypass surgery, and enhanced external counterpulsation. Currently, the only directly competitive laser technology for the performance of TMR is the CO_2 Heart Laser System manufactured by Novadaq Technologies, Inc. Other medical device and pharmaceutical companies may also develop additional competitive products. The Company s revascularization technology competes on the basis of ease of use, versatility, size of laser console, and improved access to the treatment area with a smaller fiber-optic system.

HeRO Grafts. The Company s HeRO Graft competes with balloon angioplasty products, including C.R. Bard Inc. s Conquest and Boston Scientific s Mustang. These products treat central venous stenosis and may preclude the future use of the HeRO Graft due to total occlusion of the central venous system. No product on the market currently serves as a fully subcutaneous AV access graft for patients while treating central venous stenosis. Other companies either have a fully subcutaneous graft for maintaining AV access, such as Artegraft Inc. s Artegraft Bovine Carotid Artery Graft, W.L. Gore & Associates Hybrid Vascular Graft, C.R. Bard, Inc. s Impra, and Atrium s Flixene, or they have a chronic dialysis catheter for maintaining access in patients with central venous stenosis. Additional competitive products may be under development by other large medical device, pharmaceutical, and biopharmaceutical companies. The Company s HeRO Graft competes on the basis of reducing catheter dependency in ESRD patients with central venous stenosis, and benefiting patients through fewer infections, superior dialysis adequacy, higher patency rates, and reduced costs compared to catheters.

General

Other recently developed technologies or procedures are, or may in the future be, the basis of competitive products. There can be no assurance that the Company s current competitors or other parties will not succeed in developing alternative technologies and products that are more effective, easier to use, or more economical than those which have been or are being developed by the Company or that would render the Company s technology and products obsolete and non-competitive in these fields. In such event, the Company s business, financial condition, profitability, and cash flows could be materially, adversely impacted. See Part I, Item 1A, Risk Factors Risks Relating To Our Business Rapid Technological Change Could Cause Our Services And Products To Become Obsolete.

Research and Development and Clinical Research

The Company uses its expertise in chemistry (protein, material, organic, and bio), cell biology, and engineering, and its understanding of the needs of the cardiac and vascular surgery medical specialties to attempt to expand its preservation services and surgical adhesives, sealants, and hemostats businesses and to develop or acquire products and technologies for these specialties. The Company identifies market areas that can benefit from preserved tissues, medical devices, and other related technologies and then attempts to develop innovative techniques, services, and products within these areas, to secure their commercial protection, to establish their clinical efficacy, and then to market these techniques, services, and products. The Company employs approximately 36 people in its research and development and clinical research departments, including five Ph.D.s with specialties in the fields of chemistry (protein, material, organic, and bio); biomaterials; molecular biology; and engineering.

In order to expand the Company s service and product offerings, the Company is currently in the process of obtaining approvals, developing, or investigating several technologies and products, including technologies related to additional applications of its SynerGraft technology, including the CryoValve SGAV and ProPatch, the PHT product platform used in BioGlue, BioFoam, and other PHT derivatives, PerClot, revascularization technologies, human tissue preservation, and the HeRO Graft.

To the extent the Company identifies additional applications for its products, the Company may attempt to license these products to corporate partners for further development of such applications or seek funding from outside sources to continue the commercial development of such technologies. The Company may also attempt to acquire or license additional technologies from third-parties to supplement its product lines.

The Company s research and development strategy is to allocate available resources among the Company s core market areas of cardiac and vascular surgery, sealants, and hemostats, based on the size of the potential market for any specific product candidate, the estimated development time and cost required to bring the product to market, and the expected efficacy of the potential product. Research on these and other projects is conducted in the Company s research and

development laboratory or at universities or clinics where the Company sponsors research projects. The Company s medical and scientific advisory board consults on various research and development programs. The Company s preclinical studies are conducted at universities and other locations outside the Company s facilities by third-parties under contract with the Company. In addition to these efforts, the Company may pursue other research and development activities.

In 2012, 2011, and 2010 the Company spent approximately $7.3 million, $6.9 million, and $5.9 million, respectively, on research and development activities on new and existing products. These amounts represented approximately 6%, 6%, and 5% of the Company s revenues for each of the years 2012, 2011, and 2010, respectively. Of these amounts spent on research and development activities, $604,000, $398,000, and $490,000 was funded by the U.S. Department of Defense (DOD) in 2012, 2011, and 2010, respectively.

CryoValve SGPV. At the FDA s request, the Company has committed to conducting a post-clearance study to collect long-term clinical data for the CryoValve SGPV. Data collected in this study will be compared to data from a defined control group implanted with a standard processed human pulmonary heart valve. The Company believes the information obtained from this study may help ascertain whether the SynerGraft process extends the long-term durability of pulmonary valves. Additionally, explant analyses may help determine if the heart valve s collagen matrix recellularizes with the recipient s own cells. The study is expected to be completed in early 2014.

CryoValve SGAV. In September 2009 the FDA granted a Humanitarian Use Device (HUD) designation for the CryoValve SGAV for aortic valve replacement in patients aged 0 to 21 years. An HUD is a medical device intended to benefit patients in the treatment or diagnosis of a disease that affects fewer than 4,000 people in the U.S. per year. The HUD designation is the first step in obtaining a Humanitarian Device Exemption (HDE), which if obtained would allow the Company to market the CryoValve SGAV in the U.S. market. The Company submitted an HDE application in February 2012. The FDA responded with comments and requested additional information in September 2012. The Company is currently developing plans to respond to these questions. Additional jurisdictions for potential shipments of CryoValve SGAV also include Austria and the U.K.

BioFoam. In November 2012 CryoLife received an additional indication in Europe to also market its BioFoam as an adjunct to hemostasis in cardiovascular surgery when cessation of bleeding by ligature or other conventional methods is ineffective or impractical. The Company will be conducting a 45 patient post-market study in Europe on BioFoam used in cardiovascular applications in 2013. BioFoam received initial approval by the FDA in late 2009 for an IDE to conduct a pilot human clinical trial to help seal liver tissue in patients for whom cessation of bleeding by ligature or other conventional methods is ineffective or impractical. The first patient was enrolled into the trial in 2011 after receiving the required DOD and Institutional Review Board (IRB) approvals. Due to slower than expected enrollment, CryoLife worked with the FDA to further modify the protocol to enhance the ability to enroll patients. This modification was received in the fourth quarter of 2011. Even with the protocol modifications, the study design made it extremely difficult to recruit patients, due to the restrictive inclusion/exclusion criteria. As a result, CryoLife made the decision in the third quarter of 2012 to discontinue the U.S. BioFoam IDE study. CryoLife has been awarded a total of $6.1 million in funding allocated from U.S. Congress Defense Appropriations Conference Reports in 2005 through 2010 for the continued development of PHT for use on the battlefield. CryoLife has received $5.4 million of that funding. Unused funds will be returned to the DOD.

PerClot. In September 2010 CryoLife entered into a worldwide distribution agreement and a license and manufacturing agreement with SMI for PerClot, a polysaccharide hemostatic agent used in surgery. As part of the consideration paid to SMI, the Company allocated $3.5 million to an intangible asset for PerClot distribution and manufacturing rights in the U.S. and certain other countries which do not have current regulatory approvals. This $3.5 million is considered in-process research and development as it is dependent upon regulatory approvals which have not yet been obtained. Therefore, CryoLife expensed the $3.5 million as in-process research and development upon acquisition. CryoLife filed an IDE with the FDA in March 2011 seeking approval to begin clinical trials for the purpose of obtaining PMA to distribute PerClot in the U.S. In April 2011 the FDA disapproved CryoLife s IDE filing. In March 2012 CryoLife refiled its IDE and the FDA responded with comments in the second quarter of 2012. CryoLife filed a revised IDE in November 2012 and received questions from the FDA in December 2012 related to this filing. CryoLife is currently working to address the questions and expects to respond to the FDA in the first quarter of 2013.

Revascularization Technologies. In May 2011 CryoLife completed its acquisition of Cardiogenesis. Along with the TMR technology, Cardiogenesis has developed the Phoenix System, which is designed to combine the delivery of biologic materials with TMR. The synergy of injecting biologics, such as stem cells or growth factors, with TMR may provide greater angina reduction and improve cardiac function in patients with diffuse coronary artery disease who are not candidates for surgical bypass or intervention. The Phoenix System has received a CE Mark designation allowing commercial distribution into the European Community. CryoLife intends to continue to investigate requirements to obtain an IDE for clinical evaluation of the Phoenix System in the U.S.

The PEARL 8.0 handpiece received FDA approval in February 2012. A condition of approval is to conduct a post approval study on 10 to 22 patients at up to 5 centers with 30 day follow-up.

HeRO Grafts. The Company is currently working on improvements to the HeRO Graft which may include product enhancements to facilitate easier implantation of the device. Additionally a CE Mark application for the HeRO graft is currently under review by the Company s Notified Body.

ProPatch. In late 2006 CryoLife received 510(k) clearance from the FDA for ProPatch. In 2011 CryoLife implemented modifications to streamline the manufacturing process. These modifications resulted in the submission of a new 510(k), which was cleared in January 2012. CryoLife intends to commercialize ProPatch, which may include partnering with one or more third-parties as well as obtaining clinical data to support indications to be marketed directly.

Patents, Licenses, and Other Proprietary Rights

The Company relies on a combination of patents, trademarks, confidentiality agreements, and security procedures to protect its proprietary products, preservation technology, trade secrets, and know-how. The Company believes that its patents, trade secrets, trademarks, and technology licensing rights provide it with important competitive advantages. The Company owns or has licensed rights to 65 U.S. patents and 66 foreign patents, including patents relating to its technology for human cardiac and vascular tissue preservation, decellularization of tissue, tissue revitalization prior to freezing, tissue transport, tissue packing, BioGlue manufacturing, PHT manufacturing, revascularization technologies, and HeRO Graft. The Company has approximately 11 pending U.S. patent applications and 18 pending foreign applications that relate to the Company s tissues, PHT, and other areas. There can be no assurance that any patents pending will ultimately be issued. The remaining duration of the Company s issued patents ranges from 2 months to 15 years. The main patent for BioGlue expired in mid-2012 in the U.S. and expires in mid-2013 in the rest of the world. However, for a competitor to copy BioGlue they would have to develop parts of the manufacturing process that are trade secrets of the Company and then seek FDA approval, which would likely require human clinical trials, or other regulatory approvals. The Company has an agreement with a third-party that calls for the payment of royalties based on BioGlue revenues while the main BioGlue patent is in effect. Once the Company begins to manufacture PerClot, it will also be required to pay royalties based on revenues of PerClot manufactured by the Company. The Company has $1.5 million in prepaid royalties under this agreement. In addition, the Company has a distribution agreement with a third-party for the distribution of PerClot. These products have license rights and trade secrets that provide competitive advantages.

There can be no assurance that the claims allowed in any of the Company s existing or future patents will provide competitive advantages for the Company s preserved tissues, products, and technologies or will not be successfully challenged or circumvented by competitors. There can also be no assurances that the claims allowed in patents licensed or owned by third-parties for products distributed by the Company will not be successfully challenged or circumvented by competitors. To the extent that any of the Company s products, whether manufactured by the Company or distributed by it, are not effectively patent protected, the Company s business, financial condition, profitability, and cash flows could be materially, adversely impacted. Under current law, patent applications in the U.S. and patent applications in foreign countries are maintained in secrecy for a period after filing. The Company cannot be sure that products manufactured or distributed by it, or the technologies developed by it, do not infringe patents that may be granted in the future pursuant to pending patent applications or that they do not infringe any patents or proprietary rights of third-parties.

The Company may incur substantial legal fees in defending against a patent infringement claim or in asserting claims against third-parties, and if it loses litigation, could be forced to no longer market the services or products that are related to the infringing technology or pay significant license fees or damages. In the event that any relevant claims of third-party patents are upheld as valid and enforceable, the Company could be prevented from marketing certain of its products, could be required to obtain licenses from the owners of such patents, or could be required to redesign its services or products to avoid infringement. There can be no assurance that such licenses would be available or, if available, would be on terms acceptable to the Company or that the Company would be successful in any attempt to redesign its services or products to avoid infringement. The Company s failure to obtain licenses or to redesign its services or products could have a material, adverse impact on the Company s business, financial condition, profitability, and cash flows. For example, in September of 2012, the Company received a letter from Medafor stating that PerClot, when introduced in the U.S., will, when used in accordance with the method published in our literature and with the instructions for use, infringe their U.S. patent. See Part I, Item 1A, Risk Factors Risks Relating To Our Business Our Investment In Our Distribution And License And Manufacturing Agreements With Starch Medical, Inc. Is Subject To Significant Risks.

The Company has entered into confidentiality agreements with its employees, several of its consultants, and third-party vendors to maintain the confidentiality of trade secrets and proprietary information. There can be no assurance that the obligations of employees of the Company and third-parties with whom the Company has entered into confidentiality agreements will effectively prevent disclosure of the Company s confidential information or provide meaningful protection for the Company s confidential information if there is unauthorized use or disclosure, or that the Company s trade secrets or proprietary information will not be independently developed by the Company s competitors. Litigation may be necessary to defend against claims of infringement, to enforce patents and trademarks of the Company, or to protect trade secrets and could result in substantial cost to, and diversion of effort by, the Company. There can be no assurance that the Company would prevail in any such litigation. In addition, the laws of some foreign countries do not protect the Company s proprietary rights to the same extent as do the laws of the U.S.

Preservation, Manufacturing, and Operations

The Company s corporate headquarters and laboratory facilities consist of approximately 200,000 square feet of leased manufacturing, administrative, laboratory, and warehouse space located on a 21.5-acre setting in suburban Atlanta, Georgia, with an additional 14,400 square feet of off-site warehouse space and an additional 9,000 square feet of combined manufacturing and office space in Atlanta, Georgia. Approximately 20,000 square feet are dedicated as class 10,000 clean rooms. An additional 8,000 square feet are dedicated as class 100,000 clean rooms. The extensive clean room environment provides a controlled aseptic environment for tissue preservation, manufacturing, and packaging. Approximately 55 liquid nitrogen freezers maintain preserved tissue at or below 135º C. Two back-up emergency generators assure continuity of Company manufacturing operations. The Company s corporate complex includes the Ronald C. Elkins Learning Center, a 3,600 square foot auditorium that holds 225 participants, and a 1,500 square foot training lab, both equipped with closed-circuit and satellite television broadcast capability allowing live broadcasts from and to anywhere in the world. The Elkins Learning Center provides visiting surgeons with a hands-on training environment for surgical and implantation techniques for the Company s technology platforms.

Tissue Preservation

The tissue processing laboratory is responsible for the processing and preservation of human cardiac and vascular tissues for transplant. This laboratory contains approximately 15,600 square feet with a suite of seven clean rooms dedicated to tissue processing. Currently, there are approximately 76 technicians employed in this area, and the laboratory is staffed 24 hours per day, 365 days per year. In 2012 the laboratory packaged approximately 12,000 tissues. The current processing level is estimated to be at about 35% of total capacity. To produce at full capacity levels, the Company would have to increase the amount of donated tissues, which the Company could attempt to do by revising its tissue acceptance criteria, increasing the number of relationships with OTPOs, or working to increase donor awareness to increase tissue donation. Any attempt to increase the amount of tissues processed could be constrained by the availability of donated tissues. If significant additional donated tissues were obtained, the Company would also need to increase the number of employees or increase the number of hours worked by employees.

BioGlue and BioFoam

BioGlue and BioFoam are presently manufactured at the Company s headquarters facility. The laboratory contains approximately 13,500 square feet, including a suite of six clean rooms. Currently, there are approximately 19 technicians employed in this area. The laboratory has a potential annual capacity of approximately 2 million syringes of BioGlue and BioFoam. The current production level is about 5% of total capacity. To produce at full capacity levels, the Company would need to increase the number of employees, add work shifts, and install automated filling and pouching equipment.

Revascularization Technologies

Revascularization technologies consist of laser consoles and handpieces. The manufacturing of the laser consoles is outsourced to a single contract manufacturer. The manufacturing and assembly of the handpieces is outsourced to a different single contract manufacturer. The Company s corporate headquarters has approximately 1,100 square feet of laser maintenance and evaluation laboratory space.

HeRO Grafts

The HeRO Graft manufacturing was in the process of relocating at the end of 2012 to Atlanta, Georgia from Eden Prairie, Minnesota. The manufacturing space for the HeRO Grafts in Atlanta, Georgia contains approximately 4,000 square feet including a suite of two clean rooms. There are approximately 4 technicians employed in this area. The Company believes that once manufacturing commences in early 2013, the production levels will be at approximately 12% of total capacity, increasing to approximately 25% of full capacity by the end of 2013. To produce at full capacity levels the Company would need to install a second component spraying hood and purchase some additional small equipment, as well as increase the number of technicians and the number of shifts worked.

Other Medical Devices

The Company s headquarters and off-site manufacturing has additional laboratory space consisting of approximately 20,400 square feet with a suite of eight clean rooms. This laboratory space is expected to house the manufacturing of PerClot and ProPatch.

Europa

The Company s European subsidiary, Europa, maintains a leased facility located in Guildford, England, which contains approximately 3,400 square feet of office space. In addition, Europa leases shared warehousing space through its third-party shipper.

Suppliers, Sources, and Availability of Tissues and Raw Materials

The Company s preservation services business and its ability to supply needed tissues is dependent upon donation of tissues from human donors. The Company must rely on the OTPOs that it works with to educate the public on the need for donation and to foster a willingness to donate tissue. The Company must also maintain good relationships with its OTPOs to ensure that it will receive donated tissue. In addition, future regulations could reduce the availability of tissue available for implantation. The Company also uses various medicines and solutions in its processing. Some of these medicines and solutions are only manufactured by single suppliers which means if the single supplier ceased or was unable to manufacture a medicine or solution this could have a material, adverse impact on the Company s ability to accept or process tissue which could materially, adversely impact the Company s revenues. See also Part I, Item 1A, Risk Factors.

The Company s BioGlue and BioFoam products are comprised of bovine protein and a cross linker that is delivered to the surgical site through a delivery device. The delivery devices are manufactured by a single supplier. Although the Company maintains an inventory of devices, if the single supplier ceased producing delivery devices for other than a short period of time, this would have a material, adverse impact on our ability to manufacture BioGlue and would materially, adversely impact the Company s revenues.

PerClot is produced by SMI for the Company pursuant to a distribution agreement. If SMI was unable to obtain the appropriate raw materials for PerClot in order to manufacture it for the Company or if SMI was unable to manufacture PerClot due to other factors, it would materially, adversely affect the Company s ability to sell PerClot and could therefore have a material, adverse impact on the Company s revenues. In addition, if SMI breached its distribution agreement or attempted to terminate the distribution agreement, it would materially, adversely impact the Company s ability to sell PerClot and obtain revenue growth from the product.

The contract manufacturers for the revascularization technologies laser console and handpieces generally acquire certain components from multiple sources. Other laser and fiber-optic components and subassemblies are purchased from single sources. Any significant supply interruption would materially, adversely impact the Company s ability to sell the revascularization technologies products and obtain revenue growth from these products.

HeRO Graft components are purchased from single sources in some instances; however, secondary suppliers can be approved. Any significant supply interruption would materially, adversely impact the Company s ability to sell HeRO Graft and obtain revenue growth from the product.

Quality Assurance

The Company s operations encompass the preservation of human tissue and the manufacturing of medical devices. In all of its facilities, the Company is subject to regulatory standards for good manufacturing practices, including current Good Tissue Practices (cGTPs), which are the FDA regulatory requirements for the processing of human tissue, and current Quality System Regulations, which are the FDA regulatory requirements for medical device manufacturers. The FDA periodically inspects Company facilities to review Company compliance with these and other regulations. The Company also operates according to International Organization for Standardization (ISO) 13485 Quality System Requirements, an internationally recognized voluntary system of quality management for companies that design, develop, manufacture, distribute, and service medical devices. The Company maintains a Certification of Approval to the ISO 13485. Lloyd s Register Quality Assurance Limited (LRQA) issues this approval. LRQA is a Notified Body officially recognized by the EU to perform assessments of compliance with ISO 13485 and the Medical Device Directive. The Medical Device Directive is the governing document for the EEA that details requirements for safety and risk. LRQA performs periodic on-site inspections, generally at least annually, of the Company s quality systems.

The Company s quality assurance staff is comprised primarily of experienced professionals from the medical device manufacturing and tissue processing industries. The quality assurance department, in conjunction with the Company s research and development department, routinely evaluates the Co