Taxus Cardium Pharmaceuticals Group Inc.
Form 10-K
April 15, 2014
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

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

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2013

001-33635

(Commission file number)

TAXUS CARDIUM PHARMACEUTICALS GROUP INC.

(Exact name of registrant as specified in its charter)

Delaware	**27-0075787**
(State of incorporation)	**(IRS Employer Identification No.)**
11750 Sorrento Valley Rd., Suite 250	
San Diego, California 92121	**(858) 436-1000**
(Address of principal executive offices)	**(Registrant s telephone number)**

Securities registered under Section 12(b) of the Exchange Act:

None

Securities registered under Section 12(g) of the Exchange Act:

Common Stock, par value $0.0001 per share

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

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

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 for 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. x Yes ¨ No

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the 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. x

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company.

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

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

The aggregate market value of common equity held by non-affiliates, computed on the basis of the closing sale price for the common stock as reported on the NYSE MKT on June 28, 2013, was $8.7 million. Shares of common stock held by executive officers, directors and by persons who own 10% or more of the outstanding common stock of the registrant have been excluded for purposes of the foregoing calculation in that such persons may be deemed to be affiliates. This does not reflect a determination that such persons are affiliates for any other purpose.

As of March 30, 2014, 9,652,710 shares of the registrant s common stock were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Part III (Items 10, 11, 12, 13 and 14) of this Form 10-K incorporates by reference portions of the registrant s definitive proxy statement for its Annual Meeting of Stockholders to be filed on or before April 30, 2014.

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EXPLANATORY NOTE

Unless the context requires otherwise, all references in this report to the Company, Taxus Cardium, Cardium, we, our, and us refer to Tax Cardium Pharmaceuticals Group Inc. (formerly Cardium Therapeutics, Inc.) and, as applicable, its wholly-owned subsidiaries Tissue Repair Company, To Go Brands, Inc. and LifeAgain Insurance Solutions, Inc.

Effective July 18, 2013 we effected a reverse split of our outstanding common stock, par value $0.0001 per share, in a ratio of 1 for 20. All common stock and per share amounts included in this report have been retroactively adjusted to reflect a 1 for 20 reverse stock split, as if such split had been effective at the beginning of the period reported.

SPECIAL NOTE ABOUT FORWARD-LOOKING STATEMENTS

Certain statements in this report, including information incorporated by reference, are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, Section 21E of the Securities Exchange Act of 1934, and the Private Securities Litigation Reform Act of 1995. Forward-looking statements reflect current views about future events and financial performance based on certain assumptions. They include opinions, forecasts, intentions, plans, goals, projections, guidance, expectations, beliefs or other statements that are not statements of historical fact. Words such as may, will, should, could, would, expects, plans, believes, anticipates, intends, estimates, ap projects, or the negative or other variation of such words, and similar expressions may identify a statement as a forward-looking statement. Any statements that refer to projections of our future financial performance, our anticipated growth and trends in our business, our goals, strategies, focus and plans, and other characterizations of future events or circumstances, including statements expressing general optimism about future operating results and the development of our products, are forward-looking statements. Forward-looking statements in this report may include statements about:

- our ability to fund operations and business plans, and the timing of any funding or corporate development transactions we may pursue;
- planned development pathways and potential commercialization activities or opportunities;
- the timing, conduct and outcome of discussions with regulatory agencies, regulatory submissions and clinical trials, including the timing for completion of clinical studies;
- our ability to increase revenues, and raise sufficient financing to meet our working capital requirements;
- our beliefs and opinions about the safety and efficacy of our products and product candidates and the anticipated results of our clinical studies and trials;
- our ability to enter into acceptable relationships with one or more contract manufacturers or other service providers on which we may depend, and the ability of such contract manufacturers or other service providers to manufacture biologics, devices, nutraceuticals or other key products or components, or to provide other services, of an acceptable quality on a timely and cost-effective basis;
- our ability to enter into acceptable relationships with one or more development or commercialization partners to advance the commercialization of new products and product candidates and the timing of any product launches;
- our growth, expansion and acquisition strategies, the success of such strategies, and the benefits we believe can be derived from such strategies;

our ability to pursue and effectively develop new product opportunities and acquisitions and to obtain value from such product opportunities and acquisitions;

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our intellectual property rights and those of others, including actual or potential competitors;

the outcome of litigation matters;

the anticipated activities of our personnel, consultants and collaborators;

expectations concerning our operations outside the United States;

current and future economic and political conditions;

overall industry and market performance;

the impact of new accounting pronouncements;

management s goals and plans for future operations; and

other assumptions described in this report underlying or relating to any forward-looking statements.

The forward-looking statements in this report speak only as of the date of this report and caution should be taken not to place undue reliance on any such forward-looking statements. Forward-looking statements are subject to certain events, risks, and uncertainties that may be outside of our control. When considering forward-looking statements, you should carefully review the risks, uncertainties and other cautionary statements in this report as they identify certain important factors that could cause actual results to differ materially from those expressed in or implied by the forward-looking statements. These factors include, among others, the risks described under Item 1A and elsewhere in this report, as well as in other reports and documents we file with the United States Securities and Exchange Commission (the SEC).

PART I

ITEM 1. BUSINESS

Overview

Taxus Cardium Pharmaceuticals Group is a development-stage regenerative medicine biotechnology company. We are focused on the development of advanced regenerative therapeutics designed to promote the activation and growth of (1) microvascular circulation to enhance perfusion of ischemic cardiac tissue as a potential treatment for heart disease; and (2) granulation tissue as a treatment for chronic non-healing wounds. We have a commercial FDA-cleared wound care product, a late clinical stage cardiovascular gene therapy product candidate and corresponding technology platforms as outlined below. We also own non-core interests in the Healthy Brands Collective, a health products company, and LifeAgain Insurance Solutions, Inc., an advanced medical data analytics business.

Lead Product	Technology Platform	Formulation	Status
Excellagen® Commercial	Advanced Tissue Regeneration for Wounds &	Aseptic Pharmaceutically-Formulated Fibrillar	Initial Product FDA-Cleared

Product	Biologics Delivery Platform	Collagen	
Generx®	Gene Therapy		
Product	Cardiovascular	Ad5FGF-4 DNA Construct	Phase 3 Registration Study
Candidate	Growth Factor Therapeutics		

Our business model is designed to create a portfolio of multiple opportunities for success while avoiding reliance on any single technology platform or product type, and to leverage our skills in late-stage product development in order to bridge the critical gap between promising new technologies and product opportunities that are ready for commercialization. Consistent with our long-term strategy, we intend to consider various corporate development transactions designed to place our products or product candidates into larger organizations or with

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partners having existing commercialization, sales and marketing resources, and a need for innovative products. Such transactions could involve the sale, partnering or other monetization of particular product opportunities or businesses. In parallel, as our businesses are advanced and corresponding valuations established, we plan to pursue new product opportunities and acquisitions with strong value enhancement potential.

Based on our recent sale of the Company s non-core health sciences business To Go Brands® and the commercial market launch of the first program under the LifeAgain® advanced medical data analytics platform, we now plan to primarily focus on the clinical and commercial development of our core biotechnology assets and technology platforms as described above. Our business strategy focuses on achieving key milestones with the potential to offer significant valuation inflection points of our core technology assets, as well as asset sales or other monetizations of Cardium s non-core investments. The key elements of our strategy include:

The advancement of our ASPIRE international Phase 3 registration clinical study for Generx® which is currently underway in the Russian Federation, and the release of findings from interim data analysis in mid-2014. With clinical success, the Company plans to meet with the U.S. FDA to seek harmonization between the international clinical study with Cardium s already FDA-cleared Generx Phase 3 clinical study in an effort to advance U.S.-based clinical studies supported by a strategic partner.

Strategically partner and monetize our FDA-cleared pharmaceutically formulated collagen commercial wound care product Excellagen® for select U.S.-based vertical market channels, and build on Cardium s capabilities and resources to leverage Excellagen as an advanced regenerative medicine delivery platform by identifying innovative product extensions for tissue regeneration based on stem cells, biologics, peptides and/or small molecule drugs for future development. Consistent with the Company s long-term business strategy, as previously reported, Taxus Cardium does not plan to establish an internal marketing and sales force to directly support the commercialization of Excellagen, but continues to credentialize Excellagen in preparation for the completion of strategic partnerings for various vertical channel market opportunities or asset monetization. The Company has continued to pursue a CE mark certification for Excellagen, has fully responded to all information requested by the notified body, and looks forward to completing this process. The Excellagen website is www.excellagen.com.

Advance the commercialization of our non-core LifeAgain advanced medical data analytics business investment, which is focused on the development, marketing and sale of survivable risk term life insurance for cancer survivors or others with medical conditions who are currently considered uninsurable based on traditional underwriting standards. We may seek to support the growth and development of this non-core business and technology platform through the sale of a minority stake in our LifeAgain business to a strategic partner or financial investors. The LifeAgain website address is www.lifeagain.com.

Monetize our equity stake in Cardium s non-core Healthy Brands Collective Cell-nique Corporation investment. We acquired this investment through the recent sale of our To Go Brands® health sciences business through an asset exchange for a preferred equity position in Healthy Brands. Healthy Brands has been making significant acquisitions and has previously reported plans to move forward as a public company as its current businesses advance and grow through further acquisition. The Healthy Brands Collective website address is www.healthybrandsco.com.

Advance our strategic cooperation agreement with Shanxi Taxus Pharmaceuticals Ltd., a strategic Chinese investor, which includes the evaluation of opportunities to distribute our Excellagen product and Generx product candidate in China, and distribution of Shanxi Taxus Pharmaceutical Ltd. s oncology related products in the United States.

Deploy capital strategically to develop our portfolio of product candidates and create shareholder value.

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Core Biotechnology Focus

Generx® [Ad5FGF-4]

The Company s Cardium Therapeutics operating unit is a leader in the field of cardiovascular gene therapy. Generx (alferminogene tadenovec), Cardium s lead Phase 3 clinical study product candidate, is a transformative disease-modifying angiogenic gene therapy growth factor therapeutic that is being developed to promote the growth of cardiac microvascular circulation to enhance perfusion (blood flow) for patients with advanced coronary artery disease.

Generx is designed for the potential treatment of patients with Cardiac Microvascular Insufficiency or CMI due to advanced coronary artery disease. CMI is a principal cause of Coronary Microvascular Dysfunction (CMD), a well-recognized clinical condition characterized by functional and structural abnormalities of the microvasculature (smaller blood vessels of the heart), which leads to myocardial ischemia and angina pectoris in the absence of large artery/obstructive disease. CMD, which is also sometimes referred to as microvascular angina, frequently cannot be addressed using traditional surgical approaches such as coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI, i.e. angioplasty and stents). In particular, many patients (1) have coronary artery disease that is not limited or localized to large vessels, (2) continue to experience angina after CABG or PCI, and/or (3) are not suitable candidates for surgical interventions.

Generx represents a new class of therapeutic designed to address a large and unmet medical need among patients with heart disease. It is estimated that 12% of patients with obstructive coronary artery disease continue to experience angina because their underlying medical condition is not fully addressed or cannot be resolved by chronic drugs or surgical/mechanical interventions. In addition, a recent meta-analysis reported that approximately 20% of patients who have a coronary angiography due to ongoing angina do not have obvious large vessel disease, a condition generally referred to as Cardiac Syndrome X, many of whom are presumed to have coronary disease that is diffuse and/or affects smaller vessels within the heart that are not reachable through surgical intervention. Generx is designed to be a one-time non-surgical treatment that may help many of such patients by directly addressing their underlying microvascular angina, as well as providing a non-surgical option for patients in whom coronary intervention is either contraindicated or not desirable.

Myocardial ischemia, including that associated with CMI, can be effectively diagnosed and its potential treatment quantified using SPECT imaging (Single-photon emission computed tomography). SPECT has both diagnostic and prognostic value in the management of patients with coronary artery disease because it identifies and quantitatively measures regions of the heart muscle that are at greatest risk during periods of ischemia, such as that brought on during exertion. Cardium believes that other catheter-based diagnostic techniques including catheter-based imaging diagnostics to measure fractional flow reserve and washout collaterometry will be further developed, which may enhance and broaden clinical adoption of non-surgical Generx angiogenesis therapy following initial Generx registration. Cardium believes that Generx therapy may also apply to patients with Cardiac Syndrome X, which is also characterized by microvascular dysfunction.

Based on the data from four completed clinical studies, Generx appears to be safe and well tolerated and capable of improving myocardial perfusion, as measured by validated diagnostic Single-Photon Emission Computed Tomography or SPECT imaging, in patients with Reversible Perfusion Defect Size or RPDS of greater than 9%. Generx also improved exercise tolerance time or ETT, based on an analysis of pre-specified patient sub-groups with stable angina pectoris due to advanced coronary artery disease who were unresponsive to optimal medical therapy and are not considered suitable candidates for traditional coronary artery by-pass surgery, angioplasty and/or stenting.

Upon completion of the current ASPIRE international clinical study, data from the our five Generx clinical studies will represent one of the largest clinical and regulatory dossiers for a cardiac gene therapy product candidate in the world covering the treatment of over 750 patients in the United States, Canada, South America Western Europe and the Russian Federation at over 100 medical centers.

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In December 2013, we reported encouraging initial positive findings from our ASPIRE international clinical study, which is consistent with the results obtained in our AGENT Phase 2a clinical study which showed that Generx appeared to be safe and well tolerated and that observed effects for patients with advanced coronary artery disease receiving Generx were similar in magnitude to those reported in the medical literature for patients undergoing surgical revascularization procedures such as cardiac by-pass surgery, or angioplasty and stenting, as measured by improvements of reversible perfusion defects of comparable size following such procedures. We expect to be in a position to provide findings from an interim data analysis in mid-2014, to support the advancement and completion of the Generx international clinical study in Russia, which could then support advancement of other studies and product development efforts in the U.S. and elsewhere.

Coronary Artery Disease Market Data and Potential Economic Opportunity

According to the Centers for Disease Control and Prevention, heart disease is the leading cause of death for both men and women in the U.S. and the industrialized world. In the U.S. the American Heart Association (AHA) reports that there are approximately 15.4 million patients with coronary artery disease, and that the lifetime risk of developing the coronary heart disease after 40 years of age is 49% for men and 32% for women. The AHA reports there are currently 7.8 million Americans that have been diagnosed with angina pectoris due to coronary artery disease, and it is estimated that approximately 12% of patients with angina are unresponsive to optimal medical therapy and are considered not suitable for coronary artery bypass surgery and angioplasty and stenting. In addition, the AHA reports that each year there are over 2.4 million percutaneous interventional procedures, inpatient cardiac by-pass surgeries and diagnostic cardiac catheterizations in the U.S. Likewise, cardiovascular disease is the leading cause of death in the Russian Federation and other countries in the Commonwealth of Independent States (CIS). However, comparative health statistics show that in the Russian Federation there is an early onset of heart disease in the general population, and the mortality rate is even more severe than in the U.S. For example, the current average life expectancy for males in the U.S. is 76 years of age in comparison to 64 years of age in Russia. The U.S. cardiovascular death rate for males is 80 per 100,000 in the general population compared to almost 300 per 100,000 in the Russian Federation. The cardiovascular death rates in certain countries of the CIS are even more severe than in the Russian Federation and are reported to exceed 400 per 100,000 in the general population, over five times the U.S. cardiovascular death rate.

Of the approximately 7.7 million Americans with symptomatic angina pectoris, the Cleveland Clinic Foundation reports that approximately 12% (i.e. more than 900,000 patients) are relatively unresponsive to optimal medical therapy and are considered not suitable for coronary artery bypass surgery and angioplasty and stenting. If the safety and effectiveness of Generx continue to be demonstrated in clinical trials, it could potentially be labeled for the treatment of this very significant patient population. Overall, we project that this patient population could represent a $3.0 billion addressable market opportunity in the United States, and is significantly larger when considered on a global basis given the large and increasing number of patients worldwide who are affected by coronary artery disease.

Cardium s commercialization program has also established a six year shelf life for Generx based on validated real time cGMP studies validated studies conducted by Cardium researchers. As a result, Cardium anticipates that Generx would be campaign-manufactured in large quantity and held for marketing, sale and distribution during the six year stability period by SAFC, our cGMP contract manufacturer which is located in Carlsbad, California. This facility has the capacity to scale the manufacture of Generx to larger batch quantities (up to approximately 2.0 million doses annually) without the need for significant additional capital investment or major process technology engineering. This flexibility allows Cardium to manufacture Generx at a highly economical direct cost, which could potentially yield economic gross margins that would be approximately equivalent to a small molecule drug model, as opposed to many traditional biologic products having much higher costs of manufacture. This would represent a significant commercial advantage in the market, since cost per dose could be many fold lower than that typically associated with the manufacture of complex donor-based autologous cell therapies and similar approaches currently under development by other biotechnology companies for cardiovascular applications.

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How Does Generx Work?

Generx is designed to be administrated to patients as a single non-surgical treatment during a standard catheter-based procedure by an interventional cardiologist in an out-patient setting using well established diagnostic angiography. Generx is an adenovector (serotype 5) DNA-based gene therapy construct that encodes the Fibroblast Growth Factor-4 (FGF-4) gene. Following administration by a catheter into the three major coronary arteries of the heart, Generx is designed to allow the cellular expression of FGF-4 protein which has been shown to stimulate the release and action of other angiogenic growth factors including Platelet-Derived Growth Factor (PDGF), Hepatocyte Growth Factor (HGF) and Vascular Endothelial Growth Factor (VEGF). This process is believed to orchestrate and promote the growth of cardiac microvascular circulation (a functional collateral network) in ischemic cardiac tissue. Cardium s methods of gene therapy utilize an intra-coronary angioplasty balloon catheter that produces transient myocardial ischemia. The induction of transient ischemia during intra-coronary Generx administration, together with the introduction of nitroglycerin, significantly facilitate the transfection of Generx into heart cells, apparently via enhanced penetration through microvessel endothelium and upregulation of Coxsackie-Adenovirus Receptor or CAR. Company-sponsored research demonstrates that Generx has the capacity to promote and enhance cardiac microvascular circulation through the formation of new capillary vessels, a process referred to as angiogenesis, as well as enlargement of pre-existing collateral arterioles, a process referred to as arteriogenesis.

Generx Clinical Development Strategy

Generx has been cleared by the U.S. FDA for a Phase 3 clinical study, and has also been cleared for a Phase 3 registration study in the Russian Federation, the international clinical study called ASPIRE. In 2012, Cardium initiated the ASPIRE study, which is expected to involve up to 100 patients with myocardial ischemia, defined as patients with a reversible perfusion defect of 9% or greater based on SPECT imaging. The international study is a randomized, multi-center study with two parallel arms conducted at leading medical centers in Moscow and Novosibirsk to supplement previously-obtained data from the four prior clinical studies. The study s primary efficacy endpoint is improvement in Reversible Perfusion Defect Size or RPDS, as measured by SPECT imaging eight weeks following Generx administration

In December 2013, we reported encouraging initial positive findings from the ASPIRE international clinical study, which is consistent with the results obtained in the AGENT Phase 2a clinical study which showed that Generx appeared to be safe and well tolerated and that observed effects for patients with advanced coronary artery disease receiving Generx were similar in magnitude to those reported in the medical literature for patients undergoing surgical revascularization procedures such as cardiac by-pass surgery, or angioplasty and stenting, as measured by improvements of reversible perfusion defects of comparable size following such procedures. We expect to be in a position to provide findings from an interim data analysis in mid-2014, which could then support completion of the ASPIRE registration study in Russia, as well as other studies and product development efforts in the U.S. and elsewhere.

If we achieve clinical success in the current international clinical study, we plan to secure initial regulatory approval and enter into a strategic partnership to have Generx marketed and sold in the Russian Federation, as well as other countries in the CIS. We also plan to pursue the registration of Generx in other international markets based on the extensive Generx clinical database and regulatory dossier which includes the safety and efficacy data derived from the five clinical studies in nine countries. In addition, we plan to meet with the U.S. FDA to discuss the Generx registration in the Russian Federation and seek to harmonize the clinical study design of the international clinical study with the U.S. clinical study in concert with a strategic partner.

Generx Clinical Study Data Summary

Upon completion of the international clinical study, Generx will have been the subject of five randomized and controlled multi-center clinical studies involving approximately 750 patients with advanced coronary artery disease at over 100 medical centers in the United States, Canada, Western Europe, South America and the

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Russian Federation. The study results from each of the completed AGENT clinical studies have been published in peer-reviewed journals and have supported, from a safety and preliminary efficacy perspective, the clearances by the U.S. FDA and the Russian Federation Health Ministry for Cardium to conduct two Phase 3 clinical studies. With completion of the current international clinical study, data from the five clinical studies will represent one of the largest clinical and regulatory dossiers in the world. In summary, based on the clinical data from the four completed clinical studies, Generx appears to be safe and well tolerated and capable of improving myocardial perfusion, as measured by SPECT imaging, in patients with myocardial ischemia due to advanced coronary artery disease. Generx also improves ETT based on an analysis of pre-specified patient sub-groups with stable angina pectoris due to advanced coronary artery disease who are not optimal candidates for traditional coronary artery by-pass surgery, angioplasty and/or stenting.

The international clinical study was designed based on positive results from the prior Generx Phase 2a clinical study (Grines et al., J Am Coll Cardiol 2003; 42:1339-47) showing that Generx improved myocardial blood flow in the ischemic region of the hearts of men and women following a single intracoronary infusion as measured by the objective efficacy endpoint of SPECT imaging. As noted in the publication, the mean change observed in Generx-treated patients was a 4.2% absolute reduction (which represents a 20% relative reduction) in the reversible perfusion defect size from baseline at eight weeks ($p<0.001$), while the placebo group showed only a 1.6% absolute reduction from baseline (not significant) at eight weeks following treatment. The observed treatment effect for patients receiving Generx was similar in magnitude to that reported in the literature for patients undergoing angioplasty/stent or revascularization procedures with reversible perfusion defects of comparable size at one year following these procedures.

An independent long-term prospective study published in Circulation (Meier et al, Circ. 2007; 116:975-983) provided key evidence indicating that men and women with more recruitable collateral circulation have a better chance of surviving a heart attack than patients who have less developed collateral circulation. This important study quantitatively evaluated coronary collateral blood flow in 845 patients with coronary artery disease during a 10-year follow-up period and showed that long-term cardiac mortality was approximately 66% lower in patients with a highly developed collateral vessel blood supply ($p=0.019$). For the first time, this study showed the importance of collateral circulation beyond simply the relief of angina and provided further support of the potential for long term benefits from angiogenic therapy, the primary premise behind Generx s therapeutic potential.

Cedars-Sinai Medical Center Nuclear Cardiology Core Laboratory is the core lab responsible for data collection and quality control of SPECT data from the Russian based clinical study sites. This Center is considered to be one of the world s leading core laboratories for SPECT imaging. It has operated as an independent core laboratory for over 20 years and has participated in numerous multi-center clinical trials, including the recent COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) clinical study enrolling over 3,200 patients at over 60 clinical study sites. The scope of work performed by the Cedars-Sinai Core Laboratory includes imaging protocol design, quality assurance and control, interpretation, and data analysis of nuclear myocardial perfusion studies. The Core Laboratory is led by Daniel S. Berman, M.D., who has been the head of Nuclear Cardiology at Cedars-Sinai Medical Center for over 30 years, and is the Associate Director for Cardiac Imaging at the Cedars-Sinai Heart Institute. Dr. Berman is considered a leader in the field of SPECT myocardial perfusion imaging and has authored over 300 original peer-reviewed manuscripts dealing with non-invasive cardiac imaging.

Generx Technological Advances Supporting the Enhanced Delivery of Cardiovascular Therapy

Cardium researchers have developed an enhanced method of delivering Generx and potentially other agents to the heart, which has been tested in preclinical studies conducted at Emory University and is now being employed in the ASPIRE human clinical study. Cardium s innovative technique employs transient cardiac ischemia, which has been found to dramatically enhance gene delivery and transfection efficiency after one-time intracoronary administration of adenovector in mammalian hearts. Two consecutive but brief periods of coronary

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artery occlusion combined with co-administration of nitroglycerin increased both adenovector presence (measured by PCR) and transgene expression (assessed by luciferase activity) by over two orders of magnitude (>100 fold) in the heart, as compared to prior intracoronary artery delivery methods. Preclinical testing using Cardium s new approach, which was published in 2012 (Shi et al., Human Gene Therapy, 23(3): 204-212), effectively confirmed that the new technique for adenovector gene delivery in the heart can be used to dramatically boost vector delivery and therefore gene transfer. By enhancing uptake even in patients with less severe forms of disease and ischemia, it would be expected to reduce response variability and allow for the potential treatment of patients with a broader range of associated coronary artery disease. The new treatment protocols for Cardium s international clinical study have been developed to use this improved knowledge about induced transient ischemia techniques to enhance the non-surgical, catheter-based delivery of Generx to the heart.

Generx Manufacturing Capabilities and Simplified Product Handling

Cardium has also been actively advancing its Generx product candidate s engineering and process technology in preparation for potential commercialization. The Company has successfully transferred a refined, improved and fully-validated manufacturing process from Schering AG (now part of Bayer AG) to SAFC, the custom manufacturing and services business unit of Sigma-Aldrich Corporation, a global specialty chemicals and biologics supplier, located in Carlsbad, California. As a result of the rigorous technical transfer process, important process improvements were achieved enabling much higher manufacturing process yields.

Generx s long-term product stability (at the current storage temperature of -70°C) has been established and validated at a minimum of six years making it possible to manufacture Generx in large, cost effective batch sizes. Based on the current Generx validated cGMP manufacturing processes, and a recommended dosage of 6 x 10^9 viral particles per treatment, Cardium believes that it has the capacity to scale the manufacture of Generx to larger batch quantities (up to approximately 2.0 million doses annually) without the need for significant additional capital investment or major process technology engineering. Due to the validated six year stability of Generx, Cardium anticipates Generx can be campaign manufactured in large quantity and held for marketing, sale and distribution during the stability period. This flexibility will allow Cardium to manufacture Generx at a highly economical direct cost, which could potentially yield economic gross margins that would be approximately equivalent to a favorable classic small molecule drug model.

In addition, the dose preparation process for Generx has been simplified through the integration of a fully-validated, closed-system drug transfer process incorporating the use of the Becton Dickinson PhaSeal® System passive safety technology to streamline and simplify the cath-lab preparation process and eliminating the need to prepare Generx in a sterile, biological safety hood. The use of the PhaSeal system has now been integrated into the international clinical study and will be utilized for Generx commercialization. The Company has also developed a new and unique, fully-validated bio-activity performance-based, quality release assay to measure and evaluate the pro-angiogenic potency of each newly manufactured batch of Generx.

Excellagen®

Excellagen is an FDA-cleared, pharmaceutically-formulated acellular biological modulator that has been engineered to activate and promote wound healing through the growth of granulation tissue in chronic non-healing diabetic foot, pressure and venous ulcers, as well as other dermal wounds (including traumatic and surgical wounds). We believe that Excellagen is a cost-effective, easy to use professional product that has now been classified for reimbursement purposes by the U.S. Centers for Medicare and Medicaid Services as a unique skin substitute - a designation which is consistent with other forms of skin substitutes including living skin equivalents Dermagraft® and Apligraf® and human dermal and amnion placental tissue-based products including Graftjacket® and EpiFix®.

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Excellagen is prepared as a sterile professional-use syringe, physiologically formulated homogenate of purified atelopeptide bovine dermal collagen (Type I) in its native 3-dimensional fibrillar configuration, providing a structural scaffold for chemotaxis, cellular adhesion, migration and proliferation to promote wound healing. Cardium research and published scientific literature also support Excellagen s capability to activate blood platelets to release growth factors, including Platelet-Derived Growth Factor (PDGF), an important endogenous wound healing mediator.

In a U.S.-based, multi-center, randomized and controlled clinical study (the Matrix study), a single protocol specified application of Excellagen was found to accelerate the rate of tissue granulation at one week by 204% compared to standard of care (p=0.018), and this accelerated healing response continued for two weeks (104%; p=0.032). While Excellagen is FDA-cleared for use in a broad array of dermal wounds, initial clinical focus has been on the treatment of chronic non-healing diabetic foot, pressure and venous ulcers. In December 2013, the Centers for Medicare and Medicaid Services (CMS) made a final determination to assign Excellagen a unique, product-specific Q code, classifying Excellagen as a skin substitute, after reviewing Cardium s HCPCS Level II Code Modification Request and subsequent supporting information for Excellagen as a wound care product indicated for the treatment of hard to heal wounds such as diabetic foot ulcers and pressure ulcers as well as other dermal wounds. This new reimbursement code took effect January 1, 2014, although a reimbursement rate has not yet been determined.

In addition to its application for dermal wounds, Excellagen s pharmaceutically formulated collagen has been engineered to serve as a biologics delivery platform, potentially enabling multiple device, tissue scaffolding and therapeutic product extensions for tissue regeneration based on stem cells, biologics, peptides and small molecule drugs. This technological attribute of Excellagen is expected to enable product extensions, which could be co-developed for commercialization with a variety of different strategic partners.

Excellagen is Cardium s initial commercial product developed based on technology through its acquisition of the Tissue Repair Company. Consistent with Cardium s business strategy, Excellagen has been substantially credentialized and we are now seeking strategic partners to market and sell Excellagen in the United States and elsewhere through multiple marketing channels. Consistent with the Company s long-term business strategy, as previously reported, Taxus Cardium does not plan to establish an internal marketing and sales force to directly support the commercialization of Excellagen, but continues to credentialize Excellagen in preparation for the completion of strategic partnerings for various vertical channel market opportunities or asset monetization. The Company has continued to pursue a CE mark certification for Excellagen, has fully responded to all information requested by the notified body, and looks forward to completing this process.

Recent Excellagen Wound Healing Case Studies

We have recently completed two clinical evaluation studies in collaboration with wound care practitioners to assess the use of Excellagen to treat chronic pressure ulcers in elderly patients in residence at long-term care facilities. The wounds studied in these patients were of over 18 months in duration and located in hard to treat areas, including the buttocks or coccyx, the most prevalent locations for pressure ulcers. Following weekly treatment regimens consisting of sharp debridement immediately followed by application of Excellagen, the three case study patients exhibited robust formation of new granulation tissue within their previously non-healing pressure ulcers, which led to either complete wound closure or substantial wound reduction after only 5 to 6 weeks of treatment. The results of this study, entitled Serial Sharp Debridement and Formulated Collagen Gel to Treat Pressure Ulcers in Elderly Long-term Care Patients , was published in the in the November 2013 issue of the peer-reviewed journal Ostomy Wound Management (Ostomy Wound Manage. 2013;59(11):43 49). The second case study involved elderly long-term care facility patients with chronic (>12 months duration) pressure ulcers located on the heel, the second most prevalent location for pressure ulcers. The weekly treatment regimen consisted of sharp debridement immediately followed by application of Excellagen. The study period was eight weeks in duration and all three case study patients exhibited rapid and robust formation of new granulation tissue within their previously non-healing heel pressure ulcers (decrease in wound volume of 93-100%). The patients

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were monitored for four weeks following the official eight week study period, and all three heel ulcers continued to improve, with one going to complete closure. The results of this study have been submitted for publication in the peer-reviewed journal, Advances in Skin and Wound Care.

Excellagen Stem Cell Delivery Platform Studies

We believe that Excellagen can also be useful for the delivery of stem cells to promote the growth of an engineered tissue graft using autologous mesenchymal fetal stem cells, and to promote diabetic wound healing using allogeneic stem cells, respectively. Ongoing collaborations are designed to confirm the opportunity to develop product line extensions using Excellagen as a delivery vehicle in combination with stem cells and other biologics for the development of new and innovative advanced regenerative therapeutics.

Researchers at Boston Children s Hospital are evaluating the use of Excellagen® as a delivery scaffold to seed autologous mesenchymal fetal stem cells for ex-vivo engineering of tissue grafts for transplantation into infants to repair prenatally diagnosed birth defects. Autologous mesenchymal fetal stem cells are derived prenatally from infants with a medical defect requiring life-saving tissue repairs. These stem cells are sourced from amniotic fluid, the placenta or umbilical cord blood. The stem cells are then seeded into a scaffold to promote the growth of an engineered tissue graft. These grafts will potentially be used to surgically repair, either in the fetus or immediately following birth, certain prenatally diagnosed birth defects that could include congenital diaphragmatic hernia, tracheal and chest wall defects, bladder extrophy and various cardiac anomalies. Preliminary pre-clinical research has confirmed that Excellagen collagen homogenate maintains mesenchymal fetal stem cell viability. Additional proof-of-concept studies are currently underway.

The Company is also engaged in a collaboration with Orbsen Therapeutics in a European study that is designed to confirm the role of Excellagen in a diabetic wound model, with and without stem cells. The study is being conducted by researchers led by Professor Timothy O Brien at the National University of Ireland, in Galway and Orbsen Therapeutics Ltd., to evaluate the medical utility of Excellagen as a delivery agent for Orbsen s human mesenchymal stem cells (MSC) for the potential treatment of diabetic wounds. The research is sponsored by the European-funded ReddStar initiative.

Excellagen U.S. Market Opportunity

The U.S. advanced wound care market exceeds $5 billion annually with seven million Americans suffering from chronic wounds. The skin substitutes market segment, which includes Excellagen, as well as Dermagraft®, Apligraf®, EpiFix® and Graftjacket®, represents a $500 million annual market opportunity. This market is expected to grow due to the aging population and the rise in diabetes, obesity and the increased number of seniors living in long-term care facilities now and in the coming decade. According to the National Diabetes Fact Sheet (2011), over 25 million Americans are living with diabetes. Annually healthcare professionals treat approximately 900,000 diabetic foot ulcers. The National Institutes of Health estimates that 15% of people with diabetes will develop a foot ulcer. In addition, approximately 68,000 non-traumatic lower-limb amputations are performed annually in those with diabetes.

Cardium Business Strategy

With the recent preclinical, clinical and regulatory advances of our key products Generx® and Excellagen®, we are committed to applying our first-mover scientific leadership position in the field of regenerative medicine for the development and commercialization of these products in collaboration with strategic partners. The key elements of our business strategy include:

- The advancement of our ASPIRE international Phase 3 registration clinical study for Generx® which is currently underway in the Russia Federation, and release of findings from interim data analysis in mid-2014. Upon clinical success, the Company plans to meet with the U.S. FDA to seek harmonization between the international ASPIRE study with Cardium s already FDA-cleared Generx Phase 3 clinical study and advance U.S.-based clinical studies supported by a strategic partner;

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Strategically partner and monetize our FDA-cleared pharmaceutically formulated collagen commercial wound care product Excellagen® , for selected U.S.-based vertical market channels and build on Cardium s capabilities and resources to leverage Excellagen s advanced regenerative medicine delivery platform by identifying innovative product extensions for tissue regeneration based on stem cells, biologics, peptides and/or small molecule drugs for future development and commercialization with one or more strategic partners. Consistent with the Company s long-term business strategy, as previously reported, Taxus Cardium does not plan to establish an internal marketing and sales force to directly support the commercialization of Excellagen, but continues to credentialize Excellagen in preparation for the completion of strategic partnerings for various vertical channel market opportunities or asset monetization. The Company has continued to pursue a CE mark certification for Excellagen, has fully responded to all information requested by the notified body, and looks forward to completing this process;

Advance the commercialization of our non-core LifeAgain Insurance Solutions advanced medical analytics business, which is focused on the development, marketing and sale of survivable risk term life insurance for cancer survivors or others with medical conditions who are currently considered uninsurable based on traditional underwriting standards. The Company plans to potentially support the growth and development of this non-core business and technology platform through the sale of a minority stake in our LifeAgain business to a strategic partner or financial investors;

Monetize our equity stake in Cardium s non-core Healthy Brands Collective Cell-nique Corporation investment. We acquired this investment through the recent sale of our To Go Brands® health sciences business through an asset exchange for a preferred equity position in Healthy Brands. Healthy Brands has been making significant acquisitions and has previously reported plans to move forward as a public company as its current businesses advance and growth through further acquisition;

Leverage our recent cooperation agreement with Shanxi Taxus Pharmaceuticals Ltd. to distribute our Excellagen product and Generx product candidate in China, and distribute Shanxi Taxus Pharmaceuticals Ltd. s oncology related products in the United States; and

Deploy capital strategically to develop our portfolio of product candidates and create shareholder value.

Government Regulation

New drugs, biologics, devices, and nutraceuticals, are subject to extensive regulation in the United States under the federal Food, Drug, and Cosmetic Act. In addition, biologics are also regulated under the Public Health Service Act. We believe that the pharmaceutical products we are attempting to develop will be regulated either as biological products or as new drugs. Both statutes and their corresponding regulations govern, among other things, the testing, manufacturing, distribution, safety, efficacy, labeling, storage, record keeping, advertising and other promotional practices involving biologics or new drugs. FDA approval or other clearances must be obtained before clinical testing, and before manufacturing and marketing, of biologics and drugs. Obtaining FDA approval has historically been a costly and time-consuming process. Different regulatory regimes are applicable in other major markets.

In addition, any gene therapy and other DNA-based products we develop will require regulatory approvals before human trials and additional regulatory approvals before marketing. New biologics are subject to extensive regulation by the FDA and the Center for Biological Evaluation and Research and comparable agencies in other countries. Currently, each human-study protocol is reviewed by the FDA and, in some instances, the NIH, on a case-by-case basis. The FDA and the NIH have published guidance documents with respect to the development and submission of gene therapy protocols.

To commercialize our product candidates, we must sponsor and file an investigational new drug (IND) application and be responsible for initiating and overseeing the human clinical trials to demonstrate the safety and efficacy and, for a biologic product, the potency, which are necessary to obtain FDA approval of any such

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products. For our newly sponsored investigational new drug applications, we will be required to select qualified investigators (usually physicians within medical institutions) to supervise the administration of the products, and we will be required to ensure that the clinical trials are conducted and monitored in accordance with FDA regulations and the general investigational plan and protocols contained in the IND application.

The FDA receives reports on the progress of each phase of testing, and it may require the modification, suspension, or termination of trials if an unwarranted risk is present to patients. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA. The IND application process can thus result in substantial delay and expense. Human gene therapy products, a primary area in which we are seeking to develop products, are a new category of therapeutics. Because this is a relatively new and expanding area of novel therapeutic interventions, there can be no assurance as to the length of the trial period, the number of patients the FDA will require to be enrolled in the trials to establish the safety, efficacy and potency of human gene therapy products, or that the data generated in these studies will be acceptable to the FDA to support marketing approval.

After the completion of trials of a new drug or biologic product, FDA marketing approval must be obtained. If the product is regulated as a biologic, the Center for Biological Evaluation and Research will require the submission and approval, depending on the type of biologic, of either a biologic license application or a product license application and a license application before commercial marketing of the biologic. If the product is classified as a new drug, we must file a new drug application with the Center for Drug Evaluation and Research and receive approval before commercial marketing of the drug. The new drug application or biologic license applications must include results of product development, laboratory, animal and human studies, and manufacturing information. The testing and approval processes require substantial time and effort and there can be no assurance that the FDA will accept the new drug application or biologic license applications for filing and, even if filed, that any approval will be granted on a timely basis, if at all. In the past, new drug applications and biologic license applications submitted to the FDA have taken, on average, one to two years to receive approval after submission of all test data. If questions arise during the FDA review process, the approval process can take more than two years.

Notwithstanding the submission of relevant data, the FDA may ultimately decide that the new drug application or biologic license application does not satisfy its regulatory criteria for approval and may require additional studies. In addition, the FDA may condition marketing approval on the conduct of specific post-marketing studies to further evaluate safety and effectiveness. Rigorous and extensive FDA regulation of pharmaceutical products continues after approval, particularly with respect to compliance with current good manufacturing practices (GMPs), reporting of adverse effects, advertising, promotion and marketing. Discovery of previously unknown problems or failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market, as well as possible civil or criminal sanctions.

Ethical, social and legal concerns about gene therapy, genetic testing and genetic research could result in additional regulations restricting or prohibiting the processes we or our suppliers may use. Federal and state agencies, congressional committees and foreign governments have expressed interest in further regulating biotechnology. More restrictive regulations or claims that our products are unsafe or pose a hazard could prevent us from commercializing any such products.

The approval and/or clearance for marketing of medical devices, such as Excellagen and potentially other product candidates of our Tissue Repair Company subsidiary, are also subject to extensive controls by health regulatory and other authorities. Although some devices can be cleared for marketing pursuant to a procedure referred to as an FDA 501(k) clearance, other devices and/or indications may require additional clinical studies and may be subject to even more extensive regulatory and other controls.

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Nutraceuticals, dietary supplements and other products intended for human consumption, such as those included or to be included in our product portfolio , are also subject to numerous rules and regulations promulgated by the FDA and other food and health regulatory authorities, including regulations governing the sourcing, manufacture, labeling, handling, storage, marketing and use of such products.

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

We are also subject to a variety of other regulations in the United States, including those relating to bioterrorism, taxes, labor and employment, import and export, and intellectual property.

To the extent we have operations outside the United States, any such operations would be similarly regulated by various agencies and entities in the countries in which we operate. The regulations of these countries may conflict with those in the United States and may vary from country to country. In markets outside the United States, we may be required to obtain approvals, licenses or certifications from a country s ministry of health or comparable agency before we begin operations or the marketing of products in that country. Approvals or licenses may be conditioned or unavailable for certain products. These regulations may limit our ability to enter certain markets outside the United States.

Competition

The pharmaceutical, biotechnology, medical device and nutraceutical industries are intensely competitive. Our products and any product candidates developed by us would compete with existing drugs, therapies, devices or procedures and with others under development. There are many pharmaceutical, biotechnology and medical device companies, public and private universities and research organizations actively engaged in research and development of products for the treatment of cardiovascular and related diseases, and/or products for the healing of chronic wounds. Many of these organizations have financial, technical, research, clinical, manufacturing and marketing resources that are greater than ours. If a competing company develops or acquires rights to a more efficient, more effective, or safer competitive approach for treatment of the same or similar diseases or conditions we have targeted, or one that offers significantly lower costs of treatment, our business, financial condition and results of operations could be materially adversely affected.

We are aware of products currently under development by competitors targeting the same or similar cardiovascular and vascular diseases as our Generx product. These include biologic treatments using forms of genes and therapeutic proteins. For example, CardioVascular BioTherapeutics is developing injectable and topical forms of FGF-1 for the potential treatment of cardiovascular diseases. We will also face competition from entities using other traditional methods, including new drugs and mechanical therapies, to treat cardiovascular and vascular disease.

In the areas of tissue repair and wound healing, such as Excellagen and others being developed by our Tissue Repair subsidiary, there are a number of approaches being employed, including other collagen-based products, living skin equivalents, negative pressure wound therapy devices and other devices, and biologics and small molecule drugs designed to promote repair and healing. Competing products include Dermagraft®, Apligraf®, EpiFix® and Graftjacket®, and others.

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We believe that the most significant competitive factor in the field of new therapeutics and devices is the effectiveness of a product candidate, as well as its relative safety and cost as compared to other products, product candidates or approaches that may be useful for treating a particular disease condition. If validated and commercialized we expect that our Generex product will provide an effective and safe alternative for cardiac patients are no longer responsive to medical therapy, and are considered not suitable candidates for traditional percutaneous or surgical revascularization procedures such as cardiac by-pass surgery, or angioplasty and stenting. We also anticipate that treatment by Generex will cost substantially less than surgical procedures.

We believe that our product development programs will be subject to significant competition from companies using alternative technologies, some of which are described above, as well as to increasing competition from companies that