



#### **Comprehensive Solutions for Patient Temperature Modulation Therapy**

#### Cardiac Cooling











- Medical Technology Company Focused on Innovative Products that have the Potential to Transform the Practice of Medicine
  - Initially Focused on Cardiovascular Disease and Treatment of Ischemic Injury
- Building a Business Balanced on Products for "Today" with the Development of Breakthrough Products for "Tomorrow"
  - By Design, Cardium is <u>Not</u> a Binary Tech Bet or an Early-Stage Science Play
  - We have Medical Devices with FDA Clearances and Later-Stage Product Candidates with FDA Fast Track Status
  - Acquiring Undervalued Product Opportunities with Significant Growth Potential on Highly Favorable Economic Terms
    - Completed Three Acquisitions with \$270 Million Investment by Big Pharma and Institutional Investors

#### **Company Development Pipeline**

Company	Therapeutic Application & Lead Product	Clinical & Commercial Status	Disease Focus
Cardium Biologics	Cardiovascular Growth Factors <b>Generx</b> ™	AWARE Phase 3 Clinical Study FDA Fast Track Status	Heart Disease and Angina
InnerCool Therapies	Surface & Endovascular Temperature Modulation Therapies <b>CoolBlue and</b> <b>RapidBlue Systems</b> ™	FDA (510k) Clearance – Marketed & Sold in U.S.	Fever Control & Neurosurgery Research for Heart Attack, Stroke & Cardiac Arrest
Tissue Repair Company	Growth Factor Activated Matrix <i>Excellarate</i> ™	<b>MATRIX</b> Phase 2b Clinical Study	Neuropathic Diabetic Foot Ulcers and Tissue Injuries



#### **Integrative Perspectives**



#### **Diversified Portfolio of Intrinsic Value Equity Drivers**

#### **Temperature Modulation Therapy**



#### Therapies<sup>®</sup> 34.033.9 Acquired in March 2006 33.9 Fully-Validated Manufacturing Facility 34.0 34.1 **FDA Clearances for** 34.0 Surgical Applications and 34.1 **Fever Control** 34.0 34.1 34.2 Products Being Used at over 35 Major Medical 34.0 Centers 33.9 **Expanding Small Regional** 33.8 Sales Force to National Footprint 34.0 34.1 Scaling New Manufacturing 34.0 34.0 Facility for Annual Revenue 34.1of \$50 Million and Above 34.1 Alsius Acquisition Valued its 34.2 Therapeutic Hypothermia 34.1 34.0 Business at \$40 Million and 33.9 with Performance Incentives Over \$70 Million 33.9 34.0

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#### Cardiac Cooling

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#### Current InnerCool Positioning Statement

"InnerCool Therapies is a San Diego-based medical technology company focused on becoming the leader in the development, manufacture, marketing and sale of new and innovative products for the emerging field of temperature modulation therapy, which are designed to rapidly and controllably cool the body in order to reduce cell death and damage following acute ischemic events such as cardiac arrest or stroke, and to potentially lessen or prevent associated injuries such as adverse neurological outcomes. Based on industry estimates, the potential worldwide market for temperature modulation systems and related disposables could exceed \$2 billion annually.



#### **Competitive Positioning**

CoolBlue™ Surface Cooling

**INNERCOOL** 

**RapidBlue**<sup>™</sup>

Endovascular Cooling

The <u>Only</u> Total Comprehensive Solutions Company Accuiro

## Temperature Modulation Therapy: Developing a Comprehensive Solutions Approach



#### **Business Strategy**

- Leverage Unique Market Position: Establish InnerCool as first and only comprehensive, one-source provider of temperature modulation systems for hospitals and clinicians based on a "total progressive solutions approach"
- Differentiation Through Performance: Based on documented performance, establish InnerCool's endovascular catheter-based system as the best-inclass product setting standards by which all systems are measured
- <u>Drive Adoption</u>: Continue to drive adoption of InnerCool's products by promoting awareness among leading hospitals and critical care practitioners, including participating in clinical trials, training physicians and supporting the adoption of temperature management treatment guidelines
- Increase System Installations and Catheter Use: Increase system installations at target hospitals and drive catheter use among existing customers
- Enhance Existing Products and Develop New Products: Continue to improve the design of our current products and expand our pipeline of future products and continually enhance our systems, software and catheters to deliver more effective and easier-to-use temperature management products
- Improve Margins through Scale and Efficiency: Focus on improving gross margins by lowering raw material and manufacturing costs and realize economies-of -scale as sales volume increases

#### The InnerCool Strategic Advantage

- Only company worldwide that offers comprehensive temperature modulation surface and endovascular cooling systems
- RapidBlue System is the world's most powerful premium-priced endovascular cooling system that lowers body temperature by 4°-5°C per hour
- RapidBlue System is the only endovascular system to offer a fully integrated catheter-based temperature probe, marketed as the Accutrol<sup>®</sup> catheter
- CoolBlue Surface Cooling System has been designed to compete favorably against the industry leader Medivance Arctic Sun System, based on focus group research
  - CoolBlue System easier to use (no adhesives) and priced 30% 40% lower while offering comparable performance



#### The InnerCool Product Advantage





#### New Cardium Tech Center

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#### cGMP Clean Rooms





InnerCool Warehouse

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#### THERAPEUTIC HYPOTHERMIA Mechanisms of Action



#### THERAPEUTIC HYPOTHERMIA

Research



Early Cooling



Late Cooling

Region of infarction by ex vivo MRI



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## Therapeutic Cooling: A Broadening Market Opportunity Through Clinical Research



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#### **Brain Injury in Cardiac Arrest**

- Study published in The New England Journal of Medicine showed induced hypothermia reduces mortality and improves long-term neurological function
  - One in seven lives saved
  - 37% improvement in neurological function
- Other studies show cooling may also be beneficial for in-hospital cardiac arrest

#### Organizations Supporting Temperature Management



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# This Man Was Dead.

## He Isn't Anymore

How Science Is Bringing Mor Heart-Attack Victims Back To Life

> Brian Duffield, 41, whose heart stopped after a swim in May 2006

A New Route to Restoring Life...

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"By inducing hypothermia in a patient resuscitated after cardiac arrest, doctors are able to reduce cell death and increase the chance of a full recovery."

"People have a hard time believing that something as simple as cooling the patient can make such a difference."

> Newsweek 341 July 23, 2007

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#### Case Study: Spinal Cord Injury



ESPN: NFL Report, September 09, 2007

After catastrophic life-threatening injury, NFL player, Kevin Everett, received <u>hypothermic cooling</u> <u>therapy</u> in the ambulance and at the hospital which has greatly enhanced his chance of a more full recovery.

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*"I don't know if I would call it a miracle. I would call it a spectacular example of what people can do."* 

> Dr. Barth Green, chairman of the department of neurological surgery at the University of Miami school of medicine

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#### Overview of InnerCool Clinical Development Activities

Study	Clinical Status	Timing	Principal Funding Source	Study Objective
InnerCool Therapies: ICTuS-L (Stroke Study) Endovascular Cooling System	Phase 1	Initiated	U.S. National Institute of Health / National Institute of Neurological Disorders	Study endovascular hypothermia as adjunct to thrombolytic therapy to prolong tPA treatment window from 3 hours to 6 hours
InnerCool Therapies: Heart Attack Study Endovascular Cooling System	Pilot	Initiated	Lund University Hospital Sweden	Evaluate medical utility of rapid early cooling to reduce infarct size in heart attack patients
InnerCool Therapies: COMPARE (Neuro Surgery) Endovascular Cooling System	Pilot	Initiated	Harborview Medical Center Seattle, WA	Evaluate endovascular hypothermia during extended occlusion for aneurysm reconstruction surgery

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#### Hypothermia/Caffeinol as Potential Treatment for Ischemic Stroke Patients

- 4Q / 2007 Cardium licensed technology covering the use of Caffeinol for treatment of stroke patients undergoing hypothermia cooling therapy
- Caffeinol and hypothermia have both been shown to be beneficial in reducing damage to brain tissue following stroke, and data suggests that combining these neuroprotective therapies can substantially reduce neurotoxic events triggered by ischemia and allow for better tissue viability and ultimate function
- One of the objectives of the agreement is to evaluate the safety and efficacy of treating stroke patients with Caffeinol, administered by intravenous infusion (IV), in combination with InnerCool's endovascular hypothermia technology
  - A study has been proposed to the National Institute of Neurological Disorders and Stroke (NINDS), part of the National Institutes of Health (NIH)
- Data from InnerCool's ongoing NIH-sponsored ICT-uS-L trial has provided excellent evidence of the safety of InnerCool's temperature modulation system in acute ischemic stroke patients
  - A new ICT-uS-L trial is expected to expand that database and further evaluate both cooling and Caffeinol as potential new treatment paradigms for stroke

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#### **Competitive Positioning**

CoolBlue™ Surface Cooling

**INNERCOOL** 

**RapidBlue**<sup>™</sup>

Endovascular Cooling

The <u>Only</u> Total Comprehensive Solutions Company Accuiro



The ONLY Company to provide A COMPREHENSIVE SOLUTION TO **TEMPERATURE MODULATION THERAPY** 

#### Surface **CoolBlue**<sup>™</sup>

## **Progressive Therapeutic Approach**

#### Endovascular **RapidBlue**<sup>™</sup>

- Convenience for less-acute patients
- Easy-to-use surface vest and thigh pads
- No adhesives contacting the skin
- Suitable for prolonged uses

#### **High-Performance Catheter** for Rapid Cooling and Warming





Accutrol<sup>™</sup> technology enables precise temperature measurement and modulation



#### Thin flexible catheter



Powerful performance for time-critical needs

- Rapid temperature modulation Cooling rates 4-5° C/hr Warming rates 2-3° C/hr
- Powerful enough for obese patients
- Precise and automated patient temperature control
- Excellent safety profile



## Considerations When Choosing a Cooling and Warming Technology

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Setting	ED, ICU, OR, Cath Lab
Medical Indications	Neurosurgery, cardiac, brain injury, fever control, trauma
Status of Patient	Awake, inubated, inubated & parlayed 34.1 34.2 34.2
Required Performance	Speed of cooling, tight temp control, slow rewarm, fast rewarm 33.9
Risk vs. Reward Tradeoff	Non-invasive – skin necrosis, invasive - DVT 34.0 34.0 34.0 34.0 34.0 34.0 34.0 34.0
Cost-Effectiveness	Financial cost, labor cost 34.0 34.1 34.0 34.0 34.0 34.0 34.0
Other Issues	Published data, obese vs. non-obese, patient access, MRI compatibility 33.9

herapies<sup>°</sup>

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# Temperature Modulation Therapy:34Selecting the Appropriate Cooling System for Your Patient

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Criteria	Surface-Based CoolBlue System™	Endovasular-Based RapidBlue System™	
Application	Prolonged temperature management for less acute settings	Temperature modulation for <sup>33.9</sup> neuro & cardiac surgery 34.0 34.1	
Administrative	Easy to use external jacket and thigh pads, made of soft breathable brushed nylon material and velcro fasteners. Nurse administered <i>No glue required</i>	34.0 Low-profile endovascular catheter placed by the physician in the vena cava via venous puncture 34.0	
Performance	Slower cooling and rewarming. Generally less effective for larger patients (> 30 BMI)	34.2 Faster cooling and rewarming <sub>4.1</sub> in all-sized patients 34.0	
Control	Less control at target temperature Requires external temperature measurement with bladder or esophagus probes	Precise real time control at target temperature True core temperature Measured with Accutrol <sup>™</sup> 33.9 34.0	
Concurrent Medications	Requires heavy sedation and/or muscle paralytics to achieve target temperature of <35°C (because of shivering)	May be used in awake patients at 35 C and only mild sedation at 33°C No need for paralytics 34 0	
Monitoring	Requires EEG monitoring to assess seizures Requires nurse vigilance for skin interface MRI compatible	Since no paralytic drugs required, no EEG monitoring Hands free with standard catheter care Head & neck MRI compatible	
Cost Considerations	Lower cost	33.9 Higher cost with higher 33.8 performance requirements 33.9	





Therapeutics, Inc. Cardium 2008 (



#### **New Trade Show Booth**



#### The InnerCool Product Advantage





#### ACCUTROL® ENDOVASCULAR Cooling Catheter



#### TEMPERATURE CONTROL THERAPY Establishing New Standards of Care



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#### Next Generation RapidBlue System Endovascular





Patient Temperature Modulation Therapy Endovascular cooling/warming



#### **Most Powerful Design**





- Developing a Best-of-Class System
- Flexible Metal Temperature Control Element
- Enhanced Heat Transfer
- Low Profile (No Expansion)
- Cool Rates 4-6 °C/hr

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### InnerCool's Key Technologies

#### THE (Heat Transfer Element) aka Gold Heat Exchanger

- Biocompatible gold surface layer... "the gold standard"
- Proprietary multi-layer metallic laminate is strong yet ductile to prevent fracture
- Thin metallic shell maximizes heat transfer relative to polymer balloons (roughly 2 orders of magnitude difference in thermal conductivity)
- Metal shell remains flexible at operational pressure, allowing higher pressures for increased coolant flux and enhanced heat transfer
- Metal shell does not increase in diameter during operation, promoting ease of insertion and removal
- Modular production environment promotes scalable manufacturing

- Helical features promote mixing of circulating coolant and external blood flows to enhance heat transfer
- Bellows allow flexibility under pressure and contribute to mixing of circulating coolant
- Anti-thrombogenic surface treatment engineered for superior performance by class leading coating technologists
- Covalently bonded heparin coating minimizes thrombus formation while remaining tightly bonded to the metallic surface. Tests show minimal loss of activity during prolonged use
- Geometry (surface features) and manufacturing methods protected by IP

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— T control — T esoph × Tpa



 True core temp feedback

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- No esophageal or venous probe placement
- Improved safety and reliability



#### InnerCool's Key Technologies ACCUTROL<sup>™</sup> Catheter System

- Provides core temperature monitoring for feed back control of hypothermia induction, maintenance, and rewarming
- No need for external temperature probes
- Integrated temperature sensor at tip of catheter (YSI-400 compatible) <sup>340</sup>
- Truly measures core temperature during hypothermia therapy
- Excellent agreement with Swan-Ganz PA temperature (the gold standard)
- Avoids compartmental temperature differences during dynamic temperature change
  - Bladder/rectal temperature delays of 20 30 minutes
  - Temperature offset of 1-2 C
- Strong IP coverage of catheter-mounted temperature sensors and control temperature acquisition algorithms

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CoolBlue<sup>™</sup> Surface Cooling System





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# The CoolBlue<sup>™</sup> Technology Provides Less Acute Patients with the First Stage in our Progressive Therapeutic Approach

CoolBlue <sup>™</sup> Surface Pad Features	CoolBlue™         33.8           CoolBlue™         33.9           Console Features         34.0           34.1         34.1
<list-item><list-item><list-item><list-item><list-item><list-item><list-item></list-item></list-item></list-item></list-item></list-item></list-item></list-item>	<ul> <li>Compact footprint</li> <li>Nurse friendly; easy to use</li> <li>Manual and Automatic Modes to initiate therapy immediately</li> <li>High water flow rate yields quick cooling and warming</li> <li>Proven track record of performance</li> <li>Manufactured for InnerCool by Cincinnati SubZero</li> </ul>
	ERCOOL 34.0 34.0 33.9 34.0 33.9 34.0 33.9 33.9 33.9 33.9 33.9 33.9 33.9 33

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CoolBlue Surface Cooling System Summary Findings from ICU Nursing Focus Group Market Research

- Nurses believe surface temperature management works and benefits patients
- Traditional cooling systems using reusable blankets inefficient
- Nurses seek a simple cost-effective, easy-to-use therapeutic cooling systems
- Do not like adhesives contacting the skin (Medivance, Artic Sun) because the adhesive pads are difficult to remove from the skin and get tangled with I.V. lines, etc.
- Need multiple consoles to cool multiple patients simultaneously
- Expressed preference for non-adhesive, simple velcro strip based systems and lower cost replacement pads due to patient soiling

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#### **Competitive Review & Analysis**

therapies<sup>®</sup>

Surface Cooling

Medivance

**INNERCOOL** therapies<sup>®</sup>

Endovascular Cooling

ALSIUS

Technology Convergence 34.1 34.0 34.1 34.2

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#### **Hypothermia Market Segmentation**

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Surface Systems	Endovascular Systems 33.9 33.8 33.8 33.9 33.9
Surface cooling devices, which have dominated the market for a long time, are non-invasive and come in the forms of cooling blankets, gloves, pads, head wraps and vests	<ul> <li>Endovascular devices are invasive and are inserted into the patient's venous vascular system</li> <li>They require a console to control the catheter's heat exchange</li> <li>34.0 34.0 34.0 34.0 34.0 34.0 34.0 34.0</li></ul>
<ul> <li>Low cost with low regulatory burden, and they are generally easier to use</li> </ul>	<ul> <li>Cold or warm sterile saline is circulated closed loop through the catheter</li> </ul>
<ul> <li>Some units serve a dual purpose of not only cooling a patient but can also be used to warm a patient</li> </ul>	<ul> <li>Direct heat exchange with the blood is significantly more effective than surface techniques</li> </ul>
<ul> <li>Most traditional consoles are re-usable, very easy to clean and highly durable</li> </ul>	<ul> <li>Endovascular cooling is required to effectively cool patients with body mass index &gt; 30</li> <li>34.0 34.0 34.1 34.2 34.1 34.2 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.0 34.1 34.1 34.0 34.0 34.1 34.0 34.0 34.0 34.0 34.0 34.0 34.0 34.0</li></ul>
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#### Competitive Landscape for Advanced Cooling Systems

Company	Approach	Status	
<b>INNERCOOL</b> therapies®	Endovascular and Surface	34.0 34.0 <b>Commercial</b> <sup>4.1</sup> 34.0 34.1 34.1	
ALSIUS	Endovascular only	34.1 Commercial 33.9 33.9 33.9	
Medivance®	Surface only	33.8 33.9 Commercial <sup>4.0</sup> 34.1 34.0 34.0	
Radiant	Clinical Development: Endovascular only	Liquidated Technology Purchased by Zoll Medical <sup>4</sup> 2	
Companies developing advanced technology solutions to address significant 33.9 market opportunity and unmet medical need in temperature management.			

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#### Competitor Performance Comparison: Evidence-Based Marketing

	Company / Approach	Performance C°/Hour	Relative Performance Score
ar Cooling	InnerCool's Endovascular System with Accutrol Catheter <sup>1</sup> n=88	∆ 4.8°	100%
Endovascul	Alsius CoolGuard 3000 Endovascular with ICY Catheter <sup>2</sup> n=97	∆ 1.2°	25%
Cooling	Medivance Artic Sun Surface Cooling System <sup>3</sup> n=27	∆ 1.4°	29%
Surface (	Classic Surface Cooling Blankets (TCAS Study) <sup>1</sup> n=60	∆ 0.9°	19%
<sup>1</sup> Neurosurgery 2004; 55:307-315. <sup>2</sup> Stroke 2006; 37:1792-7. <sup>3</sup> Resuscitation 2007.03.001.			34.0 34.1 s

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#### Temperature Modulation Therapy: Market Strategy



## Size Matters! InnerCool Slim Metallic Catheter vs. Alsius Big Bore Plastic Inflatable Catheter



#### "The Smaller and More Powerful the Better"

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Building a Diversified Portfolio of Products for Today and Tomorrow