

# ISCHEMIX™



Pioneering Ischemic Injury Therapy

# Ischemix

---

- Clinical-stage company developing novel compounds to treat ischemic injury
- Recently completed Phase 2a, multi-dose, double-blind, proof-of-concept study, demonstrated safety and efficacy
- Lead drug based upon modification of known active natural drug
- Future plans:
  - Complete expanded Phase 2b study to lead to Phase 3
  - Advancement of pipeline compounds for additional indications

# Corporate Overview

---

- Founded in 1999
- Over \$26M equity capital invested to-date
- Experienced management team, board of directors and clinical advisors
- Initial target market - Cardiac ischemic injury
- Potential 2 million U.S. patients annually, \$1 billion per year

# Management

---

- Albert (Bert) D. Friesen, PhD - CEO
  - 40 years of experience in drug development
  - Led development of WinRho from idea to commercial success
  - Instrumental in founding and developing several life science companies including Medicure Inc., Kane Biotech Inc., Miraculins Inc., DiaMedica Inc.
  - PhD. protein chemistry from University of Manitoba
  
- Robert Weinstein, CPA, MBA - CFO
  - Chief Financial Officer four publicly-traded, two private companies
  - Expertise in development-stage, publicly-traded and reverse merger entities
  - Extensive healthcare industry experience
  - Investment Banker and Private Equity Fund Manager
  - Certified Public Accountant; MBA – University of Chicago

# Management - Continued

---

- Reinier Beeuwkes, PhD – President and Chairman
  - 40 years experience in pharmaceuticals and life sciences
  - Former Director of Renal and Cardiovascular Pharmacology at Smith Kline
  - Co-founder and Director of Braintree Laboratories
  - Former Harvard Professor of Physiology
  - B.S., MIT; PhD., Harvard University
  
- Geoffrey Clark, MD – Chief Medical Officer and Board Member
  - Co-founder and Director of Braintree Laboratories
  - >30 years clinical practice
  - B.A., Harvard University; MD SUNY Buffalo

# Core Technology

---

- Selection of known active natural molecule with established drug activity
- Modification of parent compounds to enhance activity
- Improved drug properties and efficacy
- Obtain NCE Patents
- Pipeline of modified natural molecules for additional key indications

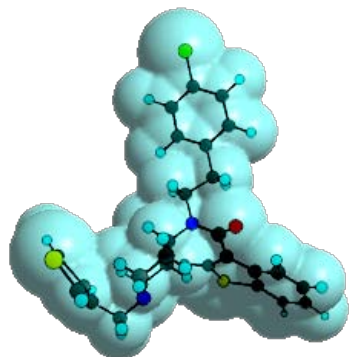
# Lead Compound - CMX-2043

---

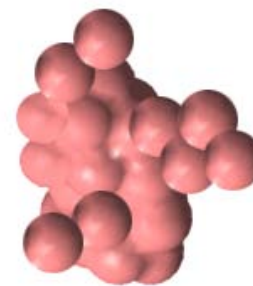
- First-in-class cardio-protective molecule
- Functions through multiple established cell survival pathways
- Modified lipoic acid scaffold
- Modification provides enhanced anti-oxidant and calcium chelating activity
- Advanced through Phase 2a (PCI patients) – No serious adverse events
- Clean pre-clinical toxicology and safety pharmacology including genotoxicity, single and repeat dose, hERG, P450

# Design Rationale - CMX-2043

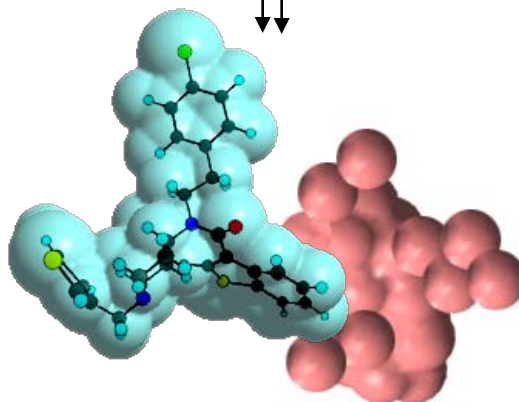
---



**Parent Molecule**



**Modifier**



**Result: CMX-2043**

- Cytoprotective
- Enhanced properties

# SUPPORT-1, Phase 2a Study

---

**A Prospective, Randomized (3:1), Comparative, Blinded, Placebo-Controlled, Three Different Intravenous Dose, Phase 2a Study of the Safety and Efficacy of CMX-2043 in Subjects Undergoing PCI and Peri-Operative Reperfusion Treatment (SUPPORT-1)**

- Multi-center
  - Three doses
  - Placebo Control
- Patient criteria
  - Elective PCI patients with stable disease
  - Receiving single stent of  $\geq 18$  mm or multiple stents

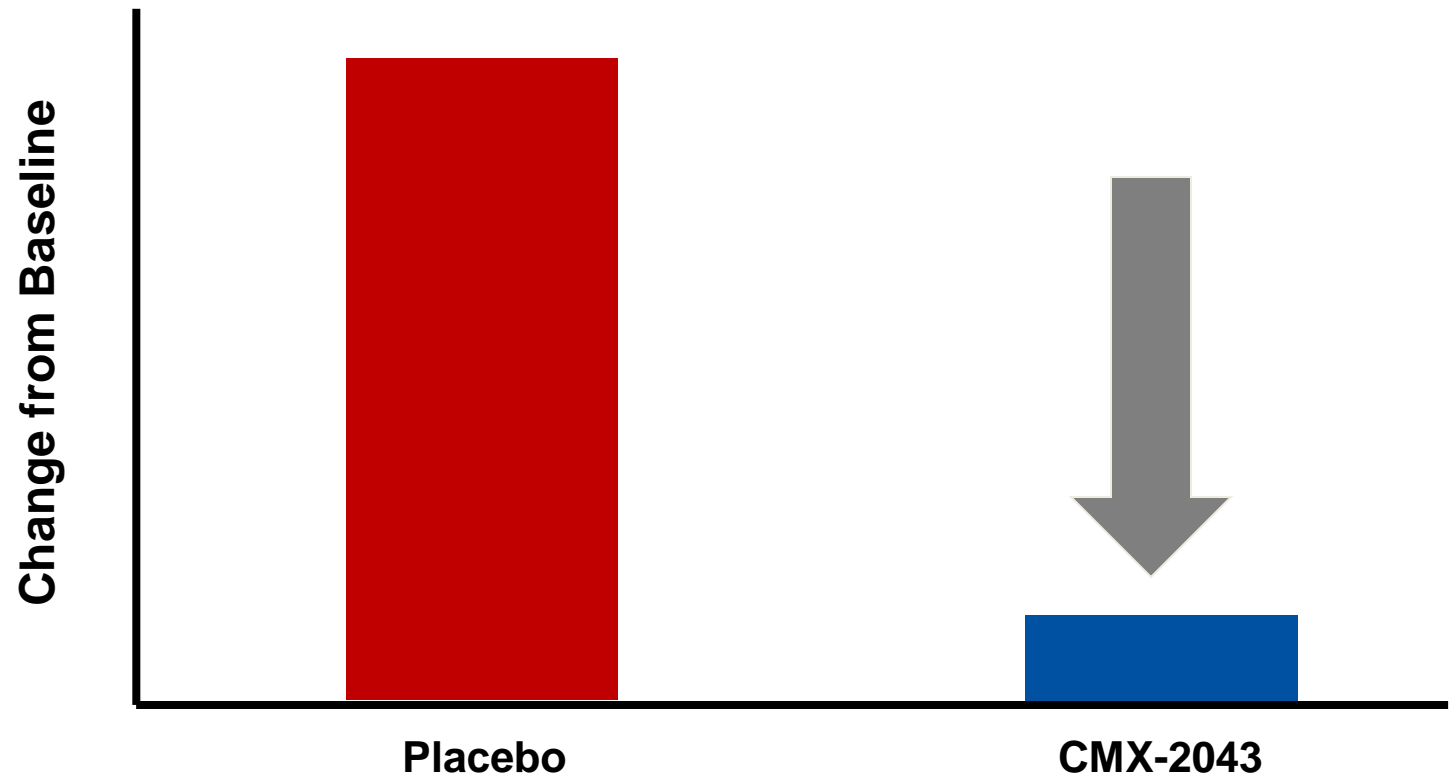
# Phase 2a Endpoints

---

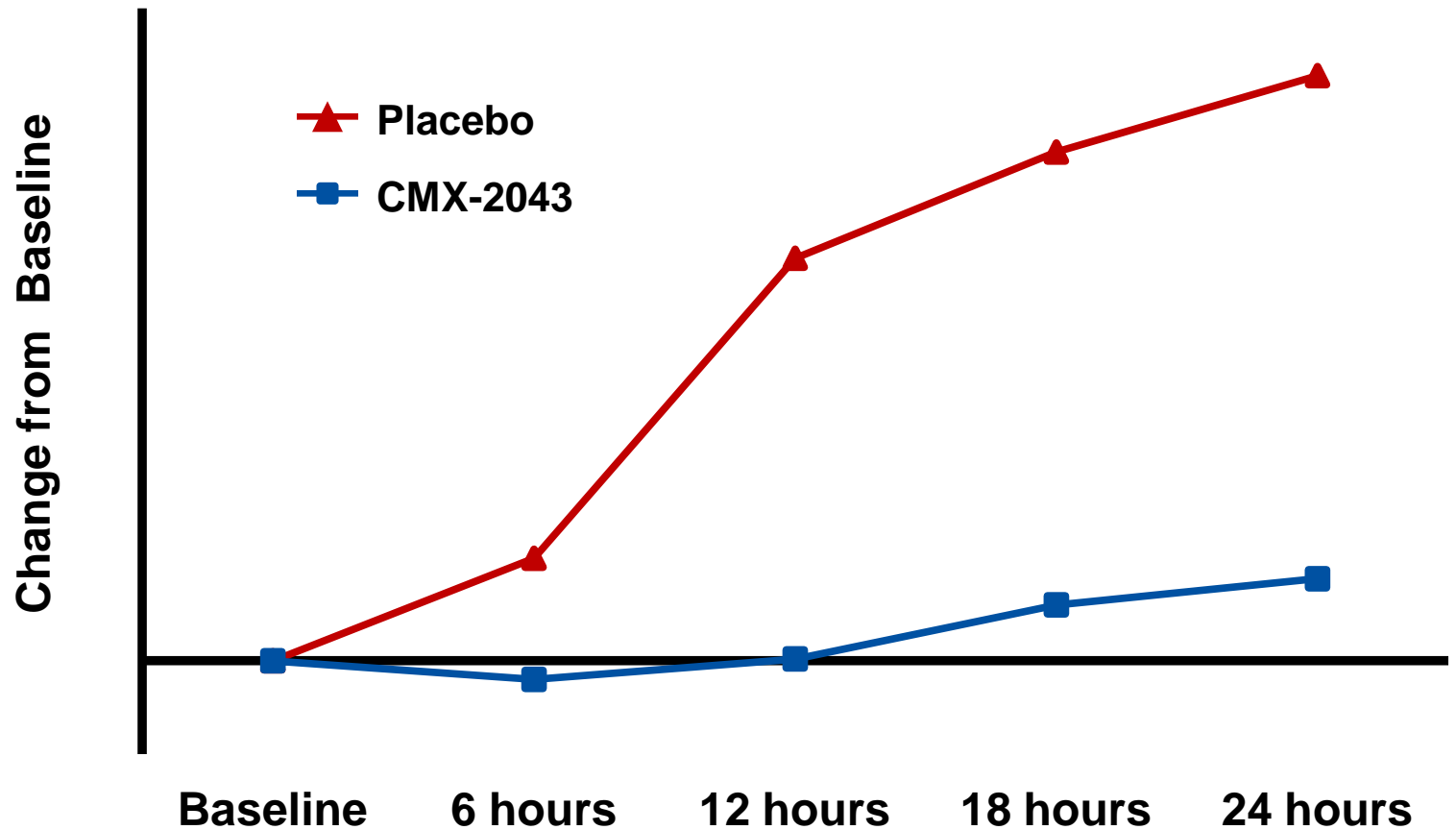
- Primary
  - Safety
    - Change in CK-MB values up to 24 hours after PCI procedure
- Secondary – Efficacy
  - Reduction in myocardial injury compared to placebo as determined by lesser increase of cardiac enzymes CK-MB and Troponin T
- Secondary – Safety
  - Treatment-emergent adverse events
  - Vital sign, ECG or clinical lab value changes compared with placebo
  - Pharmacokinetics

# Cardiac Injury Assessed by Enzyme Biomarkers

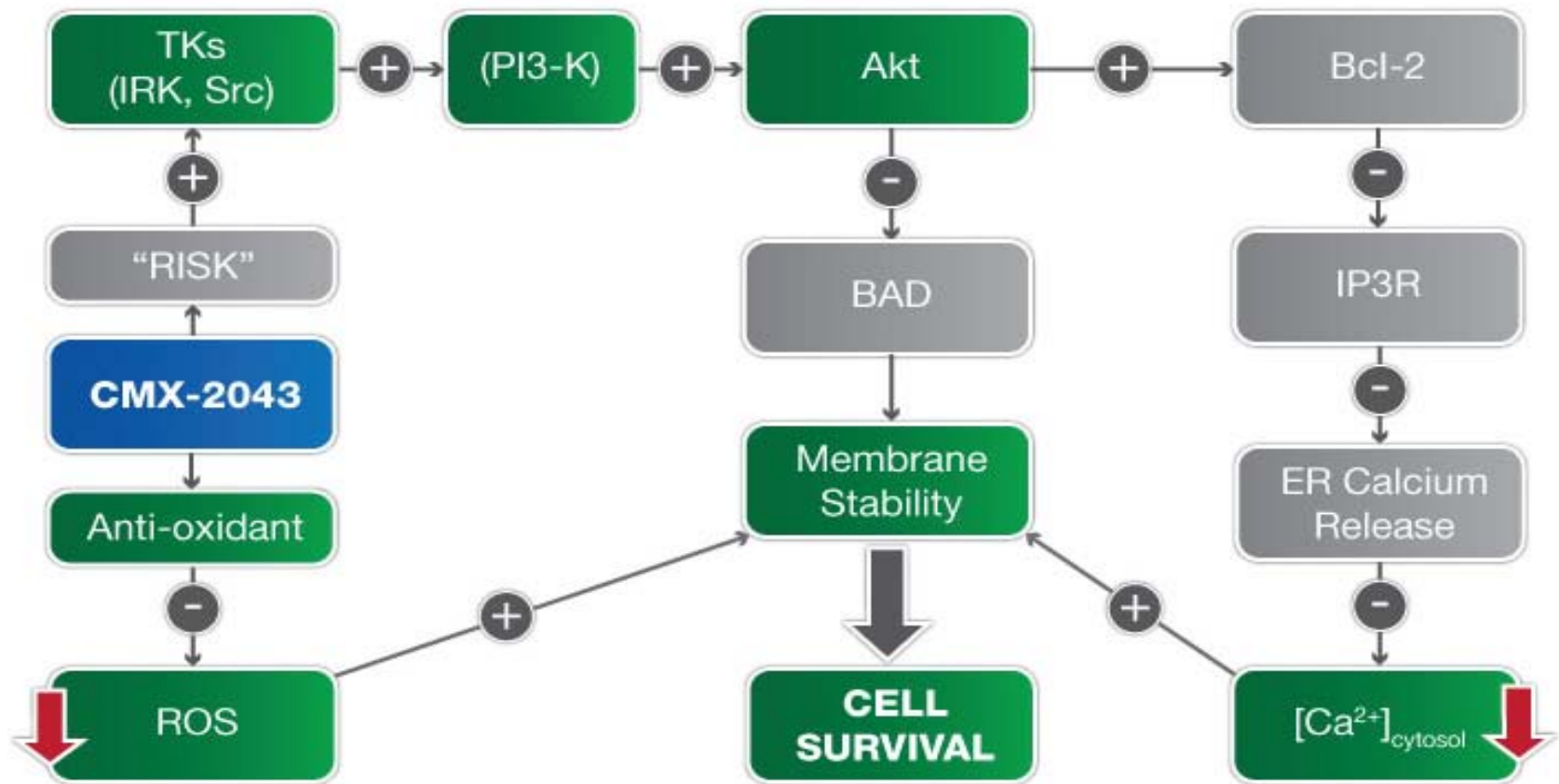
---



# Cardiac Enzyme Biomarker Concentration Following PCI Procedure



# Cell Survival Pathways - CMX-2043



Note: Green areas indicate confirmed biochemical interactions.

# SUPPORT-2, Phase 2b Study

---

**A Prospective, Randomized (2:1), Comparative, Blinded, Placebo-Controlled, Two Different Intravenous Doses, Phase 2b Study of the Safety and Efficacy of CMX-2043 in Subjects Undergoing PCI and Peri-Operative Reperfusion Treatment (SUPPORT-2)**

- Multi-center
  - Two doses
  - Placebo Control
  - IND filed in multiple countries
- Patient criteria
  - Elective PCI patients with stable disease
  - Receiving single stent of  $\geq 18$  mm or multiple stent

# Phase 2b Endpoints

---

- Primary
  - Change in Troponin T and CK-MB values up to 24 hours after PCI procedure
  
- Secondary
  - Reduction in composite endpoint of death and MI (as defined by Troponin T 3xULN) within 30 days
  
- Safety
  - Treatment emergent adverse events
  - Vital signs and physicals
  - Pharmacokinetics

# Patent Status - CMX-2043

---

- Patent Granted – March 2, 2011
- Priority date – May 2009
  - >20 years exclusivity from May 2009 (plus extensions due to FDA review, etc.)
- Compositions and Methods For Treating Ischemia and Ischemia-reperfusion Injury
- Claims
  - Composition of matter drug substance and product (salt)
  - Composition as pro-drug

# Target Market

---

- Ischemia most common in cardiovascular events
  - PCI - 1.2 million procedures / year U.S.
  - CABG - 500,000 procedures / year U.S.
- U.S. market size estimated at \$1 billion
- Worldwide market comparable to US
- Additional indications
  - Renal injury
  - Organ transplants

# CMX-2043 vs. Competition

---

- CMX-2043
  - Anti-oxidant
  - Activates AKT cell survival pathway
  - Not an anti-coagulant
- No approved drugs for ischemia treatment
- No devices
- No direct competitors

# Development Plans – CMX-2043

---

- Phase 2b study in approximately 900 patients
  - Multiple centers
  - Double-blind, placebo-controlled
- Protocol based on current catheter lab practices
- Faster recruitment by expanded inclusion criteria
- Well-defined efficacy endpoints
- Flexible data analysis plan

# Independent Directors and Advisory Board

---

- Independent Directors
  - John A. Norris, JD
    - Former Deputy Chief of the U.S. FDA
    - President and CEO, Norris Capital
  - Edward Shashoua, DO
    - Harvard Vanguard Medical Associates
  
- Advisory Board
  - James Tcheng, MD, FACC
    - Professor of Medicine – Duke University
  - Michael Gibson, MS, MD
    - Assoc. Professor of Medicine – Harvard Medical School
  - Mitch Krucoff, MD, FACC
    - Professor of Medicine – Duke University

## Summary

---

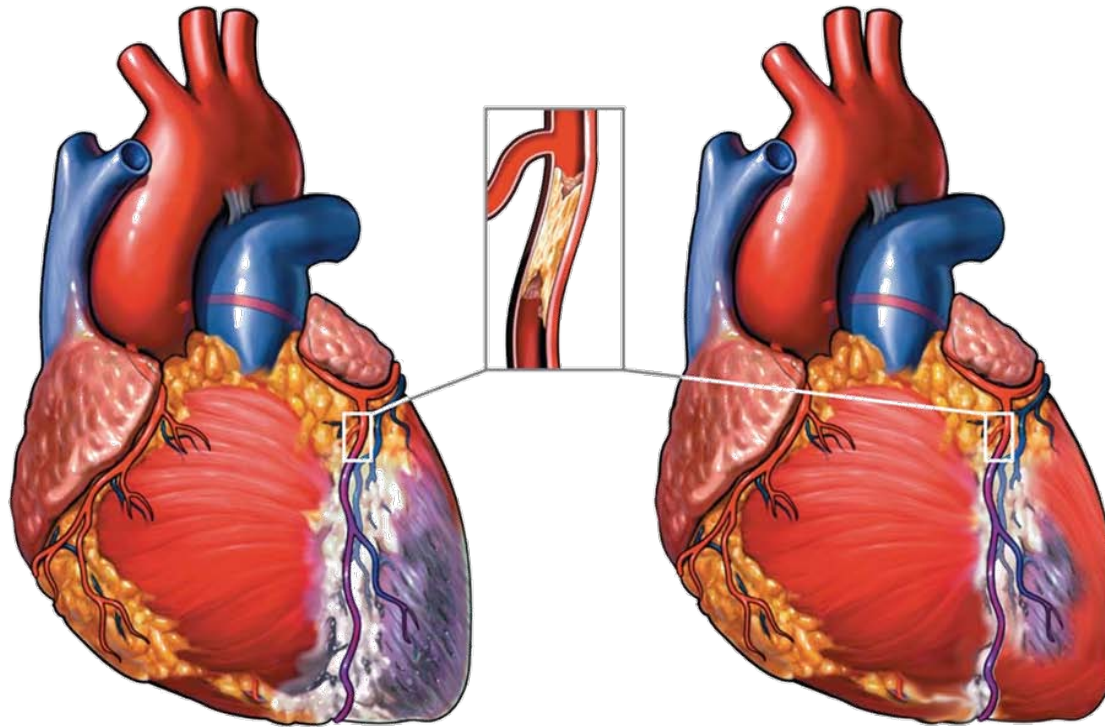
- Successful Phase 2a trial in elective PCI
- Patented NCE based on enhanced safe natural drug
- CMX-2043 targeting large, unmet market need
- Well defined endpoints
- Funding to complete Phase 2b trial
- Strong pipeline

---

# APPENDIX

# Ischemic Damage & Reperfusion Injury

---



# CMX-2043 Clinical Advisory Board

---

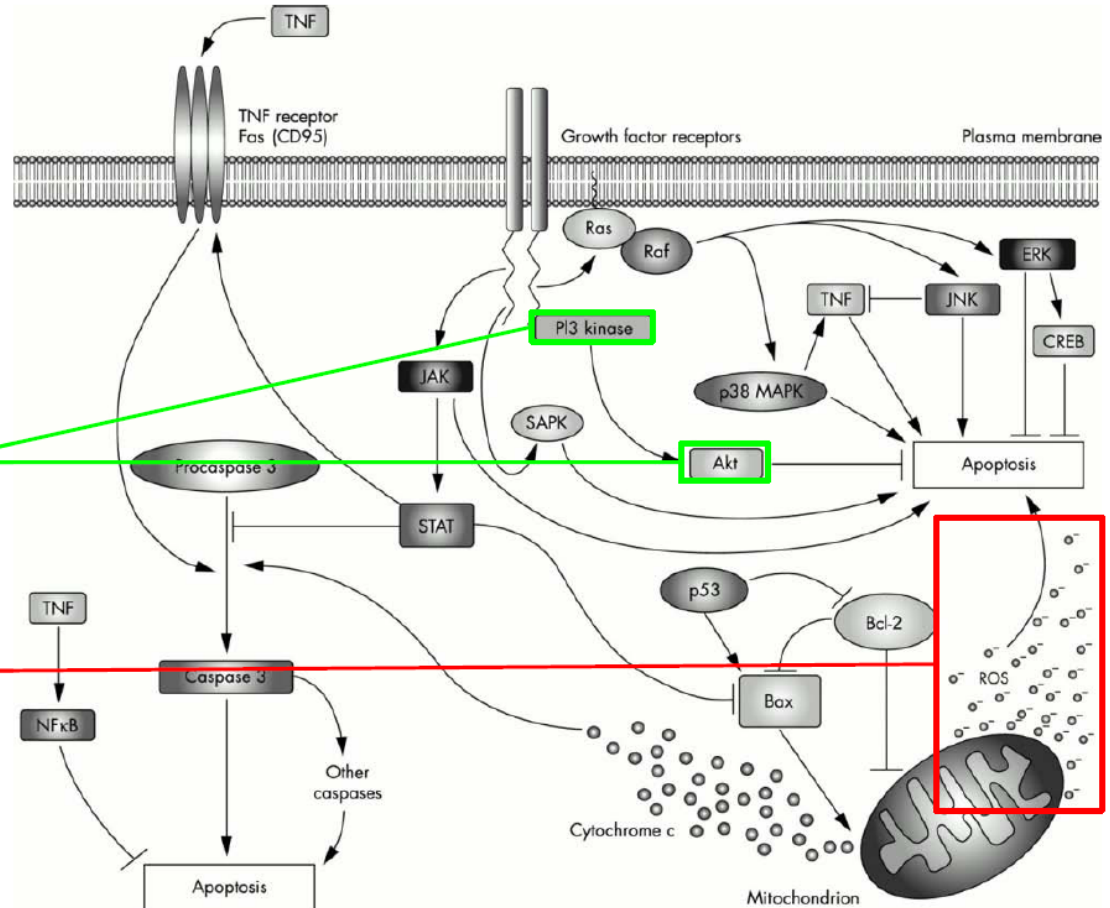
Name	Affiliation
James Tcheng MD, FACC, FSCAI, FESC	Professor of Medicine, Dept. of Medicine/Cardiology Duke University
Michael Gibson MS, MD	Assoc. Professor of Medicine, Harvard Medical School Director, TIMI Data Center Assoc. Editor, Journal American College of Cardiology
Mitch Krucoff MD, FACC, FCCP	Professor of Medicine, Dept. of Medicine/Cardiology Duke University

# Ischemia-Reperfusion Injury: Overview

## Pathways involved in Ischemia-Reperfusion Injury

CMX-2043 inhibits apoptosis and increases cell survival through two distinct mechanisms:

1. Activation of PI3K/AKT cell survival pathway which blocks apoptosis
2. Reduces levels of Reactive Oxygen Species (ROS)



Krijnen PAJ et al. J Clin Pathol 2002 55:801-811

# Universal Definition of Myocardial Infarction (MI)

---

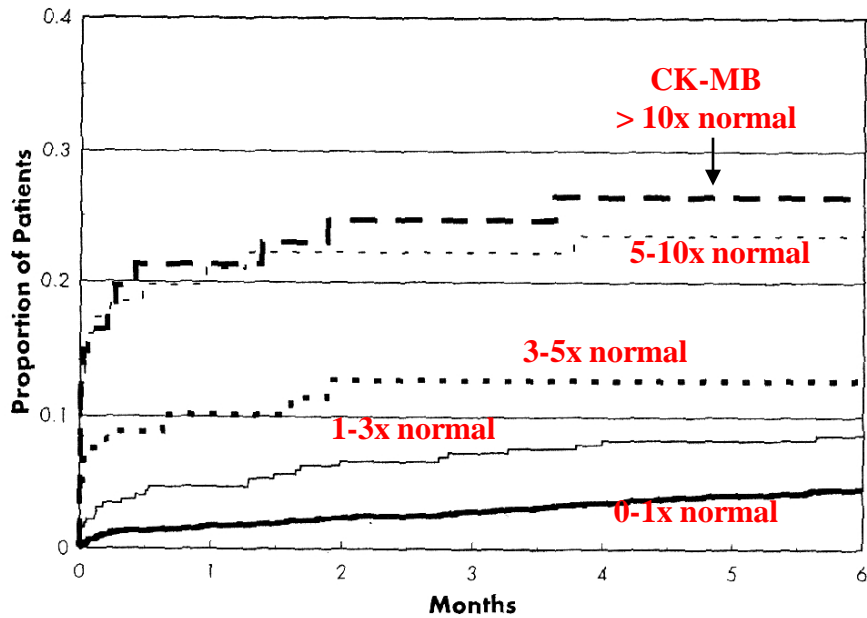
“For percutaneous coronary intervention (PCI) in patients with normal baseline troponin values, elevations of cardiac biomarkers above the 99th percentile URL are indicative of peri-procedural myocardial necrosis. By convention, increases of biomarkers greater than 3 x 99th percentile URL have been designated as defining PCI-related myocardial infarction (MI).”  
AHA, ACC, ECS, WHO

Thygesen, K., Alpert, J.S., White, H.D. et al., “Universal definition of myocardial infarction.”  
European Heart Journal (2007), 28, 2525-2538.

Accepted by FDA in direct communication with Medicare leading to SPA.  
(Dr. A. Friesen, personal communications with US FDA)

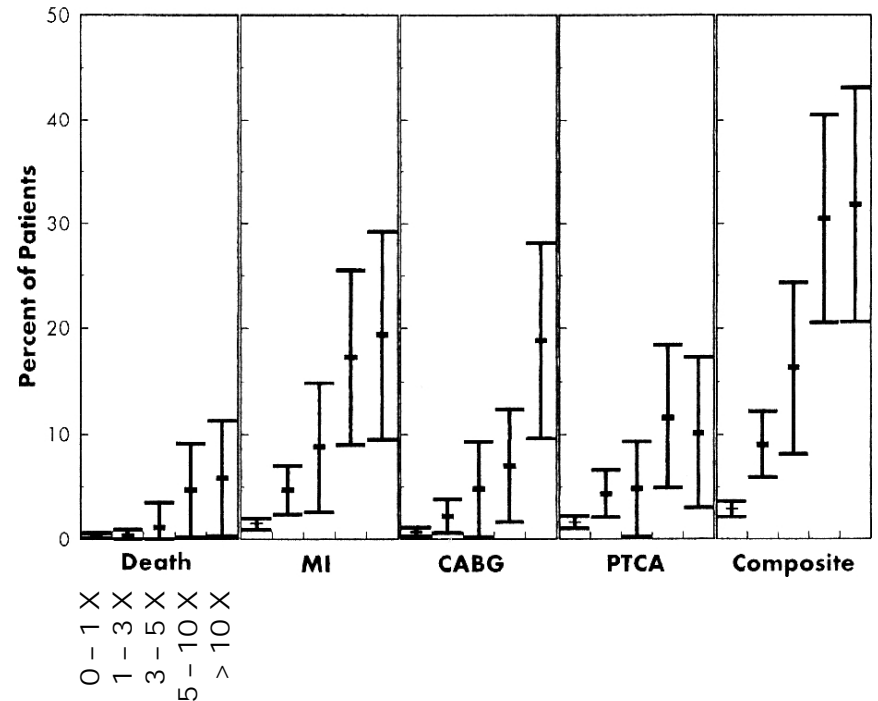
# CK-MB Correlation to Outcome

CK-MB Elevation Predicts Incidence of death and MI at 6 months post PCI

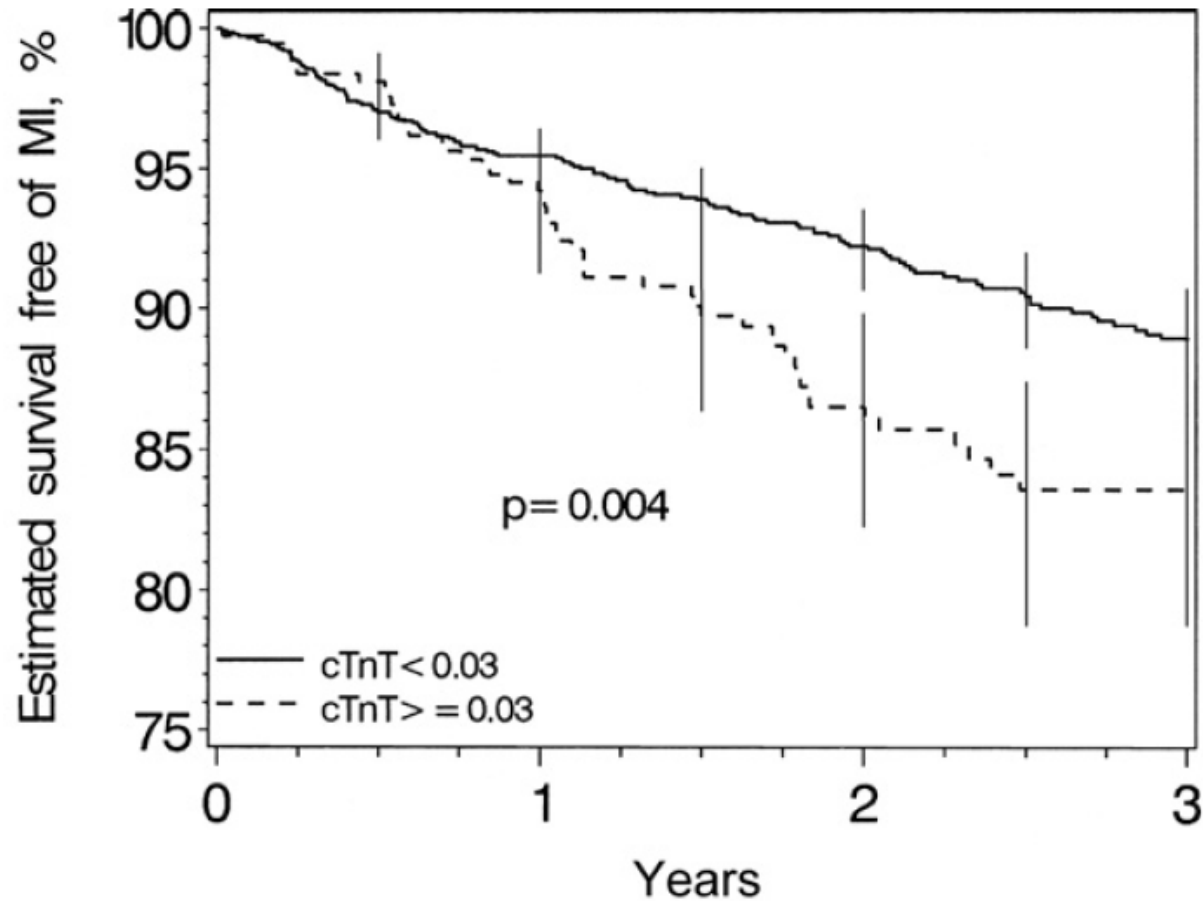


Results from IMPACT II Study  
Tardiff et. al. JACC 1999;33:88-96

CK-MB Elevation Predicts Events at 30 days post PCI (95% confid. interval)



# Mortality rates correlate with cardiac troponin T levels post PCI



Prasad A. et al., JACC 2006;48:1765-1770