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**CARDIUM REPORTS POSITIVE DATA FROM MATRIX PHASE 2b STUDY  
OF EXCELLARATE™ TOPICAL GEL FOR NON-HEALING  
DIABETIC FOOT ULCERS AND PLANS FOR PHASE 3 PROGRAM**

***Excellarate Offers Potential for Simpler and Enhanced Treatment Opportunities  
within the Spectrum of Advanced Wound Care Biologics,  
Bio-Engineered Dermal Substitutes and Medical Devices***

SAN DIEGO, CA – October 14, 2009 – Cardium Therapeutics (NYSE Amex: CXM) today reported positive data from its Matrix Phase 2b clinical trial of Excellarate™ for the potential treatment of patients with chronic non-healing diabetic foot ulcers based on the Company's Gene Activated Matrix (GAM) technology platform. The study evaluated patients treated with the Excellarate product candidate (GAM501, which is a combination of Ad5PDGF-B and 2.6% collagen) or 2.6% collagen alone (matrix), compared to patients who received only the protocol-specified standard of care without any applied Ad5PDGF-B or collagen matrix. The Company will hold a webcast and conference call to discuss the clinical results of the Excellarate Matrix Phase 2b clinical study today, October 14, 2009, at 5:00 p.m. ET (access information is provided below).

The Excellarate product candidate and its components Ad5PDGF-B and collagen matrix appear to be both safe and well tolerated by patients. The Phase 2b study was abbreviated and enrollment ended early after key efficacy measures among blinded groups were observed at rates substantially higher than those expected for patients receiving only standard of care. Consistent with those observations, the unblinded data set showed a substantial (55%) relative improvement in achieving complete wound closure by 12 weeks (the key efficacy measure for a Phase 3 product registration program) among patients treated with a single dose of Excellarate as compared to patients receiving standard of care. Nearly half of patients (48%) receiving a one-time Excellarate treatment had complete wound closure by 12 weeks, compared to a 31% wound closure rate for standard of care. Among combined one and two dose groups of Excellarate approximately 41% of patients achieved complete closure by 12 weeks. However, since re-dosing was based on group randomization rather than apparent need, a majority of patients randomized to receive a second dose of Excellarate at 4 weeks following initial product administration either did not receive one because their wounds were closed by that point, or they received only a very small second dose (less than 100 microliters) because their wounds were extremely small.

In addition to overall wound closures by 12 weeks, the Phase 2b study also evaluated wound closure rates and trajectories following product administration in order to assess the timing and extent of bioactivity. The unblinded data revealed that patients receiving Excellarate exhibited early and rapid wound healing responses as evidenced by very substantial reductions in wound radius over the first several weeks following product administration, which responses were both greater and faster than those observed among patients that had received standard of care. For example, a 108% relative improvement (decrease in ulcer radius) compared to standard of care

was observed over the first week following administration of Excellerate, and a 50% relative improvement was observed as an average over the first four weeks.

The collagen matrix, which forms an integral component of Excellerate (by promoting Ad5PDGF-B binding and PDGF-B protein retention within the wound site), had not been associated with substantial wound healing responses in preclinical animal models used for design of the clinical studies. In human diabetic patients, however, the collagen matrix appeared to contribute substantially to wound healing responses. As a result, the collagen arm was not a negative control as expected based on preclinical studies. While the clinical study was not powered to nor did it differentiate between the relative contributions of the individual Ad5PDGF-B and collagen components that make up Excellerate – both the Excellerate and the collagen matrix study arms showed substantial improvements in achieving wound closure as compared to standard of care. The standard of care (SOC) arm is the accepted control based on FDA guidance for wound healing products, and is expected to be used as the control arm in a planned Phase 3 program for product registration.

The Company's customized collagen matrix is a modified form of collagen that includes certain structural stabilizers and hydrolytic enzyme inhibitors. Based on observations from the Phase 2b clinical study, it appears that this collagen formulation which is referred to as Excellagen™, may play an active role in promoting wound healing, particularly when used in combination with standard of care (including surgical debridement).

It is believed that the collagen matrix supports the body's inherent processes of wound repair by providing a molecular scaffolding within the wound bed to promote the infiltration and proliferation of cells associated with tissue repair such as monocytes, fibroblasts and endothelial cells. Surgical debridement, a process of removing dead or damaged tissue in and around the wound site, forms a key part of standard of care and is known to promote wound healing. Regular debridement was practiced in all patients in the Phase 2b clinical study and is believed to account for a substantial portion of the wound healing response observed in the SOC group. The data from this Phase 2b and prior studies suggest that collagen may further support the wound healing process in humans and that PDGF-B, which is a growth factor known to stimulate a variety of wound repair cells, may provide an additional biologic stimulus.

Based on these data, the Company believes that its collagen matrix may prove to be very beneficial as an adjunct to existing wound care therapies, such as debridement. Since collagen has been approved by the FDA as a medical device, Cardium intends to develop a registration pathway for its collagen to be used in conjunction with debridement, which is typically applied as standard of care for all diabetic foot ulcers and many other types of soft tissue wounds. As announced today, the Company plans to advance this collagen-based product termed Excellagen™ along an abbreviated 510(k) registration process in consultation with the FDA.

Following completion of safety and preliminary efficacy data, the Company also plans to schedule a meeting with the FDA to review the complete integrated data set and outline plans for a Phase 3 clinical study program designed to confirm the safety and effectiveness of Excellerate as compared to standard of care, since PDGF-B is known to contribute to the biologic process of wound healing and is itself an approved protein product for use in advanced wound care. The Company believes that the combination of collagen and PDGF-B as provided by the Excellerate product candidate holds the potential to further promote wound healing in non-healing diabetic foot ulcers and other difficult-to-treat wounds. Based on feedback from study investigators, and with the additional positive safety data from the Phase 2b study, the Phase 3 program is also expected to allow for one or two follow-up doses in patients that exhibit a slower healing rate or who have not yet achieved substantial closure following the initial administration of product.

Regranex<sup>®</sup> (becaplermin, 0.01%) is a PDGF-B protein therapy that is currently the only FDA-approved advanced care biologic for the treatment of patients with lower extremity neuropathic diabetic foot ulcers. PDGF-B protein-based therapy is a daily use prescription medication for treatment for up to 20 weeks, which would require up to 140 daily administrations of product and an additional 140 daily wound cleansings by patients. Based on published studies reflected in the prescribing information sheet for becaplermin, daily application of product combined with daily wound cleansings resulted in a 35% relative improvement in wound closures at 20 weeks (i.e. a 50% wound closure rate for becaplermin-treated patients compared to a 37% wound closure rate for control patients). Based on additional published data from these studies, by 12 weeks (as in the shorter Excellerate study period), the wound closure rate was about 34% for becaplermin-treated patients as compared to a 25% complete closure rate for control patients, representing a 36% relative improvement in wound closure.

In contrast to becaplermin, the Excellerate product candidate is designed to stimulate a physiologic level of sustained and locally-confined PDGF-B protein by cells at the wound site. It is estimated from preclinical analyses that following a single Excellerate administration the localized cellular expression of PDGF-B would be about 55 nanograms, which is on the order of 60,000-fold lower than the approximately 3.0 million nanograms of PDGF-B protein that would be topically applied by patients over a 20-week treatment course with becaplermin. Also, unlike becaplermin, the PDGF-B protein encoded by Excellerate is a naturally-occurring version of the protein that retains its native extracellular matrix-binding domain, which further promotes retention of the growth factor within the wound site.

“The completion of the Matrix Phase 2b clinical study represents a major advance in our plans to establish an important new therapeutic class of biologics for the potential treatment of diabetic foot ulcers and other wounds. Despite years of research and effort, diabetic wounds remain a serious unmet clinical need. Lower limb amputations occur up to 30 times more often in diabetic patients, and the resulting mortality rates for these patients can be similar to or worse than many forms of cancer. We believe that, because of the complex nature of lower extremity diabetic ulcers, patients will benefit from the availability of multiple wound healing agents and therapies that can be tailored to appropriately address their specific medical conditions, and our Excellerate and Excellagen development efforts seek to expand treatment options for patients requiring advanced wound care therapy,” stated Christopher J. Reinhard, Chairman and Chief Executive Officer of Cadium.

### **Webcast and Conference Call**

The Company will hold a webcast and conference call to discuss the clinical results of the Excellerate Matrix Phase 2b clinical study today, October 14, 2009, at 5:00 p.m. ET. Participants can access the live conference call by dialing 800-259-0251 (U.S.) or 617-614-3671 (International) using the conference passcode 98344451. The call and accompanying slides can also be accessed via the webcast through the Company's website at <http://phx.corporate-ir.net/phoenix.zhtml?c=77949&p=irol-calendar>. If you are unable to attend the webcast, a replay of the conference call will be available approximately two hours after the conclusion of the call by dialing 888-286-8010 (U.S.) or 617-801-6888 (International) using passcode 68300091. The webcast will be archived for 90 days.

### **Excellerate Product Candidate Observations**

Two patients in the Matrix clinical trial were featured in local television news programs because of the rapid healing of previously non-healing wounds observed by their physicians. Data unblinding revealed that both patients had received the Excellerate product candidate. To learn more about the clinical experiences of these patients, [click here](#) to view a television segment

featuring an investigator in the study, Dr. Peter A. Blume of the Yale University School of Medicine, and [click here](#) to view a segment featuring Dr. Barbara Aung of the Aung Foothealth Clinics, and their patients enrolled in the Matrix clinical study. The Matrix study media segments can also be accessed at [www.cardiumthx.com](http://www.cardiumthx.com).

### **Matrix Phase 2b Clinical Study**

The Matrix Phase 2b clinical study was a multi-center U.S.-based study designed to evaluate Excellerate for the potential treatment of non-healing diabetic foot ulcers. Enrollment in the study was ended early after key efficacy measures among blinded groups were observed at rates substantially higher than those expected for patients receiving only standard of care. The study, which was conducted at 20 medical centers, evaluated patients that were treated with the gene-activated Excellerate product candidate (Ad5PDGF-B / 2.6% collagen) or the collagen matrix component of Excellerate, compared to patients who received only standard of care treatment without any applied Ad5PDGF-B or collagen. A per protocol data analysis included 113 patients with lower extremity neuropathic ulcers that were chronically non-healing despite receiving standard of care. Eleven additional patients who were initially recruited into the trial were excluded (7 patients were lost to evaluation or had a disqualifying surgical procedure and 4 were determined to have been mis-enrolled based on prespecified enrollment criteria, which led to exclusions before study completion and unblinding). The Matrix study evaluated safety as assessed by adverse events, clinical laboratory measurements, vital signs, concomitant medications, physical exam findings and serum antibody concentrations to collagen and adenovector. Preliminary measures of efficacy included the incidence of complete wound closure by 12 weeks and the effect of Excellerate on healing rates as measured by the change of the ulcer radius during the 4-week period following Excellerate treatment. In addition, patients whose wounds were successfully closed are being followed for up to three additional months to further evaluate wound healing durability. Durability results will be reported at a later date.

Excellerate appeared to be both safe and well tolerated in human patients with diabetic neuropathy. There were no substantial differences observed with respect to adverse events, clinical laboratory results, physical exam findings or immunological antibody responses to collagen or the adenovector in patients receiving either one or two doses of Excellerate or collagen matrix, as compared to each other or to standard of care.

Collagen, an FDA approved medical device, is an important and required element of the Company's Gene Activated Matrix technology and was also included as a key comparator group in the Phase 2b study, as an independent collagen-only treatment arm. Based on preclinical animal data suggesting that collagen would not contribute substantially to wound healing, the study was expected to demonstrate that collagen administration would be equivalent to standard of care, and that these groups would collectively form a control group. However, based on a preliminary review of the top line data, collagen appears to contribute to the healing response in human diabetic patients. While the standard of care (SOC) control group in the Phase 2b study was too small to support statistical differentiation of the groups, the 31% wound closure rate observed in the SOC group was similar to that observed in prior published studies and substantially lower than that observed for patients receiving Excellerate or collagen alone. Among patients receiving a single dose of Excellerate, there was a 55% relative improvement in complete wound closure by 12 weeks as compared to the SOC group, which is considered to be a key efficacy criterion for a Phase 3 product registration program.

During the course of the Phase 2b Matrix study, some investigators expressed an interest in having the flexibility to re-dose patients (to allow for a second or third treatment during the 12-week study period) in response to observed healing slowdowns or plateaus following an initially rapid healing response among some patients. In addition, while early rapid healing following

product administration was not a prespecified efficacy measure, the unblinded Phase 2b data revealed that patients receiving Excellerate exhibited a 108% relative improvement (decrease in ulcer radius) as compared to SOC over the first week following a one-time administration of product, and a 50% relative improvement was observed as an average over the first four weeks. The Phase 2b clinical study included a second dose treatment cohort, but the observed healing slowdowns or plateaus did not necessarily coincide with the protocol's established second dosing at week 4 following initial dosing, and a number of patients prespecified by randomization to receive a second dose either did not require it (because their wounds had already closed) or received only an extremely small second dose (because their wounds were almost closed). Based on continuing safety data from the Matrix Phase 2b study, as well as the open label Phase 1/2 clinical study and preclinical research, all of which included some re-dosing, the Excellerate product candidate appears to be both safe and well tolerated, with no significant differences observed in immunological antibody responses to either collagen or to the adenovector in patients receiving Excellerate as compared to those receiving only standard of care. These findings together with the initial healing rate change over time observed in the Phase 2b study support allowing investigators in future studies to re-dose a subset of patients who have not yet achieved a prespecified rate or extent of wound closure. As a result, subject to review with the FDA, we would consider the inclusion of a re-dosing protocol into the planned Phase 3 clinical study program. Cardium believes that this added feature may offer the potential to further enhance efficacy in practical real world clinical settings by optimizing the interaction between Ad5PDGF-B production, which is believed to occur predominantly over the first few weeks following administration, with the individual patient's underlying physiology within the wound site.

### **Planned Phase 3 Clinical Program**

Following completion of the Phase 2b study's durability phase and a complete statistical data analysis, Cardium plans to meet with the FDA to review the complete clinical trial results and to review the Company's proposed Phase 3 clinical study program. The Company will seek to establish a clinical development plan, which could include a special protocol agreement, to define the size and scope of the proposed program which will be based on the important information acquired from the Phase 1/2 and Phase 2b clinical studies. Based on FDA guidance documents and other clinical studies that have supported other product registrations, the Phase 3 program will include a prospective, randomized, double-blind, controlled multi-center study that will evaluate continued safety and definitive efficacy. Cardium is also planning that this study program will utilize a single primary efficacy endpoint, percent of complete wound closure at 12 weeks or earlier, as compared to standard of care.

### **Excellerate Product Candidate**

The Excellerate product candidate is initially being developed to facilitate wound closure in non-healing diabetic foot ulcers. Excellerate is a collagen-based topical gel employing Cardium's Gene Activated Matrix™ technology to locally stimulate the release of platelet-derived growth factor-B protein (PDGF-B) and provide a matrix for cell migration, which are believed to be important keys in the human body's wound healing process. The sustained localized release and retention of PDGF-B by a patient's own cells directly at the wound site is believed to stimulate angiogenesis and granulation tissue formation through the recruitment and proliferation of cells such as monocytes, fibroblasts and endothelial cells. These cell types are considered critical for the effective stimulation of a variety of wound healing processes.

The Excellerate product candidate is being designed to provide physicians and patients with a potentially simpler, easy-to-use treatment regimen compared to most diabetic wound healing agents or devices in use that require repeated administrations over a long term (weeks to months). Based on recently announced advancements, Excellerate is also expected to be re-

formulated as an easy-to-use single syringe that would be pre-mixed and ready to be applied to patients' wounds. The reformulation will allow Excellerate to be maintained in a physician's office using a standard refrigerator (at a temperature of about 4°C) and is expected to have a shelf life of at least 15-18 months.

### **Gene Activated Matrix Technology Platform**

Cardium's proprietary Gene Activated Matrix™ technology platform is designed to provide a therapeutic level of protein synthesis at a specific site in the body and can be used in soft tissue such as skin, ligament, tendons and cartilage, as well as in hard tissue such as bone. The technology is distinctive in that it is immobilized gene delivery that allows for gene uptake restricted to the application site. The Gene Activated Matrix comprises any biocompatible matrix containing a gene or DNA vector encoding for a growth factor or any therapeutic protein. The technology allows for a broad spectrum of formulations and the use of any biocompatible matrix, natural or synthetic, which would include, but not be limited to, collagen, de-mineralized bone, allograft and other synthetic graft materials.

The Company's studies have shown that proliferative cells migrate into the Gene Activated Matrix and then take up the immobilized gene resulting in localized and sustained production of small but physiologically active quantities of growth factor proteins or other therapeutic proteins based on the protein-producing DNA of choice. Compared with current protein therapy, which may be limited due to the inherently short half-life of proteins, the Company believes that the localized and sustained production of therapeutically significant concentrations of DNA-driven proteins at the delivery site can significantly enhance the stimulation of localized therapeutic processes such as tissue repair.

### **About Cardium**

Cardium is focused on the acquisition and strategic development of new and innovative biomedical product opportunities and businesses that have the potential to address significant unmet medical needs and definable pathways to commercialization, partnering and other economic monetizations. Cardium's investment portfolio includes the Tissue Repair Company and Cardium Biologics, medical technology companies primarily focused on the development of innovative therapeutic products for wound healing, bone repair, and cardiovascular indications. In July 2009, Cardium completed the sale of its InnerCool Therapies medical device business to Royal Philips Electronics, the first asset monetization from the Company's biomedical investment portfolio. News from Cardium is located at [www.cardiumthx.com](http://www.cardiumthx.com).

### **Forward-Looking Statements**

Except for statements of historical fact, the matters discussed in this press release are forward looking and reflect numerous assumptions and involve a variety of risks and uncertainties, many of which are beyond our control and may cause actual results to differ materially from stated expectations. For example, there can be no assurance that Excellerate or our other candidates will prove to be sufficiently safe and effective, or that results or trends observed in one clinical study or procedure will be reproduced in subsequent studies or procedures, or that clinical studies even if successful will lead to product advancement or partnering; that the Excellerate product candidate offers the potential for simpler or more cost-effective treatment for physicians and patients than other FDA-approved products that currently are or will be on the market; that the Matrix clinical study program or other human clinical trials can be conducted and completed in an efficient and successful manner; that we can develop a DNA-based orthobiologics product portfolio; that our products or product candidates will not be unfavorably compared to competitive products that may be regarded as safer, more effective, easier to use or less expensive; that FDA

or other regulatory clearances or other certifications, or other commercialization efforts will be successful or will effectively enhance our businesses or their market value; that our products or product candidates will prove to be sufficiently safe and effective after introduction into a broader patient population; or that third parties on whom we depend will perform as anticipated.

Actual results may also differ substantially from those described in or contemplated by this press release due to risks and uncertainties that exist in our operations and business environment, including, without limitation, risks and uncertainties that are inherent in the development of complex biologics and in the conduct of human clinical trials, including the timing, costs and outcomes of such trials, our ability to obtain necessary funding, regulatory approvals and expected qualifications, our dependence upon proprietary technology, our history of operating losses and accumulated deficits, our reliance on collaborative relationships and critical personnel, and current and future competition, as well as other risks described from time to time in filings we make with the Securities and Exchange Commission. We undertake no obligation to release publicly the results of any revisions to these forward-looking statements to reflect events or circumstances arising after the date hereof.

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