21-Oct-11

Generx®

(alferminogene tadenovec)

Angiogenic Therapy

Regenerative Medicine for Interventional Cardiology

GENERX®

Investor Presentation

DNA-Based Non-Surgical Angiogenic Therapy

Forward Looking Statements

This presentation may contain forward-looking statements, including comments concerning clinical trials and product development programs, evaluation of potential opportunities, the level of corporate expenditures, the assessment of Cardium's technology by potential corporate partners, capital market conditions, timing of events, cash consumption and other subjects. Actual results could differ materially from these forward-looking statements for many reasons, including the risks described under "Risk Factors" in the Company's Annual Report on Form 10-K and Quarterly Reports on Form 10-Q as filed with the Securities and Exchange Commission. No guarantee about future results, performance or achievements can be made. Neither Cardium nor its agents intend to update any of the forward-looking statements after the date of this presentation to conform them to actual results or to changes in expectations.

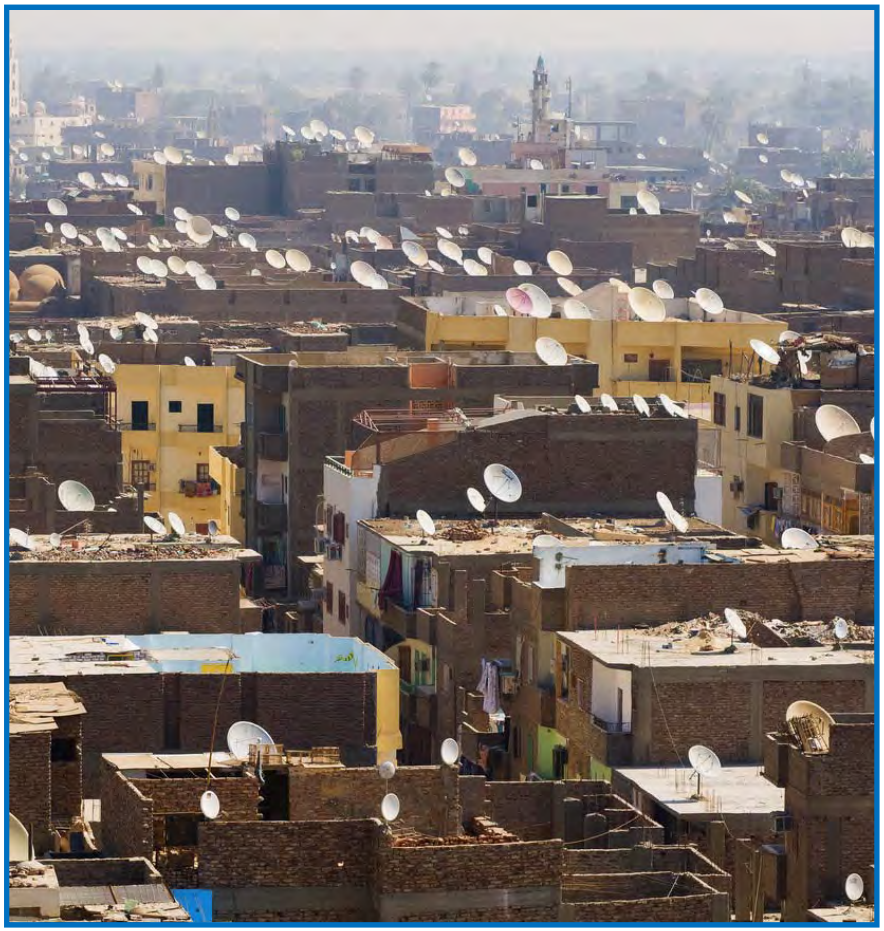
CARDIUM
MEDICAL OPPORTUNITIES PORTFOLIO

Scientific Overview and Therapeutic Rationale

DNA-Based Cardiovascular Therapeutics

- New regenerative medicine biological tools for interventional cardiology
- Leverages the healing power of cardiac plasticity
- Proprietary, catheter-based intracoronary delivery approach during an angiographic procedure
- One-time non-surgical treatment
- DNA transgene delivery and CAR receptor-based preferential cardiac uptake

- Ischemic injury (coronary heart disease) is a required precursor for effective growth factor DNA-based therapy
- Designed to stimulate microvascular cardiac angiogenesis
- Driven by upstream regulatory gene that stimulates a cascade of other important growth factors
- First DNA-based biologic to advance to U.S. FDA Phase 3 (with fast track status) and Registration / Phase 3 Study in Russia



Developing new and innovative, cost-effective advanced care for coronary heart disease patients in international markets

YouTube
NYSE Amex: CXM

Generx Cardio Chant

Generx® Highlights

- Generx [Ad5FGF-4] represents a new therapeutic class of regenerative medicine DNA-based biologics for interventional cardiology that is being designed to stimulate the natural growth of microvascular circulation for the treatment of patients with myocardial ischemia due to advanced coronary disease. Generx is administered one-time, using a cardiac catheter.

- Generx is being currently developed, in markets outside the U.S., as treatment alternative for patients who may not have access to costly and invasive advanced mechanical revascularization procedures, including coronary artery bypass surgery and angioplasty/stents, or may no longer be optimal candidates for these procedures.

- Ad5FGF-4 has been evaluated in four clinical studies in North America and Western Europe at over 100 medical centers with over 650 patients participating in these studies. Data from the clinical studies have been published in leading peer reviewed medical journals.
  - The product appears safe and capable of improving microvascular circulation in certain patients, as measured by SPECT imaging, and improvements using standard ETT assessments.

Generx® Highlights

- An independent 10-year clinical study (n=845) by Swiss researchers, published in the American Heart Association's journal Circulation, have reported that patients with high levels of collateral circulation in the heart have a statistically significant mortality advantage when compared to patients with low collateral flow.

- Generx was cleared by the FDA to initiate the AWARE Phase 3 clinical study (with Fast Track status) for certain refractory patients. Ad5FGF-4 is the only DNA-based cardiovascular biologic to be cleared for Phase 3 clinical study by the FDA.
  - The AWARE clinical trial was inactivated by Cardium based on economic considerations due to the patient recruitment challenges for a small targeted population group in the U.S. where by-pass surgery and angioplasty are commonly available to patients of all ages.

- Generx will be evaluated in a Phase 3 / registration study (the Aspire Study) for 100 patients with advanced coronary artery disease at up to six major medical centers in the Russian Federation in connection with a commercialization plan covering the marketing and sale of Generx in Russia. Ad5FGF-4 will be marketed and sold in Russia under the trade name "Cardionovo."

Generx® Highlights

- Recent discoveries from Cardium-sponsored preclinical studies at Emory University showed that induced transient ischemia (i.e. balloon catheter-based occlusion/ reperfusion as in an ordinary angioplasty, but at lower pressure) substantially increases Generx's DNA vector's transfection efficiency to heart muscle cells. These new findings offer the opportunity to further enhance angiogenic response and lower response variability in patients.
  - These findings have now been integrated into the Russian-based ASPIRE clinical study protocol.
- A senior group of current Cardium physicians and business executives have worked on the Generx research and development effort from the initial development (1996) to the present.
- During the Generx development cycle, over $250 million has been invested in the product formulation, manufacturing and clinical study by Collateral, Schering and Cardium.
- As a DNA-based bio-reactor manufactured product, Generx is projected to have favorable gross margins and offers the potential to generate substantial revenue in large markets with coronary artery disease.

Generx®: Historical Perspective

Collateral Therapeutics
(NASDAQ)

University of California San Diego

Discovery, Licensing and Initial Preclinical Studies

1996

Schering AG

As Strategic Partner with Collateral Therapeutics

Schering Acquires Collateral in 2002 for $160 Million

Phase 1/2 to Phase 2b/3

1997 - 2005

Cardium Therapeutics Formed to Acquire Technology from Schering / Bayer

FDA Phase 3 Clearance with Fast Track Status & Phase 3 Clearance for Registration Study in Russia

2005 - Present

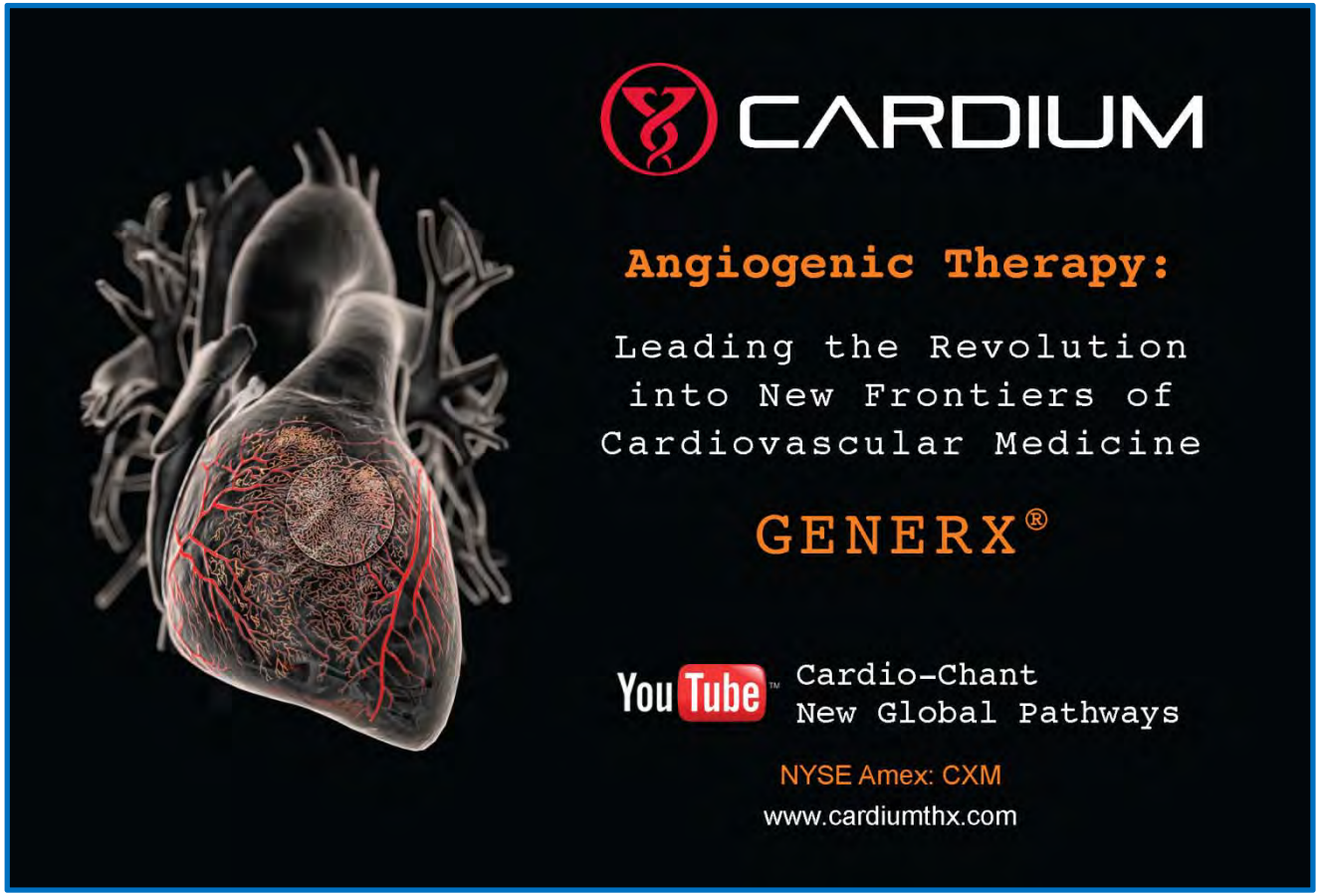
Commercial International Development Activities

Russia
Brazil
India

Current Status

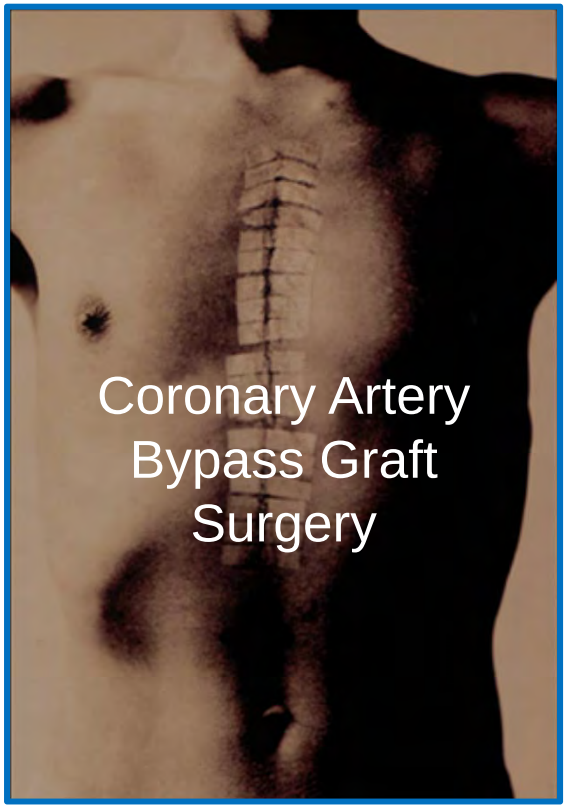
CARDIUM
MEDICAL OPPORTUNITIES PORTFOLIO

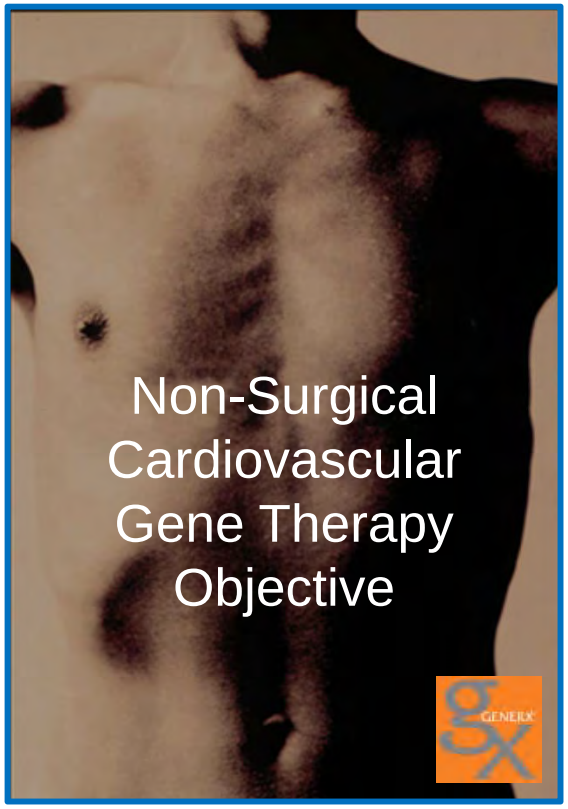
Generx® Late-Stage Clinical Development



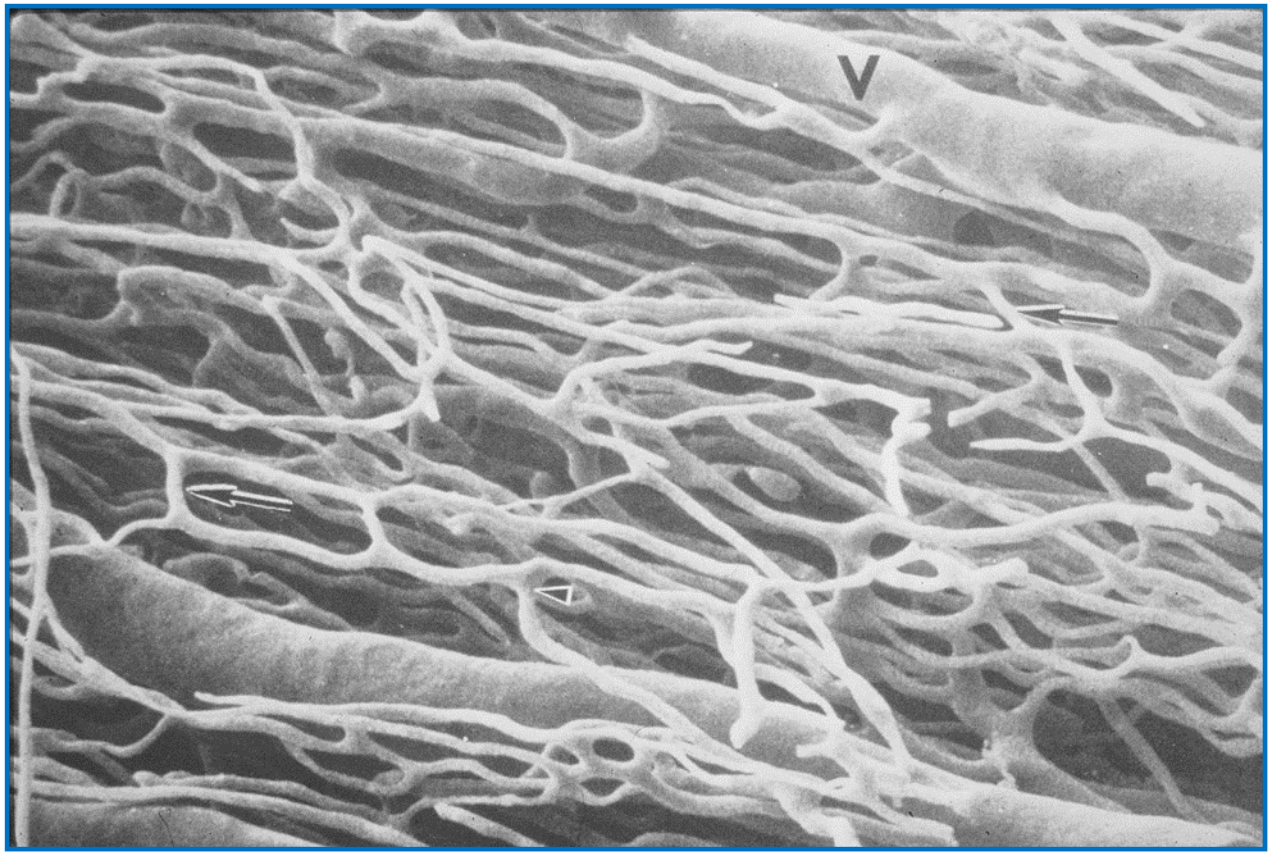
Generx® Revolutionary Alternative for Heart Disease

Patients Without Access to Advanced Surgical Care



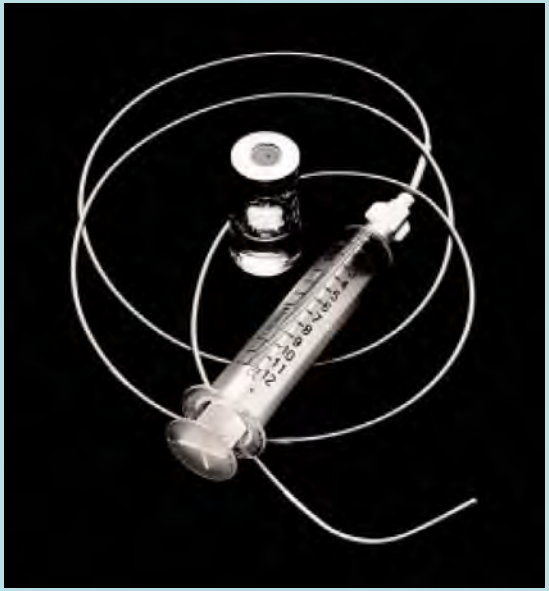


Cardiovascular Angiogenesis



CARDIUM
MEDICAL OPPORTUNITIES PORTFOLIO

GENERX™ [Ad5FGF-4]

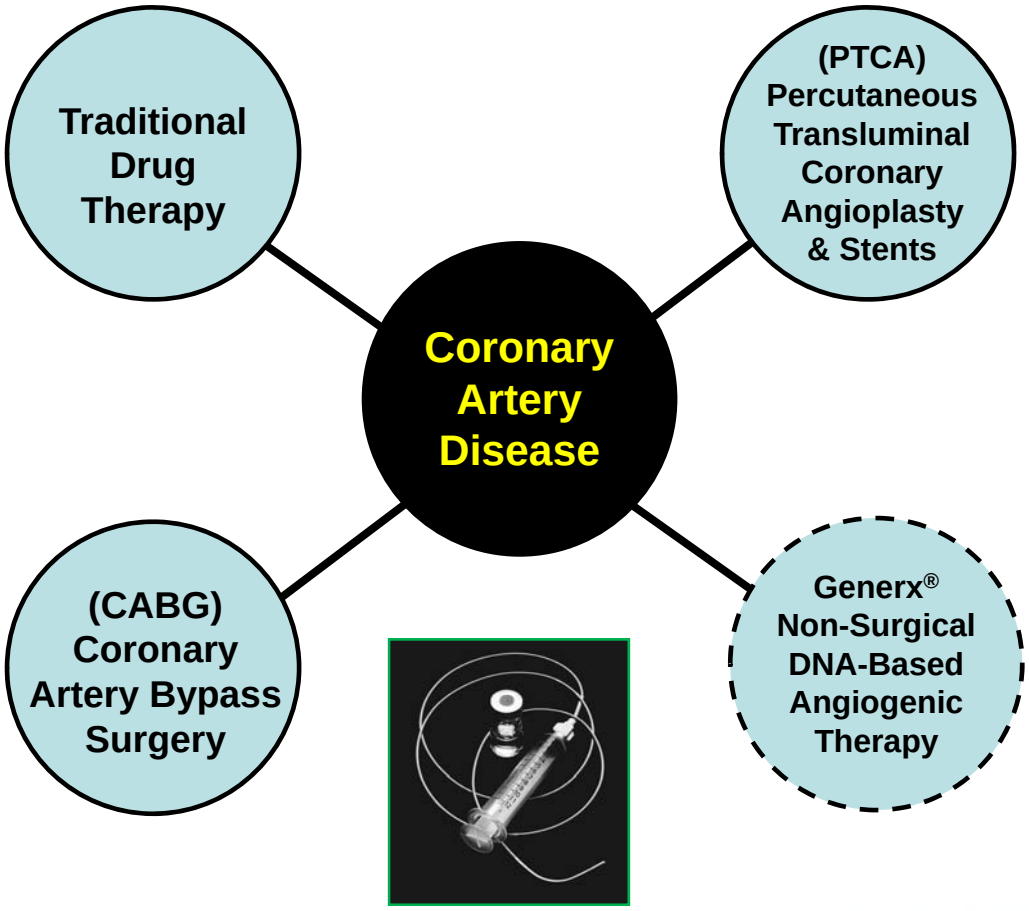


Generx [Ad5FGF-4] represents a new regenerative medicine therapeutic class of DNA-based biologics that is being developed for interventional cardiology that is designed to promote a disease-modifying physiological response which stimulates the growth of microvascular circulation based on the one-time administration, using a standard cardiac catheter, as a treatment for patients with advanced coronary artery disease.

Generx is currently being developed for international markets outside the United States as a treatment alternative for patients who may not have access to costly and invasive advanced care revascularization procedures, including coronary artery bypass surgery and angioplasty/stents, or may not be optimal candidates for these procedures.

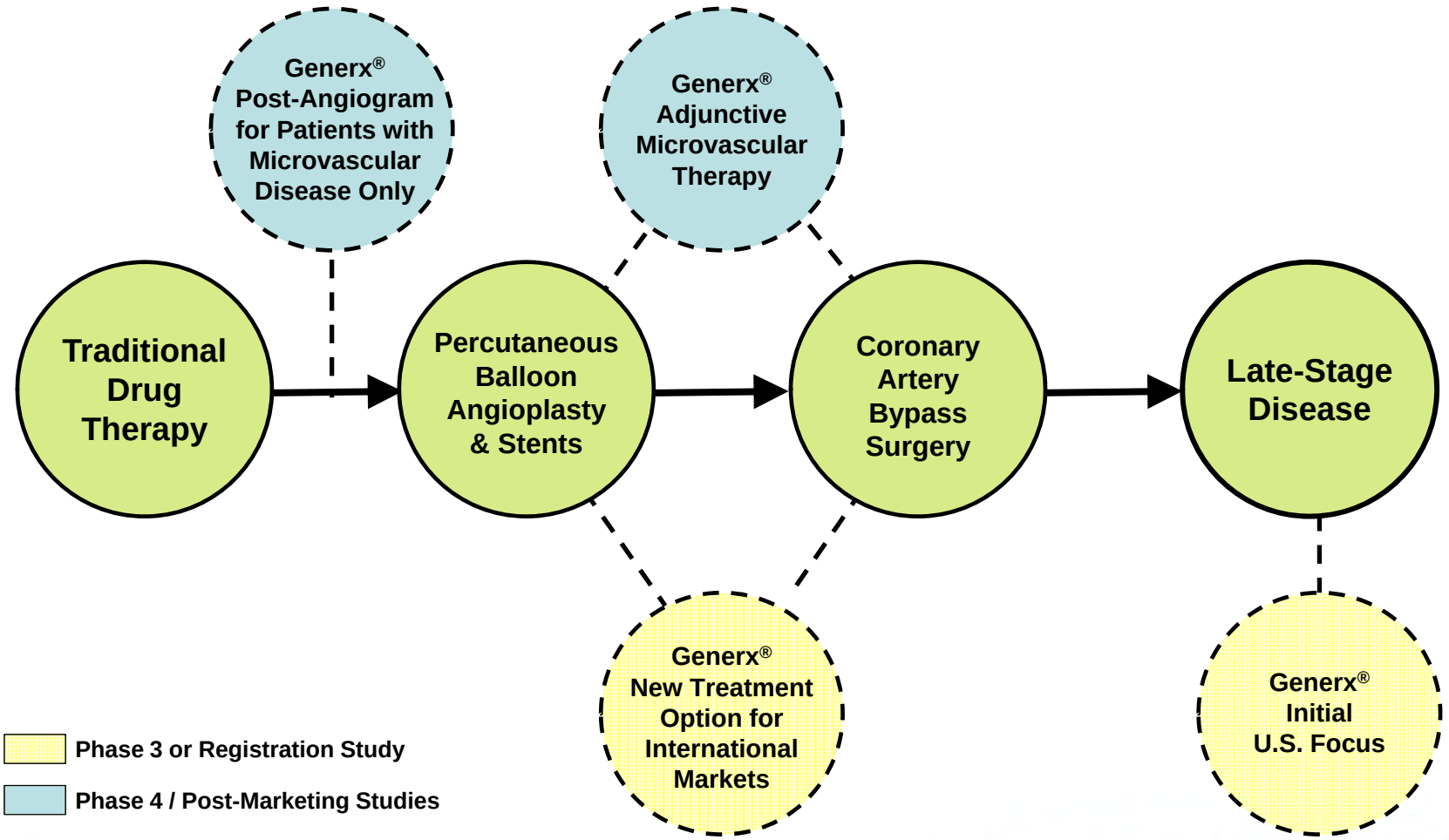
CARDIUM
MEDICAL OPPORTUNITIES PORTFOLIO

Proposed Therapeutic Positioning: Generx® / Cardionovo



Generx® Coronary Artery Disease

Pioneering New Microvascular Treatment Algorithms



Generx® [Ad5FGF-4]
Product Focus for Russian Federation

Generx is being developed to promote the growth of microvascular circulation in the heart. It is administered by a cardiologist through a cardiac catheter during an outpatient procedure.

*The product is a new treatment option for **patients with myocardial ischemia due to advanced coronary artery disease that have limited access to advanced medical care** including coronary angioplasty and stents as well as coronary artery by-pass surgery or patients who are not optimal candidates for those procedures.*

A long-term study (n = 845) has shown that patients with a higher collateral blood flow index may have an improved mortality benefit when compared to patients with a relatively lower collateral blood flow index.

Selected Health Statistics Benchmarks			
Demographic Metrics	**United States**	**Russian Federation**	**Variance**
Average Life Expectancy - **Males**	75	**57**[1]	- 24%
Cardiovascular Death Rates per 100,000 (Ages 35-74) – **Males**[2]	283	**1,555**	5.5X
Cardiovascular Death Rates per 100,000 (Ages 35-74) – **Females**[2]	145	**659**	4.5X

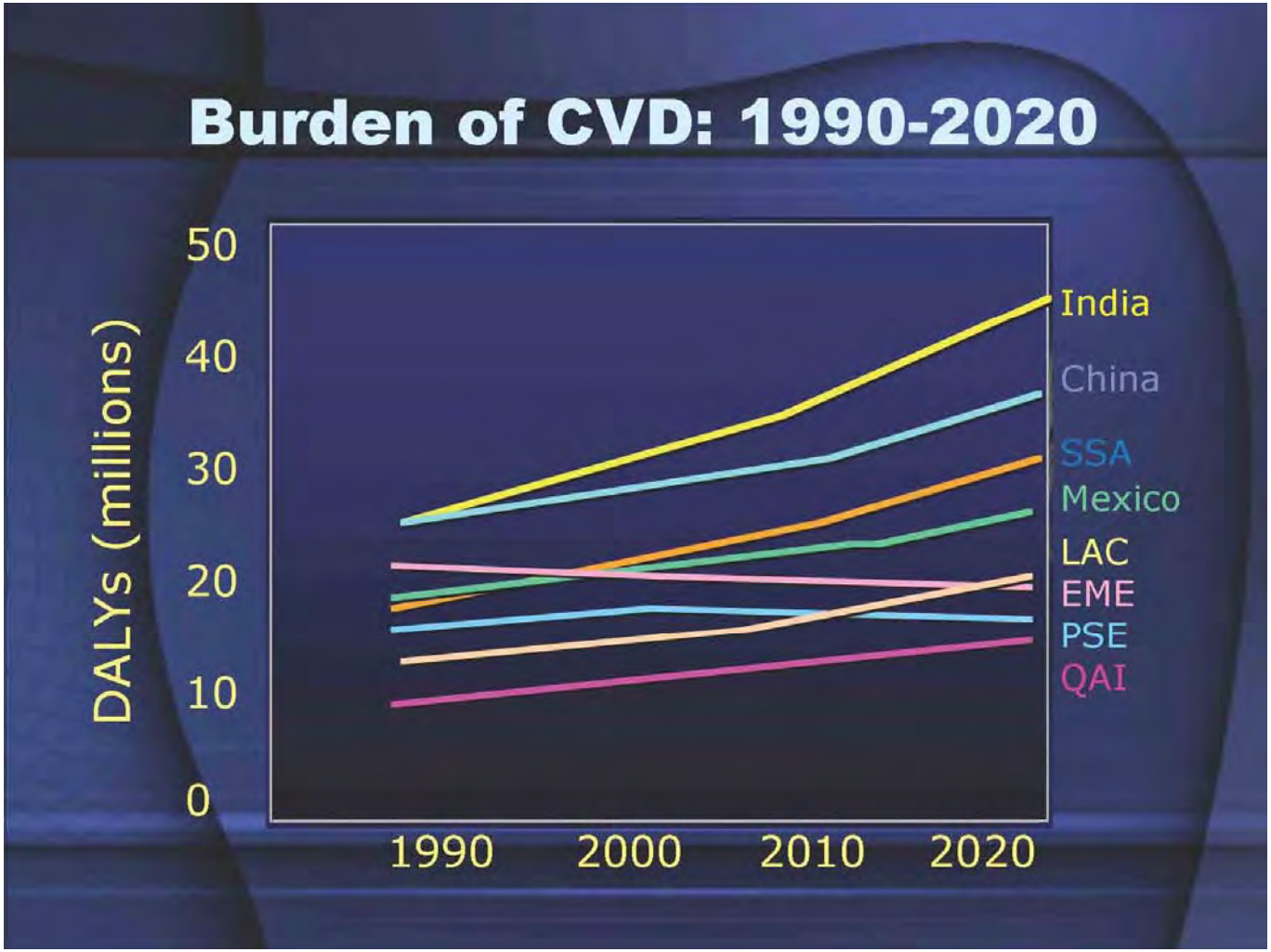
[1]R I A Novosti, Feb. 2, 2010.
[2]American Heart Association 2009.

Why Generx® for India?

64.0 Million Indians are Projected to have Coronary Artery Disease by 2015

Generx [Ad5FGF-4]	Coronary Anatomy and Cardiovascular Disease Issues in India[1]
▪ Simpler administration and cost effective treatment compared to bypass and stents	▪ Involvement at younger age
▪ First non-surgical revascularization therapy	▪ Smaller coronary arteries
▪ Stimulates the growth of microvascular circulation in patients with coronary artery disease	▪ Diffuse distal disease
▪ Women and patients with more advanced disease demonstrated significant treatment effect based on distal disease	▪ Multi-vessel disease
▪ New "induced transient ischemia" techniques may reduce treatment variability in earlier stage patients	▪ Higher incidence in women

[1]*Source: Cardiovascular Disease Trends in India*
Naresh Terhan, Escorts Heart Institute and Research Centre



Source: Cardiovascular Disease Trends in India
Naresh Terhan, Escorts Heart Institute and Research Centre

Generx® Potential Economic Opportunity

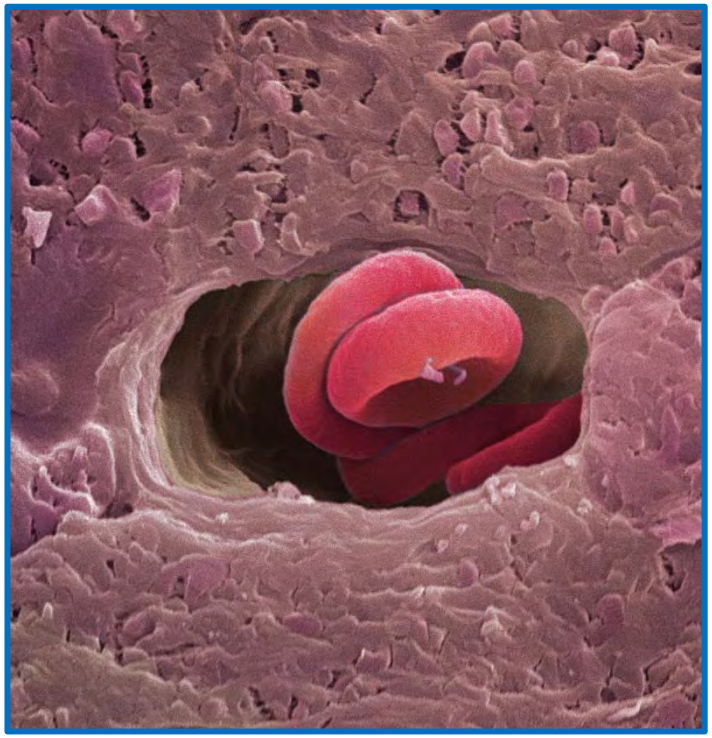
Unit Volume Opportunity per Economic Region	Target Revenue per Dose		
	Level I $2,000 / dose	**Level II $3,000 / dose**	**Level III $4,000 / dose**
50,000 doses	$100 Million	$150 Million	$200 Million
100,000 doses	$200 Million	$300 Million	$400 Million
150,000 doses	$300 Million	$450 Million	$600 Million
200,000 doses	$400 Million	$600 Million	$800 Million

Generx® [Ad5FGF-4]

Catheter-Based Intracoronary Delivery

Focus on Enhancing Angiogenic Microvascular Circulation

Generx® Understanding the Beauty of Cardiac Physiology



Colored magnification: x3000 at 6x7cm size.

Microvascular Pathways

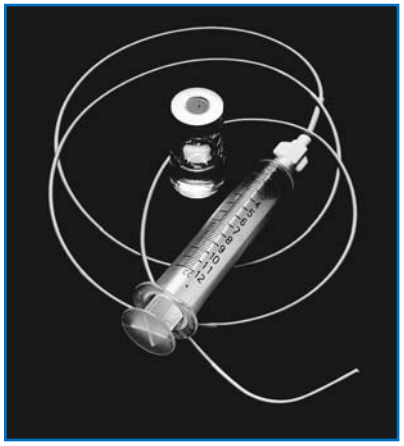
When infused into the coronary arteries using a non-surgical cardiac catheter, the Generx product candidate travels through the coronary microvascular circulation into the small caliber capillaries where it is believed to be taken up by the myocardium.

The Therapeutic Process of
Cardiac Microvascular Angiogenesis

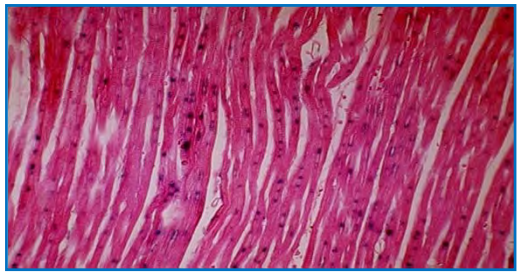
SPECT Imaging

Generx has been evaluated in studies of over 650 patients (including 450 Generx-treated patients) in four multi-center, double-blind, placebo-controlled clinical studies at 100 medical centers. Generx is the most clinically advanced DNA-based cardiovascular angiogenic growth factor therapeutic in the world.

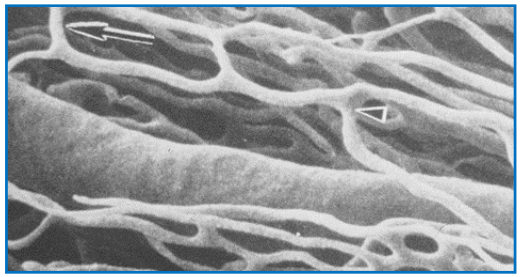
One-Time Treatment



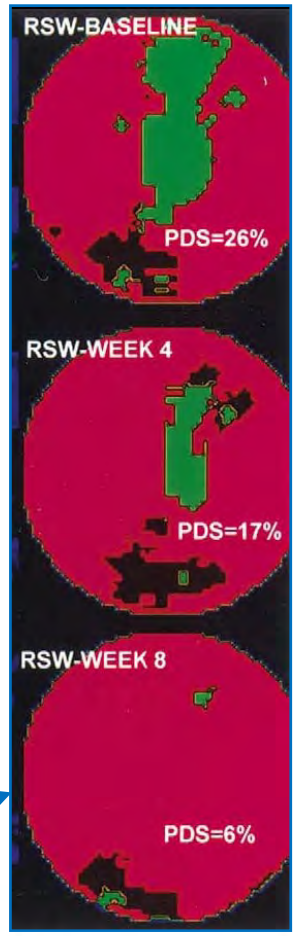
Generx [Ad5FGF-4]
(alferminogene tadenovec)



DNA-Based Delivery



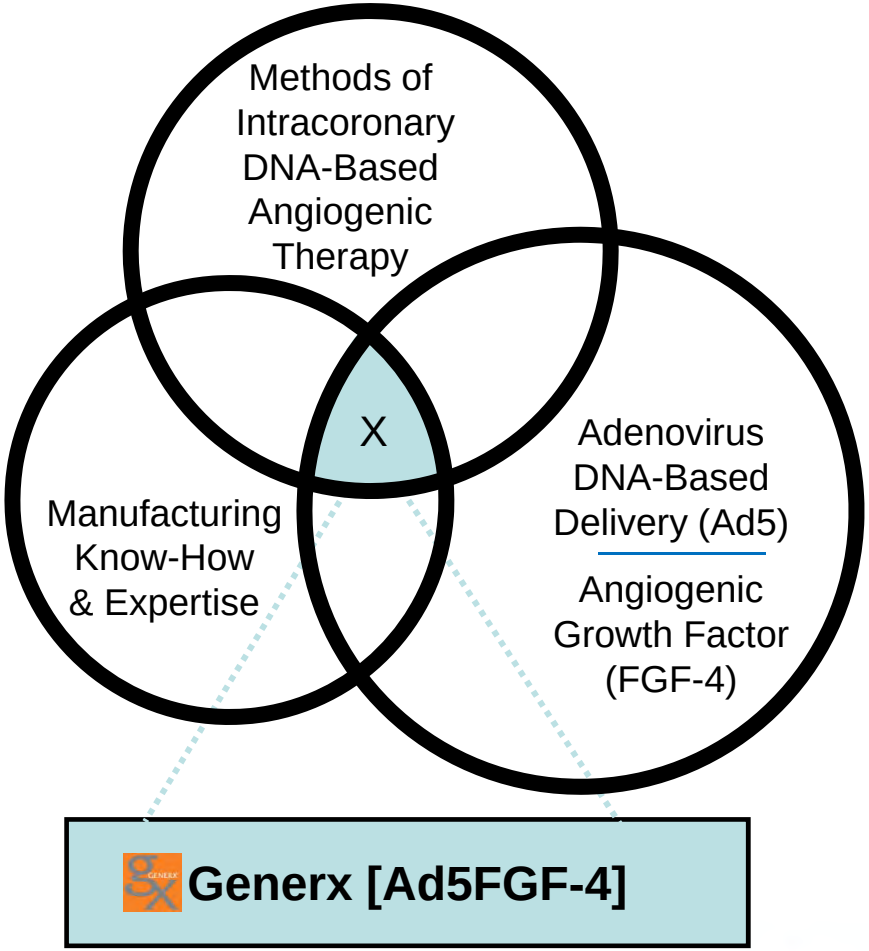
Angiogenic Response



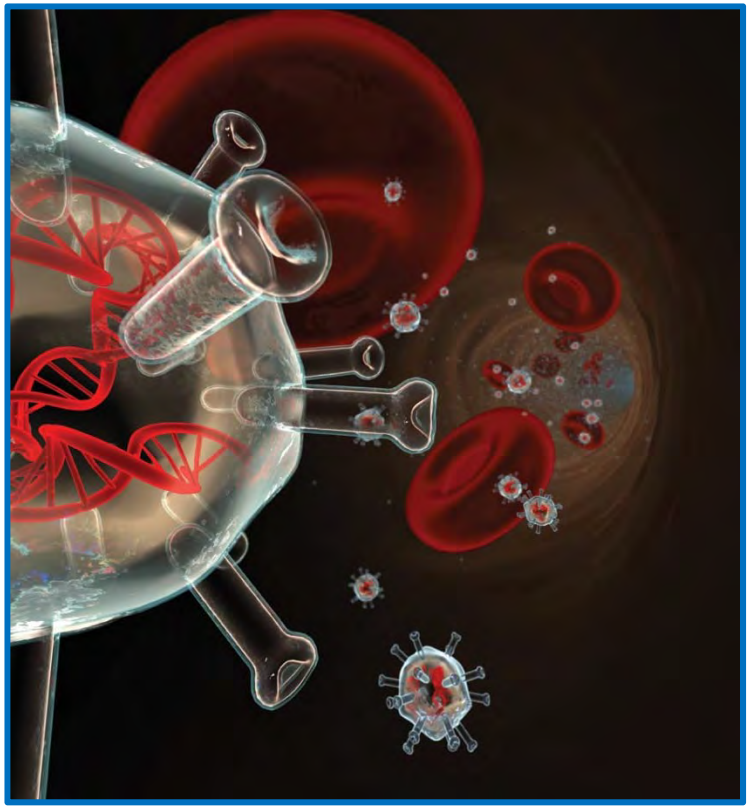
agent

AGENT-2 - Representative Generx-treated patient: 77% improvement in cardiac perfusion at 8 weeks equivalent to bypass surgery and PCI (angioplasty/stenting) at one year.

Technology Platform:
Non-Surgical DNA-Based Angiogenic Therapy

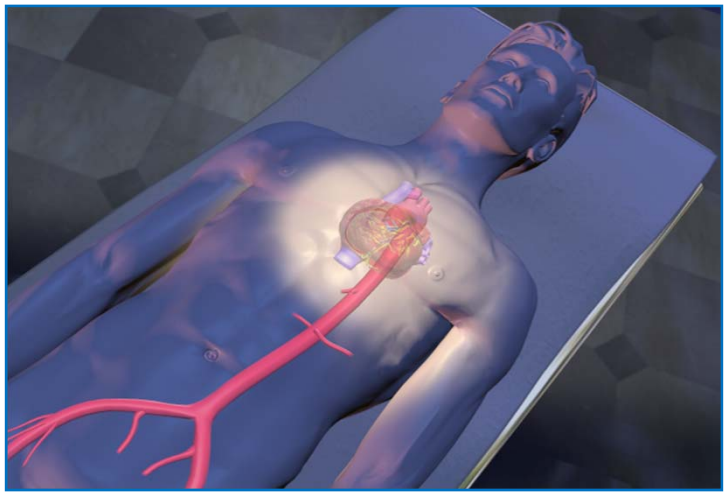


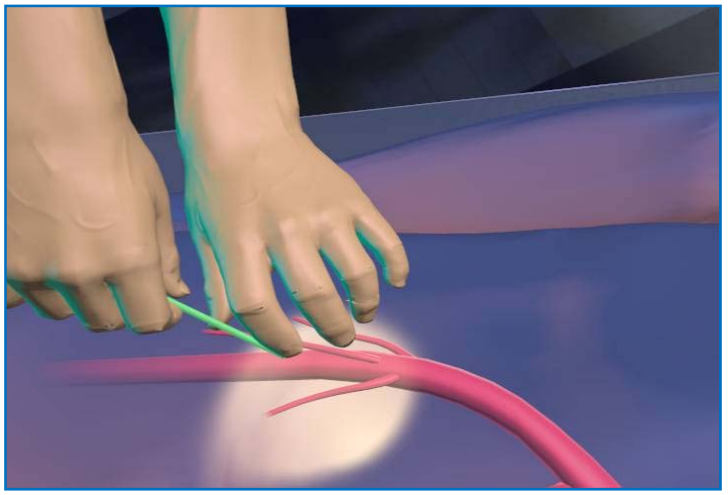
Generx® Pioneering
DNA-Based Regenerative Medicine



DNA-based therapy is designed to enable a patient's own cells to produce a therapeutic protein directly where it is needed in the body. The Generx product candidate is designed to induce localized angiogenic growth factor production following its one-time delivery to stimulate the growth of microvascular circulation.

Generx [Ad5FGF-4]
Proprietary Intracoronary Administration of
DNA-Based Cardiovascular Growth Factor Therapeutic

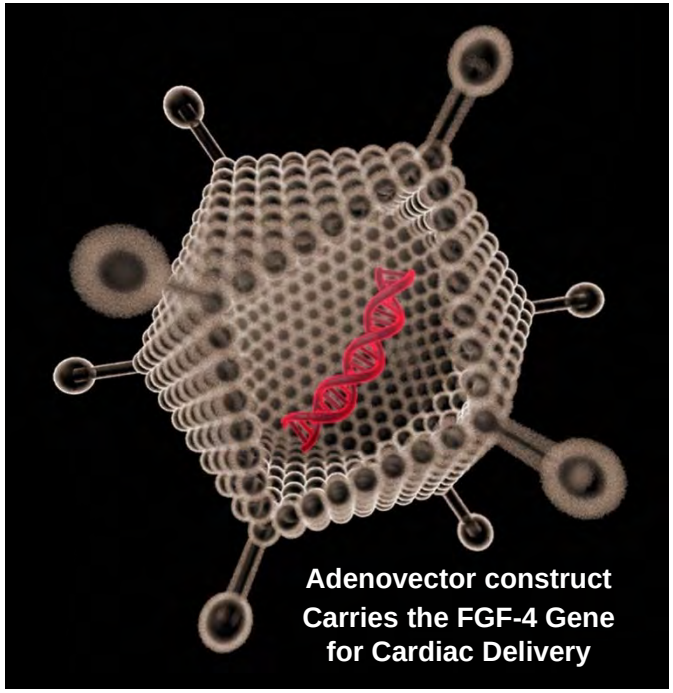




- Non-surgical delivery by intracoronary administration by interventional cardiologist during an angiogram procedure
- Utilizes standard balloon catheter which can be easily integrated into diagnostic angiogram procedures or with other percutaneous coronary interventions
- New induced transient ischemia / reperfusion techniques are designed to enhance DNA uptake and expression in the heart
- 40% administered to right coronary circulation and 60% to left coronary circulation

Generx®

(alferminogene tadenovec)



Research Studies: Intracoronary Administration	Coronary Extraction Rate
Pre-Clinical Porcine Study Giordano et al. *Nat Med* 1996;2:(5):534	98% (mean)
Phase 1/2 Clinical Study – AGENT Trial Grines et al. *Circulation* 2002;105:1291	87% (median)

DNA-Based
Adenovector Cassette

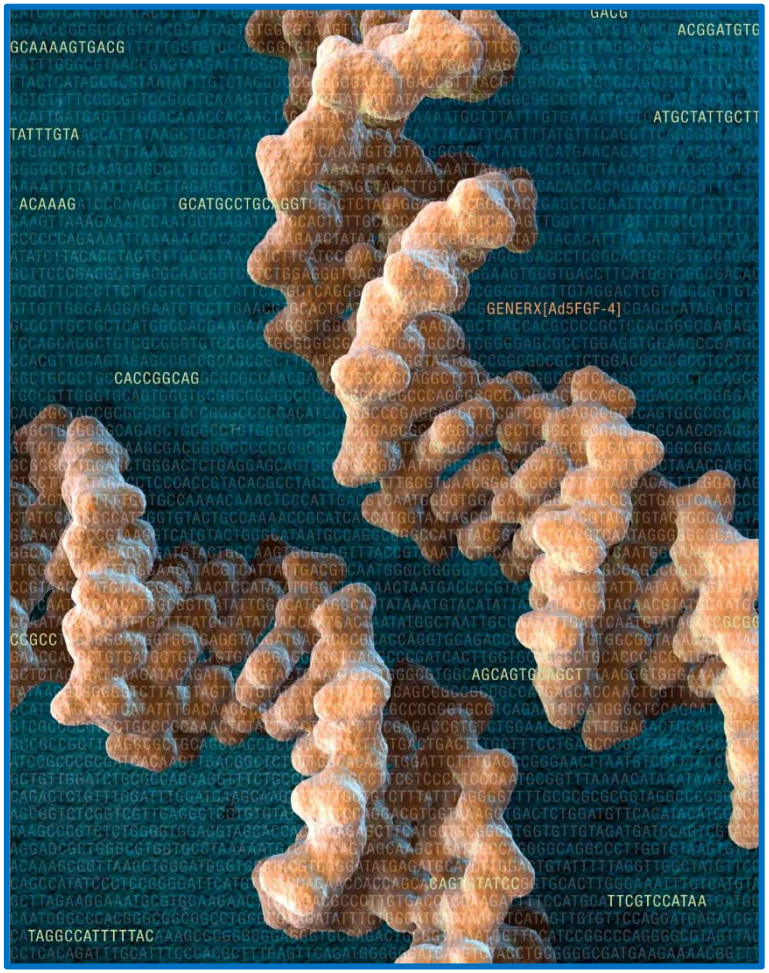
- Demonstrated CV Safety Database with FDA
- Established FDA Manufacturing Standards
- High Cardiac Transfection Levels due to a Binding Affinity with CAR Receptors and Enhanced by Ischemia
- Transient Expression - - Does Not Integrate into Host Genome
- Manufacturing in High Titer
- Easily Manipulated
- Relatively Low Cytotoxity
- Mutagenesis Improbable
- Very Favorable Manufacturing Cost

Generx® FGF-4 Gene

✓	Regulates angiogenesis
✓	Signal peptide – secreted FGF protein
✓	Binds to extracellular matrix proteins
✓	Abundant FGF-4 receptors found in cardiac tissue
✓	Upstream growth factor that can recruit and stimulate responses in downstream target cells
✓	Appears to require ischemia induced co-factors to augment the angiogenesis process

CARDIUM
MEDICAL OPPORTUNITIES PORTFOLIO

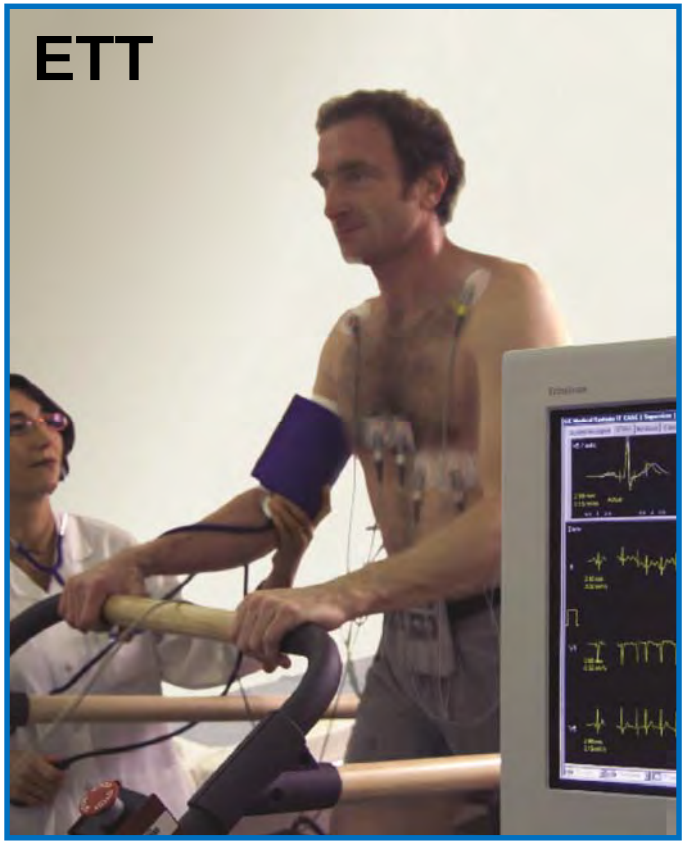
Generx® Leveraging the Power of Biology



Digital illustration of DNA.

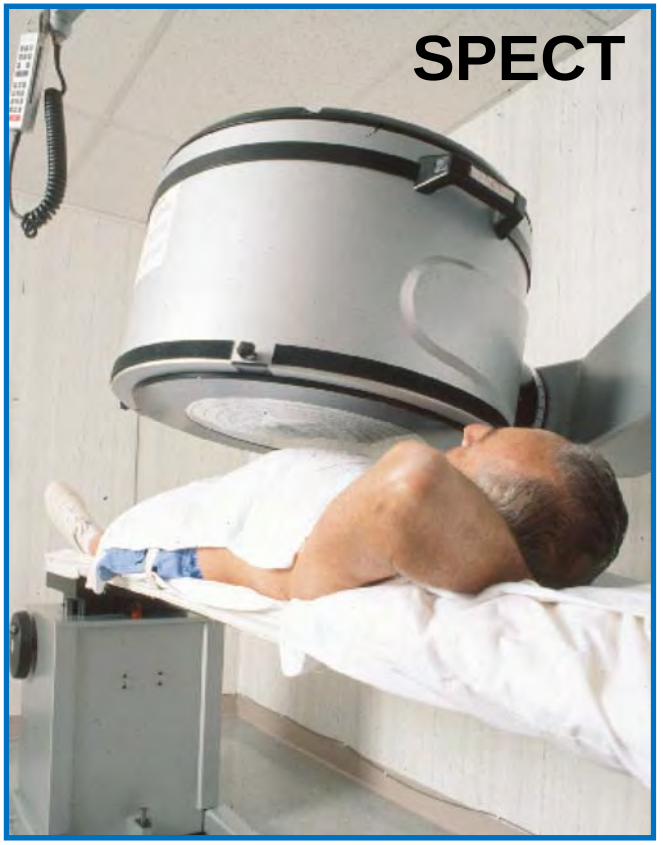
This illustration utilizes computer models of DNA-based on data generated by x-ray crystallography, a technique for determining the structure of a molecular sample, together with a portion of the DNA sequence of Generx (Ad5FGF-4), Cardium's lead clinical product candidate.

Clinical Efficacy Measures



Exercise Treadmill Stress Test

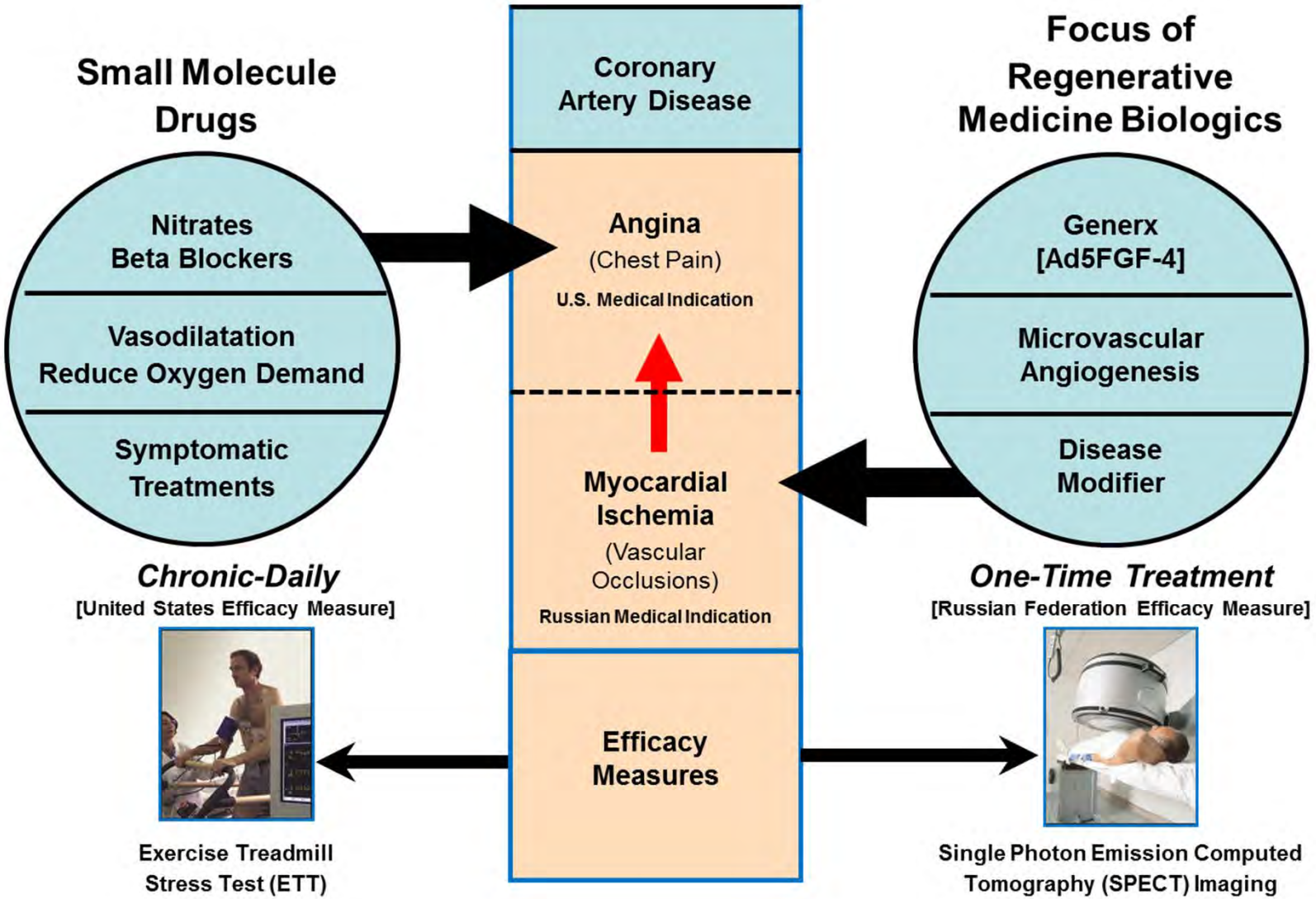
[United States Efficacy Measure]



Single Photon Emission Computed Tomography Stress Test

[Russian Federation Efficacy Measure]

Therapeutic Comparison

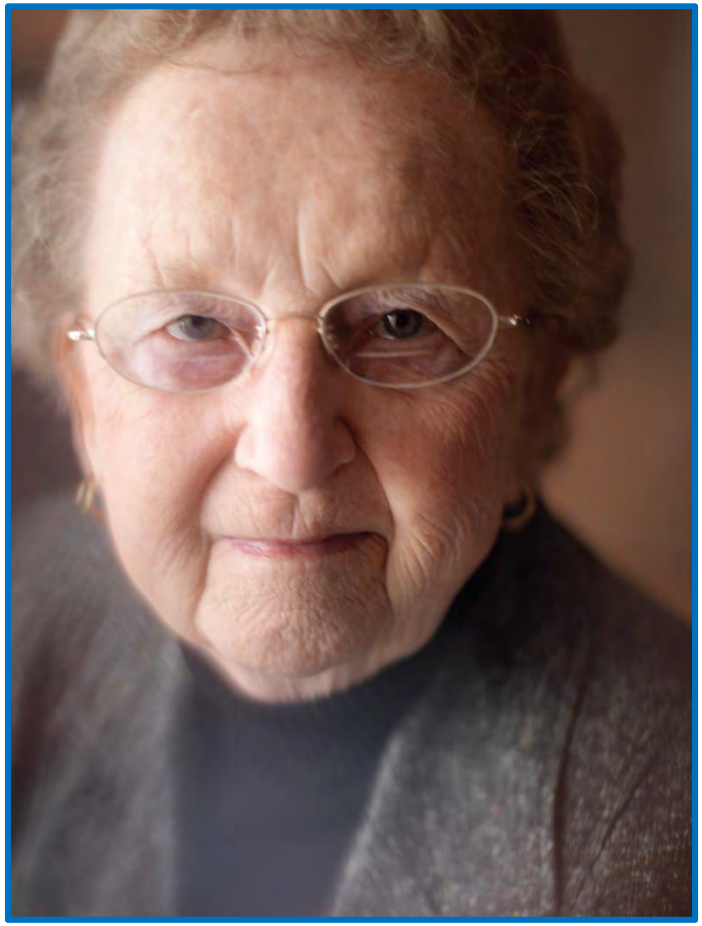


Generx® [Ad5FGF-4] Clinical Studies

Year	Study Name	Region / County	Clinical Study Phase	Patient Status	Clinical Endpoint	Number Patients Recruited
1999	AGENT-1	U.S.	Phase 1/2 Dose finding & safety	Class 2 – 3 Angina	Exercise Treadmill Time	79
2001	AGENT-2	North America	Phase 2a Mechanism of Action Study	>9% Reversible Reperfusion Defect	SPECT Imaging	52
2004	AGENT-3	North America	Phase 2b/3	Class 2 – 4 Angina	Exercise Treadmill Time	300
2004	AGENT-4	Western Europe & South America	Phase 2b/3	Class 2 – 4 Angina	Exercise Treadmill Time	252
2008	AWARE	U.S.	Phase 3 (Fast Track Status)	Class 3 – 4 Angina	Exercise Treadmill Time (Time to ST Segment Depression)	U.S. Beta Tested
2011	ASPIRE	Russian Federation	Phase 3 Registration Study	>9% Reversible Perfusion Defect	SPECT Imaging	100*
					TOTAL	**783**

*** Preparing to intiate**

Generx® Patient Pioneers



Marilyn L. was a trial participant in the AGENT-3 clinical trial. She received a one-time treatment of Generx, our DNA-based angiogenic product candidate for patients with recurrent angina due to coronary artery disease.

Generx®: Current Global Clinical Status

Elements	U.S. Market (AWARE)	International Markets (Initially Russian Federation) (ASPIRE)
Product	**Generx® [Ad5FGF-4]** (alferminogene tadenovec)	**CardioNovo [Ad5FGF-4]** (alferminogene tadenovec)
Clinical Status	FDA Clearance Phase 3 (with Fast Track Status)	RHA Cleared Phase 3 / Registration Study
Clinical Study Population	300 Women Multi-Center, Randomized, Placebo-Controlled Patient Population	100 Men & Women Multi-Center, Randomized, Controlled Parallel-Group Patient Population
Proposed Medical Indication	Anti-Angina for Refractory Patients who are not Optimal Candidates for Angioplasty / Stents & Bypass Surgery	Myocardial Ischemia as a Treatment Option for Patients Considering Angioplasty / Stents & Bypass Surgery
Clinical Endpoint	Improvement in Exercise Time Based on Treadmill	Improvement in Reversible Perfusion Deficit Based on SPECT Imaging
Clinical Study Status	Currently Inactive	Preparing to Initiate

Generx®
Key Peer-Reviewed
Scientific & Medical Journals

ARTICLES

Intracoronary gene transfer of fibroblast growth factor-5 increases blood flow and contractile function in an ischemic region of the heart

Increased coronary blood vessel development could potentially benefit patients with ischemic heart disease. In a model of stress-induced myocardial ischemia, intracoronary injection of a recombinant adenovirus expressing human fibroblast growth factor-5 (*FGF-5*) resulted in messenger RNA and protein expression of the transferred gene. Two weeks after gene transfer, regional abnormalities in stress-induced function and blood flow were improved, effects that persisted for 12 weeks. Improved blood flow and function were associated with evidence of angiogenesis. This report documents, for the first time, successful amelioration of abnormalities in myocardial blood flow and function following *in vivo* gene transfer.

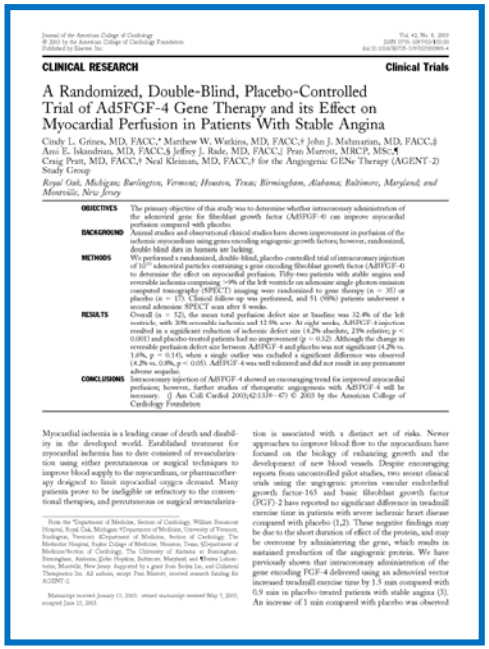
Pre-Clinical

Nature Medicine

Angiogenic Gene Therapy (AGENT) Trial in Patients With Stable Angina Pectoris

AGENT-1

Circulation (American Heart Association Journal)



CLINICAL RESEARCH — Clinical Trials

A Randomized, Double-Blind, Placebo-Controlled Trial of Ad5FGF-4 Gene Therapy and its Effect on Myocardial Perfusion in Patients With Stable Angina

AGENT-2

Journal of American College of Cardiology

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Effects of Ad5FGF-4 in Patients With Angina

An Analysis of Pooled Data From the AGENT-3 and AGENT-4 Trials

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Minneapolis, Minnesota; Royal Oak, Michigan; Burlington, Vermont; Phoenix, Arizona; Sainte-Foy, Quebec, Canada; and San Diego, California

Objectives The goal of this study was to explore the effects of angiogenic gene therapy.

Background Preclinical studies with intracoronary administration of Ad5FGF-4 (alferminogene tadenovec, Generx, Beriex Biosciences, Richmond, California) suggested it could induce angiogenesis and provide a new clinical approach to the treatment of chronic angina pectoris. Two preliminary clinical trials provided evidence that it could improve exercise treadmill test (ETT) time and myocardial perfusion. The AGENT (Angiogenic GENe Therapy)-3 and -4 trials of a low and high dose of Ad5FGF-4 for chronic angina were initiated in the U.S. and other countries and enrolled 532 patients in a randomized, double-blind, placebo-controlled fashion. Both studies were halted when an interim analysis of the AGENT-3 trial indicated that the primary end point change from baseline in total ETT time at 12 weeks would not reach significance.

Methods We performed a pooled data analysis from the 2 nearly identical trials to investigate possible treatment effects on primary and secondary end points in prespecified subgroups.

Results The effect of placebo was large and not different than active treatment in men, but the placebo effect in women was negligible and the treatment effect was significantly greater than placebo. We found a significant, gender-specific beneficial effect of Ad5FGF-4 on total ETT time, time to 1 mm ST-segment depression, time to angina, and Canadian Cardiovascular Society class in women. This is the first clinical report of a gender difference in response to cardiac angiogenic therapy.

Conclusions The potential importance of the observed gender-specific angiogenic response on the clinical treatment of refractory angina is substantial and deserves further investigation. (Efficacy and Safety of Intracoronary Ad5FGF-4 in Patients With Stable Angina; http://www.clinicaltrials.gov/ct/show/NCT00346437; NCT00346437) (Safety and Efficacy of Intracoronary Ad5FGF-4 in Patients With Stable Angina [AGENT-4]; http://www.clinicaltrials.gov/ct/show/NCT00185263; NCT00185263) (AWARE; http://www.clinicaltrials.gov/ct/show/NCT00438867; NCT00438867)
(J Am Coll Cardiol 2007;50:1038–46) © 2007 by the American College of Cardiology Foundation

Angina pectoris is a disabling manifestation of coronary artery disease (CAD). In the U.S., 8.9 million people live with chronic angina, and an additional 400,000 people are newly diagnosed each year (1). There are 2 major mechanistic approaches to the treatment of chronic angina. First, currently approved drug therapy includes beta-blockers, calcium-channel blockers, long-acting nitrates, and, most recently, ranolazine. Drug therapy alters the supply/demand relationship between the coronary arterial tree blood flow and cardiac muscle oxygen requirements. Second, revascularization by angioplasty, stent, or bypass surgery either reopens or bypasses blockages in the epicardial vessels. However, many patients continue to have recurrent angina with drug therapy and are not suitable for revascularization procedures (1). New mechanistic approaches are needed to improve blood flow to the myocardium (2).

In contrast to the mechanisms involved in approved therapeutic methods, the heart's natural responses to isch-

From the *Minneapolis Heart Institute Foundation, Minneapolis, Minnesota; †William Beaumont Hospital, Royal Oak, Michigan; ‡University of Vermont, Burlington, Vermont; §Cardiovascular and Stem Cell Consultants, Phoenix, Arizona; ‖Hôpital Laval, Sainte-Foy, Quebec, Canada; ¶Cardium Therapeutics, Inc., San Diego, California; and the #University of California, San Diego, California. Supported, in part, by Schering AG, Berlin, Germany; Berlex Laboratories, Inc., Montville, New Jersey; and Cardium Therapeutics, Inc., San Diego, California. Dr. Moreadith and Mr. Andrasfay are employees of Cardium Therapeutics, Inc. (CTI). Dr. Engler is a paid consultant to CTI. Dr. Watkins has received limited consulting fees from CTI.

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JACC
JOURNAL of the AMERICAN COLLEGE of CARDIOLOGY

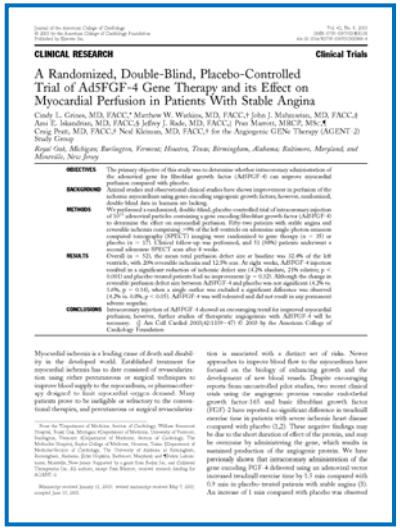
Generx®
AGENT 3 & 4
Summary Research

"We found a significant, gender-specific beneficial effect of Ad5FGF-4 on total ETT time, time to 1 mm ST-segment depression, time to angina and CCS Class in women. This is the first clinical report of a gender difference in response to cardiac angiogenic therapy."

"The potential importance of the observed gender-specific angiogenic response on the clinical treatment of refractory angina is substantial and deserves further investigation."

JACC
September 11, 2007

GENERX AGENT-2
PHASE 2A STUDY
CLINICAL EFFICACY USING SPECT



CLINICAL RESEARCH — Clinical Trials

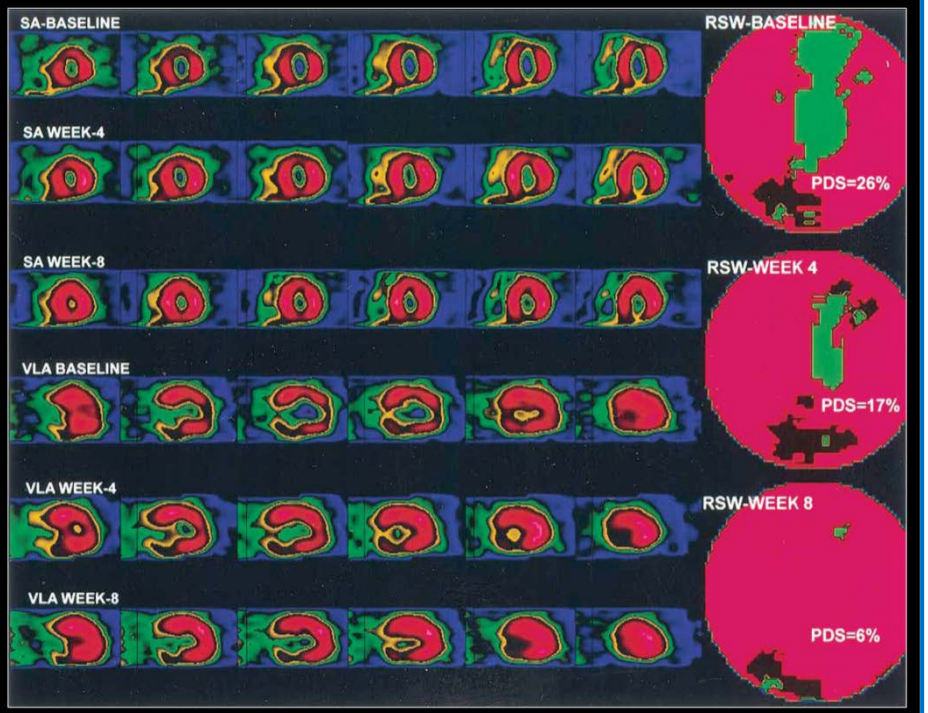
A Randomized, Double-Blind, Placebo-Controlled Trial of Ad5FGF-4 Gene Therapy and its Effect on Myocardial Perfusion in Patients With Stable Angina

Cindy L. Grines, MD, FACC,* Matthew W. Watkins, MD, FACC,† John J. Mahmarian, MD, FACC,‡ Ami E. Iskandrian, MD, FACC,§ Jeffrey J. Rade, MD, FACC,‖ Peter Marrott, MRCP, MSc,¶ Craig Pratt, MD, FACC,# Neal Kleiman, MD, FACC,† for the Angiogenic GENe Therapy (AGENT-2) Study Group

Royal Oak, Michigan; Burlington, Vermont; Houston, Texas; Birmingham, Alabama; Baltimore, Maryland; and Montvale, New Jersey

AGENT-2

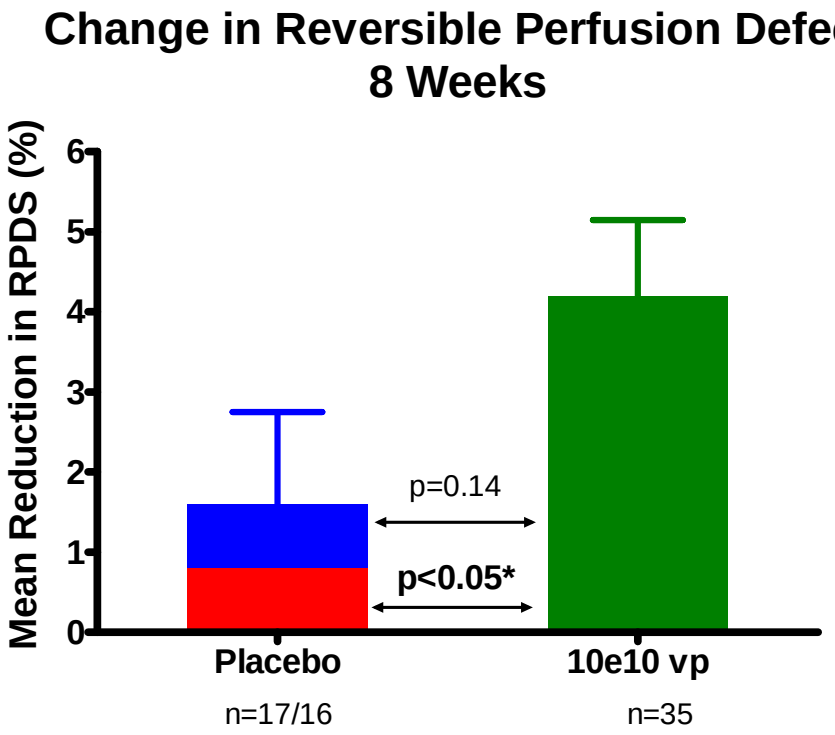
Journal of American College of Cardiology



77% Improvement

Generx-Treated Patient Demonstrating Enhanced Cardiac Perfusion (n=52 / 88% men)

AGENT 2: Primary Endpoint SPECT Imaging Angiogenic
Mechanism of Action Study



** Excludes one extreme placebo outlier*

AGENT 2 - Comparison of SPECT Results to Revascularization and Medical Therapy

Parameter	Coronary Revascular-ization	Medical Therapy	Generx AGENT-2	
			Placebo	$1x10^{10}$ vp
Number of Patients	83	206	17	35
Age	66±11	68±10	57±9	59±8
Stress defect extent (%)	18±11	16±10	20±8	20±9
Reduction of reversible defect (%)	**-5±12**	-0.8±7	-0.8±6	**-4±6**

From Berman DS, et al.
J of Nuclear Cardiol, 2001; 4:428-437

Generx AGENT 3 & 4 Clinical Studies

Clinical Efficacy Using ETT

Pooled-Analysis: Protocol-Specified Gender-Based Subgroup

Women n=76	12 weeks			6 months		
	Placebo	10^9 vp	10^{10} vp	Placebo	10^9 vp	10^{10} vp
Exercise Duration (seconds & percentage Δ)	-4	+60*	+69*	+7	+75*	+83*
	-1%	+16%	+23%	+2%	+20%	+28%
Angina Onset (seconds & percentage Δ)	+50	+111	+86	+55	+157*	+94
	+26%	+52%	+46%	+28%	+73%	+48%
Time to 1mm ST Segment ↓ (seconds & percentage Δ)	+13	+50	+63*	+14	+59*	+86*
	+4%	+16%	+27%	+5%	+19%	+36%

* < 0.05

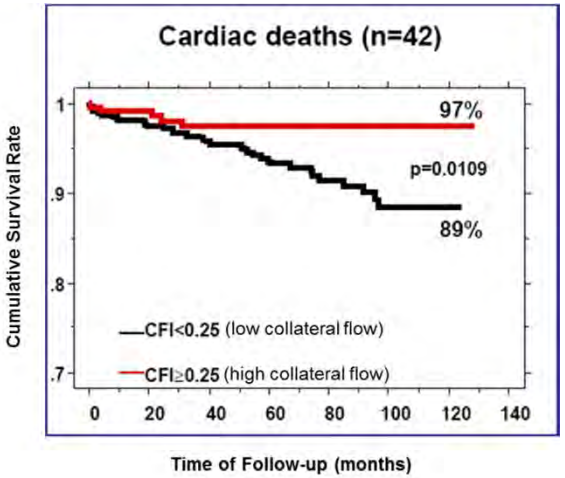
AGENT 3 & 4 Clinical Studies:
Concordance of Results from Prespecified Pooled Analysis of Gender-Based Subgroup

Women n=76	Time Point	Generx Ad5FGF-4	
		$1x10^9$ vp	$1x10^{10}$ vp
ETT Duration	12 Weeks 6 Months	p=0.032 p=0.042	p=0.002 p=0.009
Time to ECG Ischemia	12 Weeks 6 Months	NS (0.216) p=0.036	p=0.031 p=0.011
Time to Angina	12 Weeks 6 Months	NS (0.146) p=0.003	NS (0.125) NS (0.094)
CCS Class Improvement	12 Weeks 6 Months 12 Months	NS (0.222) NS (0.341) p=0.038	p=0.014 p=0.042 p=0.006

NS=Not Significant

Beneficial Effects of a Disease-Induced Angiogenic Vascularization Summary Research

"A well-functioning coronary collateral circulation saves lives in patients with chronic stable coronary artery disease."



From Meier *et al*. *Circulation* 2007; 116:975-83.

Coronary Heart Disease

Beneficial Effect of Recruitable Collaterals

A 10-Year Follow-Up Study in Patients With Stable Coronary Artery Disease Undergoing Quantitative Collateral Measurements

Pascal Meier, MD*; Steffen Gloekler, MD*; Rainer Zbinden, MD*; Sarah Beckh, BS; Stefano F. de Marchi, MD; Stephan Zbinden, MD; Kerstin Wustmann, MD; Michael Billinger, MD; Rolf Vogel, MD, PhD; Stéphane Cook, MD; Peter Wenaweser, MD; Mario Togni, MD; Stephan Windecker, MD; Bernhard Meier, MD; Christian Seiler, MD

Background—The prognostic relevance of the collateral circulation is still controversial. The goal of this study was to assess the impact on survival of quantitatively obtained, recruitable coronary collateral flow in patients with stable coronary artery disease during 10 years of follow-up.

Methods and Results—Eight-hundred forty-five individuals (age, 62±11 years), 106 patients without coronary artery disease and 739 patients with chronic stable coronary artery disease, underwent a total of 1053 quantitative, coronary pressure–derived collateral measurements between March 1996 and April 2006. All patients were prospectively included in a collateral flow index (CFI) database containing information on recruitable collateral flow parameters obtained during a 1-minute coronary balloon occlusion. CFI was calculated as follows:

$$CFI = \frac{P_{occl} - CVP}{P_{ao} - CVP}, \quad (1)$$

where P_{occl} is mean coronary occlusive pressure, P_{ao} is mean aortic pressure, and CVP is central venous pressure. Patients were divided into groups with poorly developed (CFI <0.25) or well-grown collateral vessels (CFI ≥0.25). Follow-up information on the occurrence of all-cause mortality and major adverse cardiac events after study inclusion was collected. Cumulative 10-year survival rates in relation to all-cause deaths and cardiac deaths were 71% and 88%, respectively, in patients with low CFI and 89% and 97% in the group with high CFI (P=0.0395, P=0.0109). Through the use of Cox proportional hazards analysis, the following variables independently predicted elevated cardiac mortality: age, low CFI (as a continuous variable), and current smoking.

Conclusions—A well-functioning coronary collateral circulation saves lives in patients with chronic stable coronary artery disease. Depending on the exact amount of collateral flow recruitable during a brief coronary occlusion, long-term cardiac mortality is reduced to one fourth compared with the situation without collateral supply. (***Circulation***. 2007;116:975-983.)

Key Words: angiogenesis ■ collateral circulation ■ coronary circulation ■ prognosis ■ survival

The coronary collateral circulation has long been recognized as an alternative source of blood supply to a myocardial area jeopardized by ischemia. Well-grown versus poorly grown collateral arteries in humans have been suggested to exert a beneficial effect on infarct size,[1–5] ventricular aneurysm formation,[6,7] and ventricular function.[2,7,8] A reduction in nonfatal cardiovascular events during various follow-up durations has been demonstrated among patients with versus those without angiographic coronary collaterals in the setting of chronic stable coronary artery disease (CAD).[9,10] Conversely, a study performed in a population with more extended CAD has found that the angiographic presence of collaterals may mark an unfavorable prognosis.[11] In the setting of acute myocardial infarction treated by primary percutaneous coronary intervention (PCI), there have been also controversial results regarding the effect of angiographically present collaterals, including 1 investigation without a beneficial effect on 6-month survival rate[12] and another study showing reduced in-hospital mortality.[13] This debate on the relevance of the human coronary collateral circulation has a long-lasting "tradition."[14] Much of the argument was and still is likely due to the blunt method of gauging human

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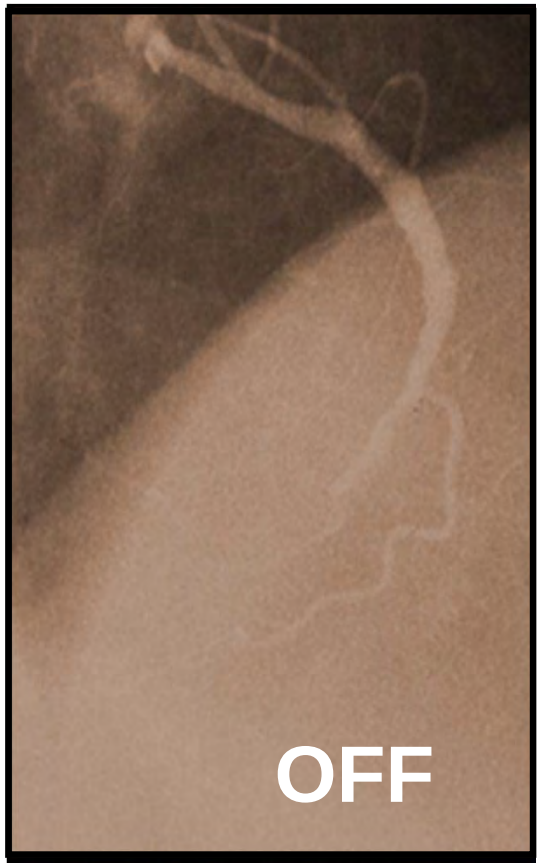
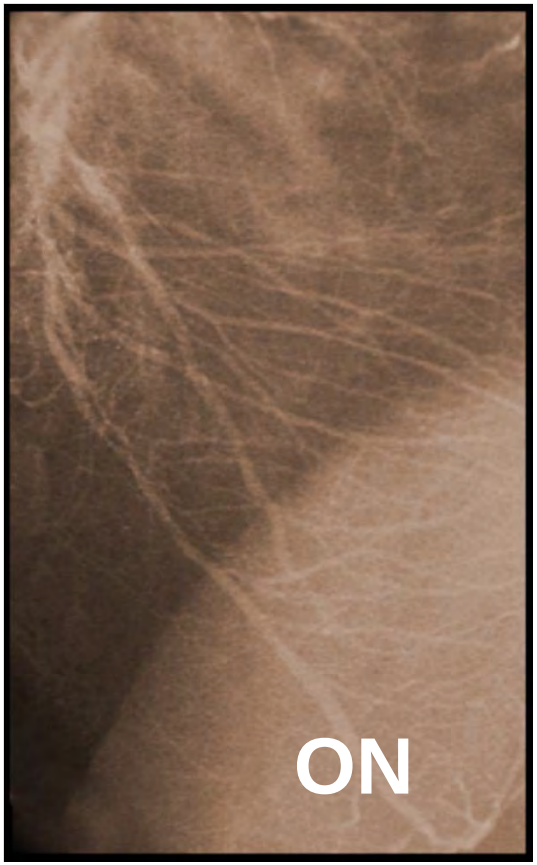
Coronary Artery Disease

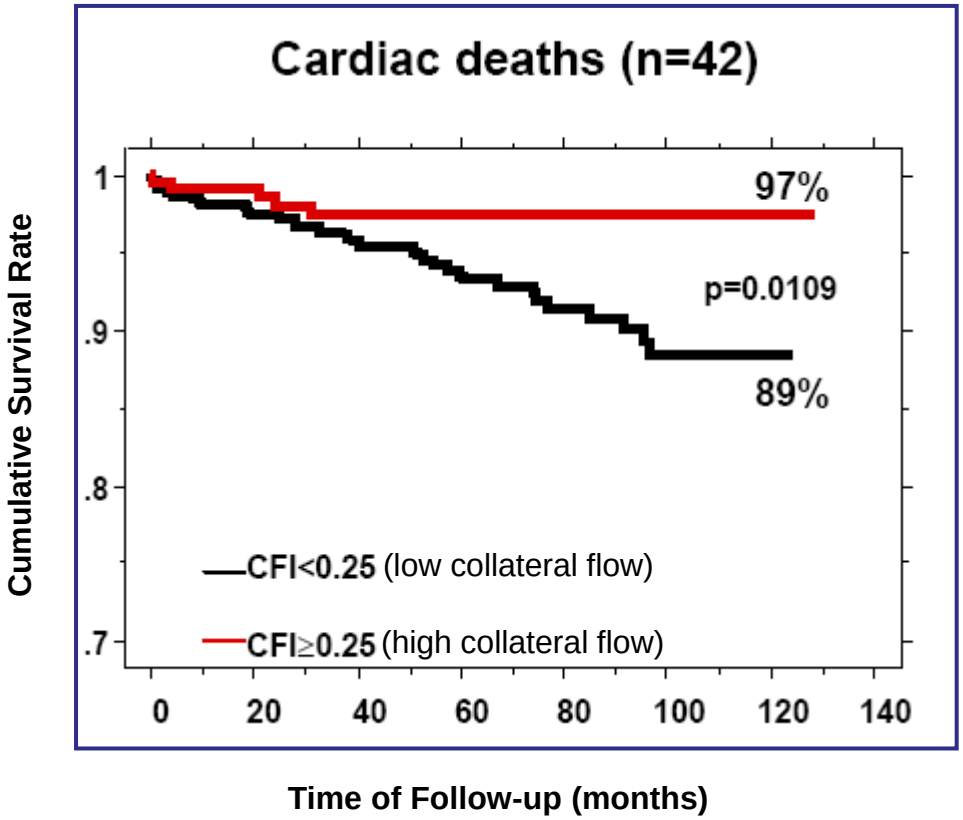
Natural Disease-Induced Angiogenic Vascularization





Beneficial Effects of Natural Disease-Induced Collateral Vessels

10-Year Follow-up in Patients with Coronary Heart Disease



From Meier *et al*. *Circulation* 2007; 116:975-83.

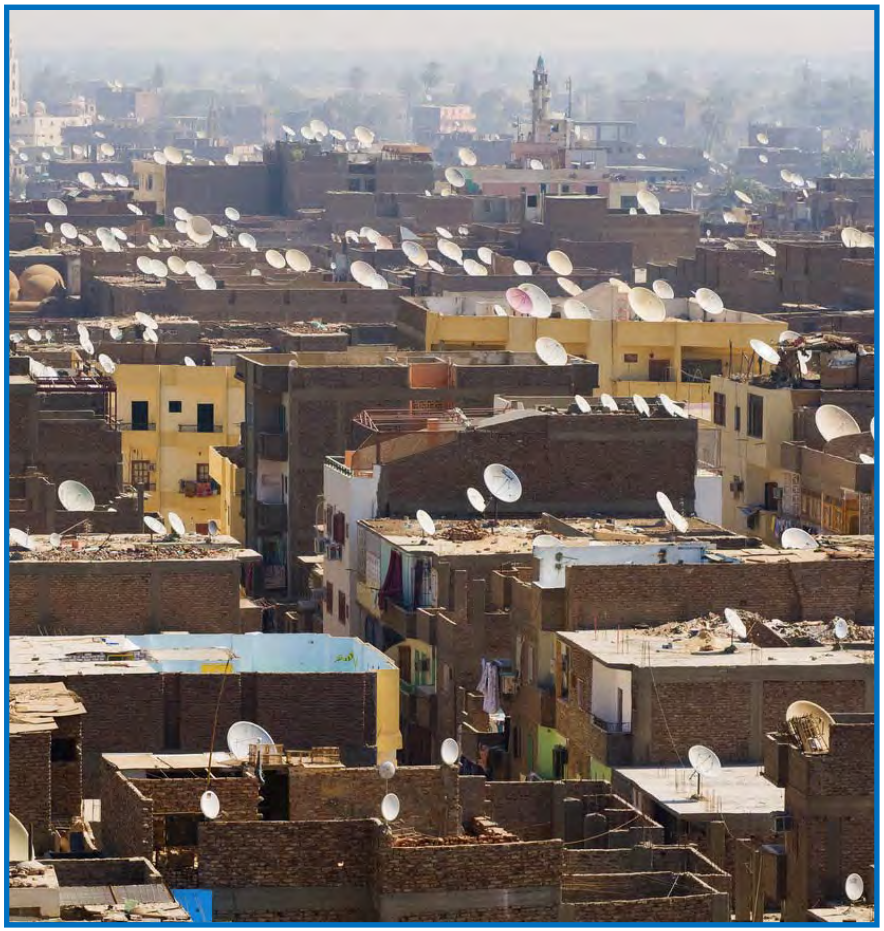
CARDIAC DEATHS:

10 year follow-up (n = 845)

High Flow:
5 (2%) Deaths

Low Flow:
37 (6%) Deaths

67% ↓
Cardiac Deaths



Developing new and innovative, cost-effective advanced care for coronary heart disease patients in international markets

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NYSE Amex: CXM

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CARDIUM

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