LEADING THE REVOLUTION INTO NEW FRONTIERS OF CARDIOVASCULAR MEDICINE
CORONARY ARTERY DISEASE
REFRACTORY ANGINA
LISTEN
PRODUCT CANDIDATE
HOPE
ANGIOGENESIS
FINDING NEW WAYS TO HEAL
CARDIAC SPECT IMAGING

- Perfusion
- Reversible Perfusion Defect

Before Treatment

4 Weeks Post-Generx Treatment

8 weeks Post-Generx Treatment

MEDICAL REVASCULARIZATION
THERAPEUTIC OBJECTIVES

Enhance Physical Exertion

Improve Cardiac Perfusion

Reduce Angina and Medication Usage

Offer New Therapeutic Options
LIVE.
Angionetics is a private, newly-formed, San Diego-based biotechnology company focused on the development of Generx™ [alferminogene tadenovec], a phase 3 angiogenic gene therapy product candidate for the treatment of Refractory Angina and Cardiac Syndrome X, and other medical indications.
INVESTMENT THESIS

• **Global Leader in Angiogenic Gene Therapy.** With clinical success, Generx will be the first cardiovascular gene-based therapeutic in the world for a large addressable population.

• **Current Management Team.** Responsible for leading Generx from pre-clinical discovery at the University of California to FDA-cleared Phase 3 clinical study. The team has a century of collective experience in fields of gene therapy, cardiovascular, biologics, and commercial development.

• **Market Opportunity.** Increasing high unmet need to manage refractory angina; eligible patient population ranges in the millions, translating into >$3 billion market opportunity.

• **Novel Mechanism of Action.** Generx provides new, innovative, angiogenic “medical revascularization” for a large population of well characterized CAD patients likely to respond and benefit.

• **Late-Stage Clinical Development.** Four completed clinical studies under FDA IND provided the basis for the Phase 3, fast track, AFFIRM study. Globally, over 650 patients were enrolled, 455 patients treated with Generx, at over 100 medical centers with over 2,500 patient years of safety data.

• **Barriers to Entry.** Know-how and trade secrets, plus 12 years of market exclusivity in the U.S under the Patent Protection and Affordable Care Act of 2010. $250 million technology & capital investment.

• **Cost-Effective Manufacture.** Fully-validated cGMP manufacturing process, and product stability enabling cost-effective batch manufacturing. Projected direct manufacturing gross margins > 85%.

• **Fits within Current Medical Practice.** Generx is a ready-to-use, one-time treatment, administered by interventional cardiologists during an angiogram-like procedure. Targeted therapeutic cost: $2,000 to $5,000 per dose comparably aligned to the economics of cardiac stents.
<table>
<thead>
<tr>
<th>Gene Therapy Product</th>
<th>Company</th>
<th>Medical Indication</th>
<th>Treatment Cost</th>
<th>FDA Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>KYMRIAH™</td>
<td>NOVARTIS</td>
<td>CAR-T Acute Lymphoblastic Leukemia</td>
<td>$475,000</td>
<td>8/2017</td>
</tr>
<tr>
<td>YESCARTA™</td>
<td>Kite</td>
<td>CAR-T Diffuse Large B-Cell Lymphoma</td>
<td>$373,000</td>
<td>10/2017</td>
</tr>
<tr>
<td>LUXTURNATM</td>
<td>Spark Therapeutics</td>
<td>Leber’s Congenital Eye Disease</td>
<td>$425,000</td>
<td>12/2017</td>
</tr>
</tbody>
</table>
GENERX: CORPORATE DEVELOPMENT HISTORICAL PERSPECTIVE

(COLLATERAL THERAPEUTICS)
(NASDAQ)
University of California
San Diego
Discovery, Licensing
and Initial
Preclinical Studies

(SCHERING)
(NYSE)
As Strategic Partner
with Collateral
Therapeutics
Schering Acquired
Collateral in 2002
for $160 Million
Phase 1/2 to
Phase 2b/3

(CARDIUM)
(NASDAQ)
Formed to Acquire
Technology from
Schering/Bayer
Phase 2b/3
& International
Pilot Study

(angionetics)
Clinical &
Commercial Development
Activities, Approved for
Phase 3 Clinical Study
United States
& China

$250 Million Invested in Preclinical Studies,
Four FDA-IND Clinical Studies
(Phase 1/2 thru 2b/3)
CORPORATE DEVELOPMENT STRATEGY

“Value Unlock”

Formerly Taxus Cardium Pharmaceuticals Group

FDA 510(K) Clearance

85%

FDA-Cleared Phase 3

Planned IPO 1Q/2019

Change of Control Comparables

<table>
<thead>
<tr>
<th>Product</th>
<th>Terminal Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ranexa® (Gilead) Small Molecule Drug for Refractory Angina</td>
<td>$1.4 Billion</td>
</tr>
<tr>
<td>Target: Generx Angiogenic Gene Therapy for Refractory Angina</td>
<td>$1.0 Billion</td>
</tr>
<tr>
<td>Kybella® Allergan Acquisition (Injectable for Chin Fat Reduction) 2015</td>
<td>$2.1 Billion</td>
</tr>
</tbody>
</table>
## ANGIOMETRICS GENE THERAPY PIPELINE

<table>
<thead>
<tr>
<th>Candidate</th>
<th>Medical Indication</th>
<th>Vector (gene)</th>
<th>Candidate Selection</th>
<th>IND-Enabling</th>
<th>Phase 1-2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generx</td>
<td>Refractory Angina</td>
<td>Ad5FGF-4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generx</td>
<td>Cardiac Syndrome X</td>
<td>Ad5FGF-4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generx</td>
<td>Congestive Heart Failure</td>
<td>Ad5FGF-4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generx</td>
<td>Moyamoya Disease</td>
<td>Ad5FGF-4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generx</td>
<td>Cerebral Ischemia</td>
<td>Ad5FGF-4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
PROPOSED GENERX TREATMENT ALGORITHM
Based on FDA-Cleared U.S. Phase 3 Clinical Study Design

Coronary Artery Disease
(16.5 million)

No Angina
(7.8 Million)

Angina
(8.7 Million)

Optimal Medical Therapy

Angiographic Risk Assessment

High Risk
(800,000)

Mechanical Revascularization

Bypass Surgery
(200,000)

PCI Stent
(600,000)

Controlled Symptoms

Uncontrolled Symptoms

(1) Range 0.6M – 1.8 [mean 1.2M] McGillion et al., Canadian J Cardiology 28:S20-S41 (2012)
other figures, Benjamin et al., Circulation, American Heart Association, Statistics 2017
PROPOSED GENERX TREATMENT ALGORITHM
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Low Risk
(1.2 Million)

High Risk
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Optimal
Medical Therapy

Medical
Revascularization

Product Candidate
Generx
(arterinogene tadenovec)

Uncontrolled
Symptoms

Controlled
Symptoms

Bypass Surgery
(200,000)

PCI Stent
(600,000)

(1) Range 0.6M – 1.8 [mean 1.2M] McGillion et al., Canadian J Cardiology 28:S20-S41 (2012)
other figures, Benjamin et al., Circulation, American Heart Association, Statistics 2017

31
Based on favorable manufacturing cost of Ad5FGF-4, Angionetics is developing a marketing strategy based on a “stent” pricing model.

Generx addressable market: $2 billion - $6 billion
## U.S. MARKET SEGMENTATION
### REFRACTORY ANGINA

<table>
<thead>
<tr>
<th>Newly-Diagnosed</th>
<th>Non-Actionable Diagnostic Angiograms</th>
</tr>
</thead>
<tbody>
<tr>
<td>100,000 Patients</td>
<td>500,000 Patients</td>
</tr>
<tr>
<td><em>Target Market Penetration:</em> 5%</td>
<td><em>Target Market Penetration:</em> 15%</td>
</tr>
<tr>
<td>Dissatisfied Ranexa Rx</td>
<td>Classic Diagnosis</td>
</tr>
<tr>
<td>200,000 Patients</td>
<td>1.2 Million Patients</td>
</tr>
<tr>
<td><em>Target Market Penetration:</em> 10%</td>
<td><em>Target Market Penetration:</em> 10%</td>
</tr>
</tbody>
</table>

220,000 Patients Annually

<table>
<thead>
<tr>
<th>Average Price</th>
<th>Revenue Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>$2,000</td>
<td>$440 Million</td>
</tr>
<tr>
<td>$3,500</td>
<td>$770 Million</td>
</tr>
<tr>
<td>$5,000</td>
<td>$1.1 Billion</td>
</tr>
<tr>
<td>Study</td>
<td>Country</td>
</tr>
<tr>
<td>---------------</td>
<td>--------------------</td>
</tr>
<tr>
<td>AGENT-1</td>
<td>United States</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>AGENT-2</td>
<td>North America</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>AGENT-3</td>
<td>North America</td>
</tr>
<tr>
<td>AGENT-4</td>
<td>Western Europe</td>
</tr>
<tr>
<td></td>
<td>&amp; South America</td>
</tr>
<tr>
<td>AWARE &amp;</td>
<td>U.S. &amp; International</td>
</tr>
<tr>
<td>ASPIRE</td>
<td></td>
</tr>
<tr>
<td>NEW AFFIRM</td>
<td>United States</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

[Generx: 622 | Placebo: 381] TOTAL 1,003
## CLINICAL EFFICACY CORRELATIONS

<table>
<thead>
<tr>
<th>Study</th>
<th>Clinical FDA Regulatory Dossier Findings</th>
</tr>
</thead>
</table>
| AGENT-1 ETT Endpoint (N = 79)              | - Safe and well-tolerated  
- Significant improvement in ETT vs. placebo when baseline ETT ≤ 10 min (p=0.01 at 4 wk; p= 0.05 at 12 wk)  
- Treatment Response Correlates to Disease Severity                                                                                                                                                                                                                                                                                                           |
| AGENT-2 SPECT Endpoint (N = 52)            | - Safe and well-tolerated  
- Significant cardiac perfusion improvement at 8 wk (p<0.05 vs placebo) similar to CABG and PCI procedures (77% Response rate)  
- Parallel trends for improvements in angina frequency and NTG use  
- Data supports improved myocardial perfusion as Generx mechanism of action                                                                                               |
| AGENT-3 / AGENT-4 Meta-Analysis ETT Endpoint (N=532) | - Safe and well-tolerated  
- In females, High Dose vs Placebo:  
  ETT: (pre-specified) 12 wk, p<0.01; 6 mo, p<0.01  
  Time to ECG Ischemia: 12 wk, p=0.03; 6 mo, p=0.01  
  CCS Class Improvements:  
    12 wk, p=0.01; 6 mo, p=0.04; 12 mo, p< 0.01  
- In AGENT-3, males and females exhibited improvement in CCS class at 12 mo (p<0.05)  
- Substantial placebo response in men  
- Treatment Response Correlates to Disease Severity                                                                                                                                                                                                                                                                                               |
| ASPIRE SPECT Endpoint (N = 11)             | - New transient ischemia delivery method safe and well-tolerated (86% Response Rate)  
- Significant cardiac perfusion improvement at 8 wk (p=0.01 vs placebo) similar to AGENT-2 and CABG/PCI                                                                                                                                                                                                                                                                                   |
Clinical & Medical Advancement: Why This? Why Now?

- FDA Phase 3 protocol approved
- FDA Fast Track designation approved Q1 2017
- Initial strategic partnership completed
- Preclinical research on Ad5 transfection efficiency **dramatically** improved using transient ischemia delivery technology
- New data supporting safety & efficacy of higher dose level
- Fundamental research on FGF-4 signaling and angiogenic process confirms VEGF interactions
- Advanced data analytics identifying Generx responders
- New simplified cath lab handling process
- A more clearly delineated refractory angina market opportunity based on Gilead’s promotion of Ranexa
- Research on limitations of mechanical revascularization supports need for “medical revascularization” Generx therapy
GENERX EFFICACY CORRELATIONS: ETT & SPECT IMAGING

AGENT-3 Clinical Study
Retrospective Analysis

Primary Endpoint:
Change from Baseline at Month 6
(CCS Class 3&4; Age ≥55, N=164)

Exercise Duration (Seconds)

Placebo  Ad5FGF-4

<table>
<thead>
<tr>
<th>Placebo</th>
<th>Ad5FGF-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>54 Seconds</td>
<td>91 Seconds</td>
</tr>
</tbody>
</table>

37 second difference
P<0.05

AGENT-2 Clinical Study

Primary Endpoint:
% Improvement in Reversible Perfusion Defect

Cardiac Perfusion Measured by SPECT

Percentage Improvement

N=52

Control Generx

<table>
<thead>
<tr>
<th>Control</th>
<th>Generx</th>
</tr>
</thead>
<tbody>
<tr>
<td>4%</td>
<td>21%</td>
</tr>
</tbody>
</table>

p<=0.05

Placebo Outlier Excluded
Phase 2A Clinical Study

Secondary Endpoint:
% Complete Remission of Angina

Grines et al., J Am Coll Cardiol. 2003; 42:1339-47. Placebo Outlier Excluded
AFFIRM PHASE 3 CLINICAL STUDY
Phase 3 Clinical Design

The FDA IND Phase 3 AFFIRM study will include only CCS Classes 3 & 4 and ages 55-75, uses a sample size of 320 patients, and is expected to be powered at 90% (5% significance) to detect a difference of 30 seconds between Generx and Placebo in the change from baseline to Month 6.

AGENT-3 Clinical Study
Retrospective Analysis
Primary Endpoint:
Change from Baseline at Month 6
(CCS Class 3&4; Age ≥55, N=164)

Henry et al., J Am Coll Cardiol. 2007; 50:1038-46

Physical Exertion (ETT)
Change from Baseline at Week 12

<table>
<thead>
<tr>
<th></th>
<th>Change in Exercise Duration (Seconds)</th>
<th>Mean Number of Weekly Angina Attacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (N=258)</td>
<td>91.7 Seconds</td>
<td>3.3 attacks</td>
</tr>
<tr>
<td>Ranexa 1000 mg (N=261)</td>
<td>115.8 Seconds</td>
<td>P=0.03</td>
</tr>
</tbody>
</table>

24 second Difference

"This is what clinical success looks like!"

### COMPARATIVE PRIMARY ETT OUTCOMES

<table>
<thead>
<tr>
<th>Metrics</th>
<th>CARISA Ranolazine&lt;sup&gt;a&lt;/sup&gt; (N = 519)</th>
<th>Generx AGENT-3 Subgroup Analysis&lt;sup&gt;b&lt;/sup&gt; (N=164)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Drug (1000 mg)</td>
</tr>
<tr>
<td>Baseline (sec)</td>
<td>418</td>
<td>415</td>
</tr>
<tr>
<td>Ending ETT (sec)</td>
<td>510</td>
<td>531</td>
</tr>
<tr>
<td></td>
<td>(12 wk)</td>
<td>(12 wk)</td>
</tr>
<tr>
<td>Abs Change (sec)</td>
<td>+92</td>
<td>+116</td>
</tr>
<tr>
<td>% Change</td>
<td>+22%</td>
<td>+28%</td>
</tr>
<tr>
<td>Abs Change Drug vs. Placebo</td>
<td>+24 sec</td>
<td>+37 sec</td>
</tr>
<tr>
<td></td>
<td>(P=0.03)</td>
<td>(P&lt;0.05)</td>
</tr>
<tr>
<td>Planned Study Designs</td>
<td>CARISA</td>
<td>AFFIRM Phase 3</td>
</tr>
<tr>
<td></td>
<td>N=823</td>
<td>N = 320; CCS 3,</td>
</tr>
<tr>
<td></td>
<td>1:1:1 Randomization</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>(Placebo, 750 mg, 1000 mg)</td>
<td>1:1 Randomization</td>
</tr>
<tr>
<td></td>
<td>118 clinical sites</td>
<td>ΔETT (6 Mo) Endpoint</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Site # pending</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Planned</td>
</tr>
</tbody>
</table>


<sup>b</sup>Post-Hoc subset analysis, CCS 3 & 4, ≥55 yr (representative of AFFIRM study criteria)
<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
<th>Logos</th>
</tr>
</thead>
<tbody>
<tr>
<td>Christopher Reinhard</td>
<td>Chief Executive Officer</td>
<td>angionetcs CARDIUM SCHERING COLLATERAL THERAPEUTICS Fisher Scientific</td>
</tr>
<tr>
<td>Lois Chandler, Ph.D.</td>
<td>Chief Operating Officer</td>
<td>angionetcs CARDIUM TISSUE REPAIR CO. SALK INSTITUTE FOR BIOLOGICAL STUDIES</td>
</tr>
<tr>
<td>Gabor Rubanyi, M.D., Ph.D.</td>
<td>Chief Innovation Officer</td>
<td>angionetcs CARDIUM COLLATERAL THERAPEUTICS SCHERING</td>
</tr>
<tr>
<td>Robert Engler, M.D.</td>
<td>Chief Medical Advisor</td>
<td>angionetcs CARDIUM Halozyme VA San Diego HEALTHCARE SYSTEM</td>
</tr>
<tr>
<td>Wei-Wei Zhang, M.D., Ph.D.</td>
<td>Chief Scientific Officer</td>
<td>angionetcs INTROGEN Genway Baxter</td>
</tr>
</tbody>
</table>
Developing New Therapeutics for a Global Market

PRODUCT CANDIDATE

Generx
[Ad5FGF-4]

angionetics
MICROVASCULAR GENE THERAPY
1985  Syntex Corporation discovers Ranexa and initiates Phase 1 & 2 clinical studies

1994  Roche acquires Syntex and discontinues the clinical development of Ranexa

1996  CV Therapeutics acquires Ranexa and begins Phase 3, encounters setbacks from efficacy and safety issues, and refocuses development from classic to “chronic” angina

2006  Ranexa approved by FDA as second-line therapy for chronic angina

2009  CV Therapeutics is acquired by Gilead Sciences for $1.4 billion (14x annualized sales)

2017  After Phase 4, FDA approved Ranexa for front-line therapy, annualized revenues reach ~$600 million in U.S. ($3,000 per year [100x generic beta blocker price] @ 200,000 patients)
# U.S. Medicare Reimbursement for Myocardial Ischemia Angina-Based Medical Therapies

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Medical Therapy</th>
<th>Reimbursement Level(1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>33510</td>
<td>Coronary Artery By-Pass Surgery for Myocardial Ischemia</td>
<td>$48,000</td>
</tr>
<tr>
<td>92928</td>
<td>Percutaneous Coronary Interventions Up to Four (4) Stent Placements for Myocardial Ischemia</td>
<td>$17,800</td>
</tr>
<tr>
<td>TBD</td>
<td>Generx Angiogenic Gene Therapy Medical Revascularization for Myocardial Ischemia</td>
<td>$4,600- $7,600</td>
</tr>
<tr>
<td>N.A.</td>
<td>Ranexa <em>(Ranolazine)</em> for Treatment of Chronic Angina <em>(Small Molecule Drug Taken Twice Daily)</em></td>
<td>$6,000 Per Year</td>
</tr>
<tr>
<td>33799</td>
<td>External Counterpulsation (ECP) for Treatment Disabling Chronic Angina <em>(35 Sessions @ $135)</em></td>
<td>$4,375</td>
</tr>
<tr>
<td>33140</td>
<td>Transmyocardial Laser Revascularization (TMLR) via Open Chest and Thoracosopic Surgery for Severe Intractable Angina</td>
<td>$3,200</td>
</tr>
</tbody>
</table>

(1) Does not include other related medical costs & expenses
NEW PATHWAYS FOR A STRUGGLING HEART

The heart sometimes has the ability to grow new tissue. Researchers are trying to grow these tissue-like tissues in the laboratory to replace damaged pieces of the organ. One potential benefit is that such patches could one day be used to repair damaged hearts. In the future, these patches might even be used to treat heart disease.

PLAN OF ACTION

1. Identify regions of the heart that are damaged or diseased.
2. Harvest living cells from these regions.
3. Use these cells to create a patch that can be used to repair the damaged heart.
4. Insert the patch into the damaged area of the heart.

The goal is to create a patch that can grow new tissue and help the heart function more efficiently.

SCIENTIFIC AMERICAN
January 2017