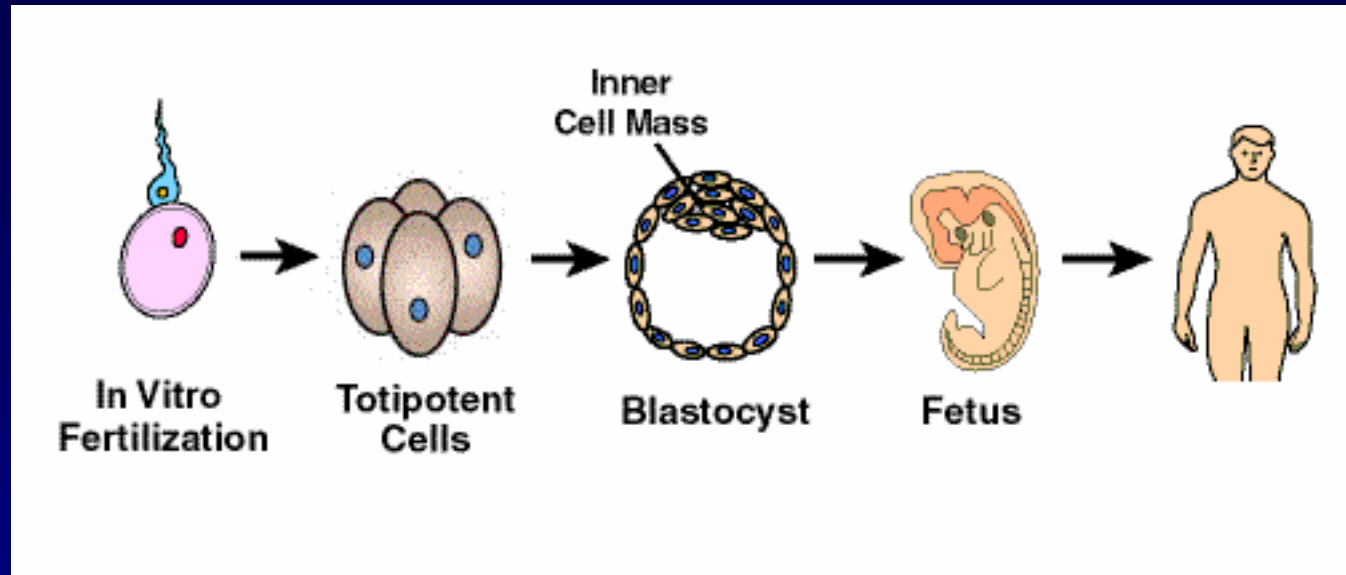




## **Road to Stem Cell Commercialisation**

**November, 2007**

# Stem Cells - Sources



**Embryonic stem cell:** present in inner cell mass of the blastocyst; pluripotential, easily grown to very large numbers, easily manipulated

**Embryonic germ cell:** primordial germ cells in the 5-10 week fetus; pluripotential, difficult to grow and access

**Adult stem cell:** present in adult tissue, e.g. bone marrow, cord blood, fat; multipotential, easy to access, grow and manipulate



## ***Advantages Of Stem Cells Over Other Medical Therapies***

- **natural biologicals, safer, less side-effects**
- **building blocks for wide range of tissues  
(blood, bone, cartilage, fat, vessels, heart muscle)**
- **regenerate tissues, reducing long-term health care costs**
- **restore function and quality of life**



## ***Embryonic Stem Cells: Major Concerns***

- ethical concerns
- need cloning to prevent immune rejection
- uncontrolled growth and risk of cancer

## ***Mesoblast's Adult Stem Cells: Significant Advantages***

- no ethical issues
- more mature, easier to regulate growth
- avoid immune rejection, unique business model



## **our patented adult stem cells deliver an efficient high margin business**

*an off the shelf product with margins equivalent to a pharmaceutical*

- one donor -- thousands of patient doses
- unrelated recipients
- frozen product immediately available -- good physician uptake
- low manufacturing costs, high margin
- centralised manufacturing (FDA and GMP compliant)
- a biologic - safer than small molecules, more rapid regulatory approval
- multiple orthopaedic and cardiovascular indications



## Major Accomplishments Since Listing

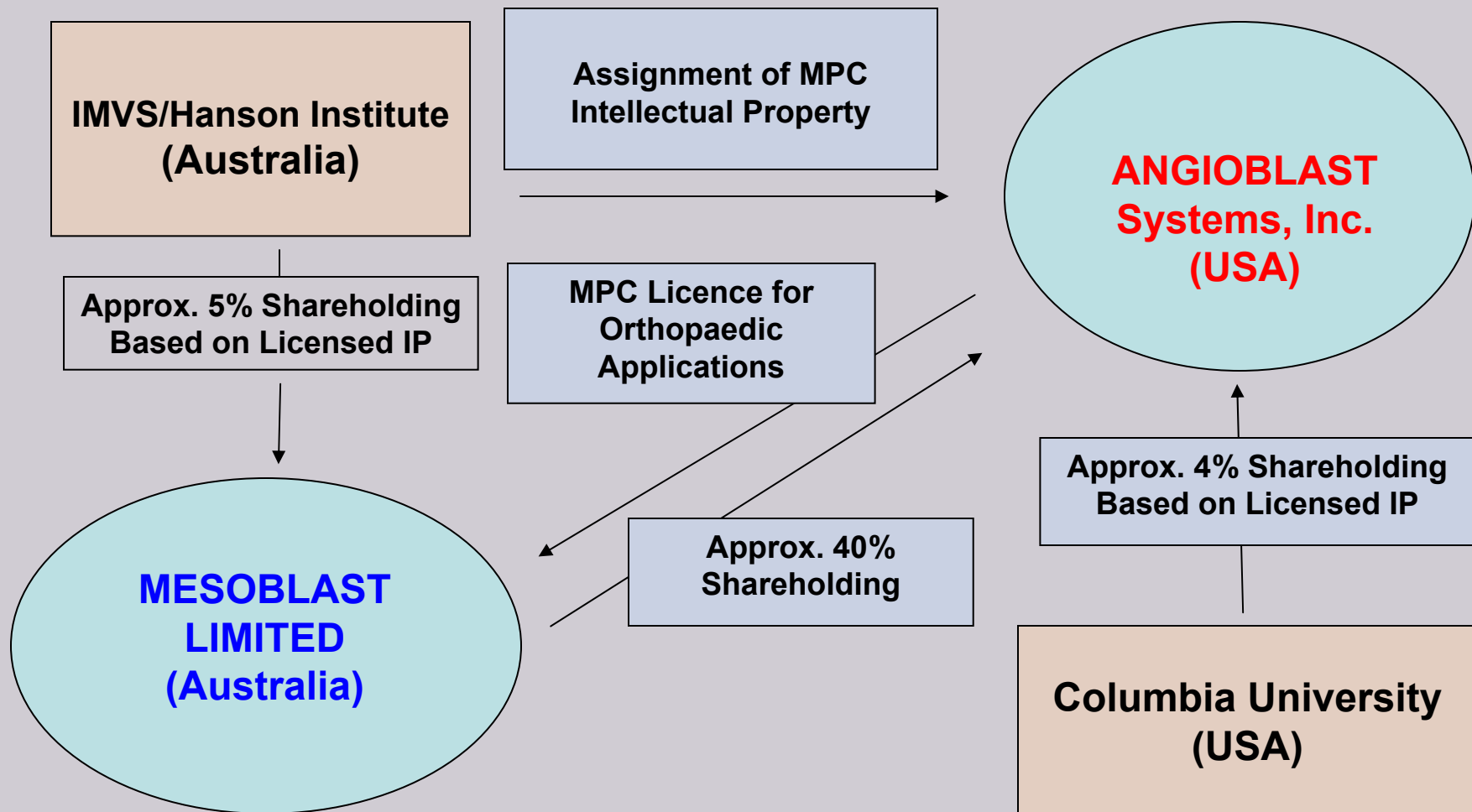
1. Granted composition-of-matter stem cell **patent in United States**, world's largest market, with further international patents pending
2. Demonstrated **scale-up** of stem cell manufacturing process
3. Demonstrated **safety** of manufacturing and cells in patients
4. Evidence of **efficacy** in pilot clinical trials in non-union fractures
5. Evidence of **efficacy** in pilot clinical trials of angina/heart failure

## Major Accomplishments Since Listing, c'td

- \_\_\_\_\_ 6. Shown effectiveness of **allogeneic** (“off-the-shelf”) stem cells in fracture repair, spinal fusion, knee osteoarthritis pre-clinical models
7. Shown effectiveness of **allogeneic** (“off-the-shelf”) stem cells in heart attack and heart failure pre-clinical models
8. Received US **FDA clearance** for **allogeneic** Phase 2 clinical trial in patients needing spinal fusion
9. Received US **FDA clearance** for **allogeneic** Phase 2 clinical trial in patients with acute myocardial infarction (heart attack)
10. Commenced both Phase 2 clinical trials in US

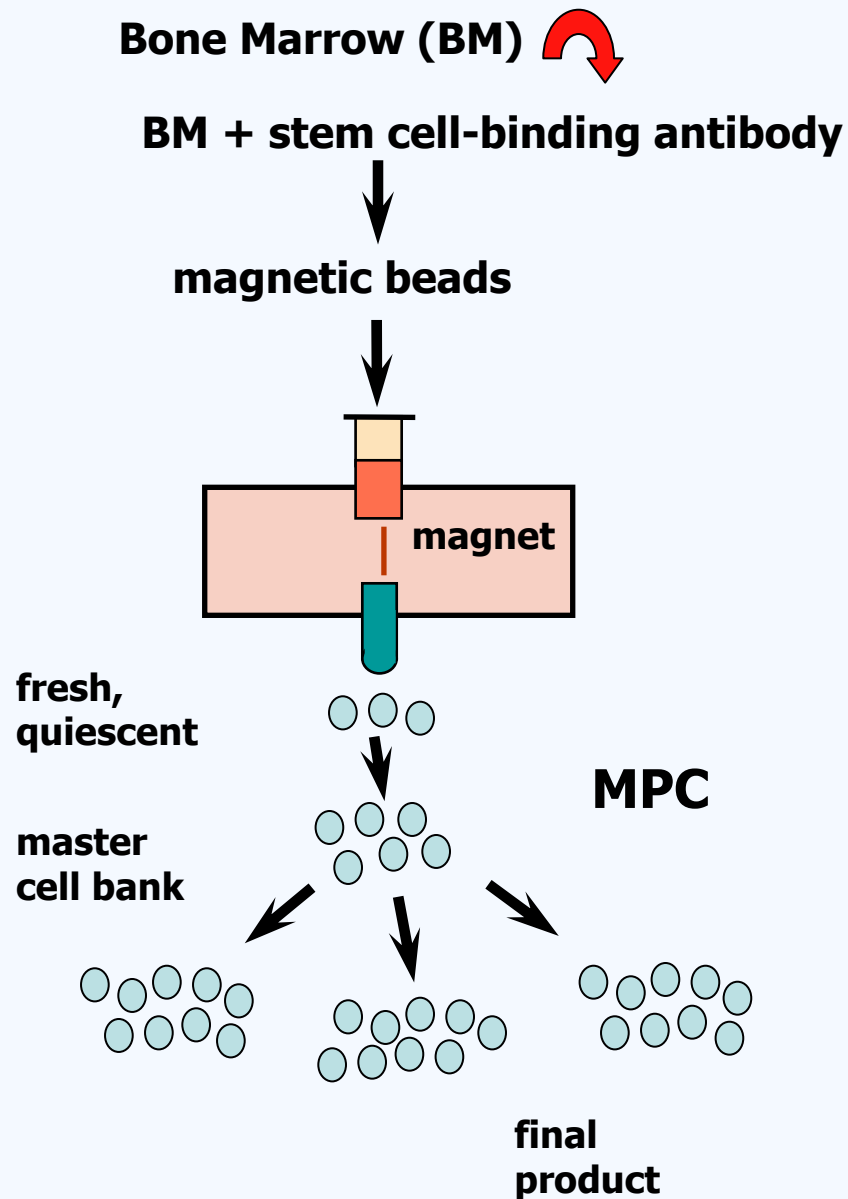


## Enhancing Shareholder Value Through Corporate Structure





## Proprietary MPC Isolation

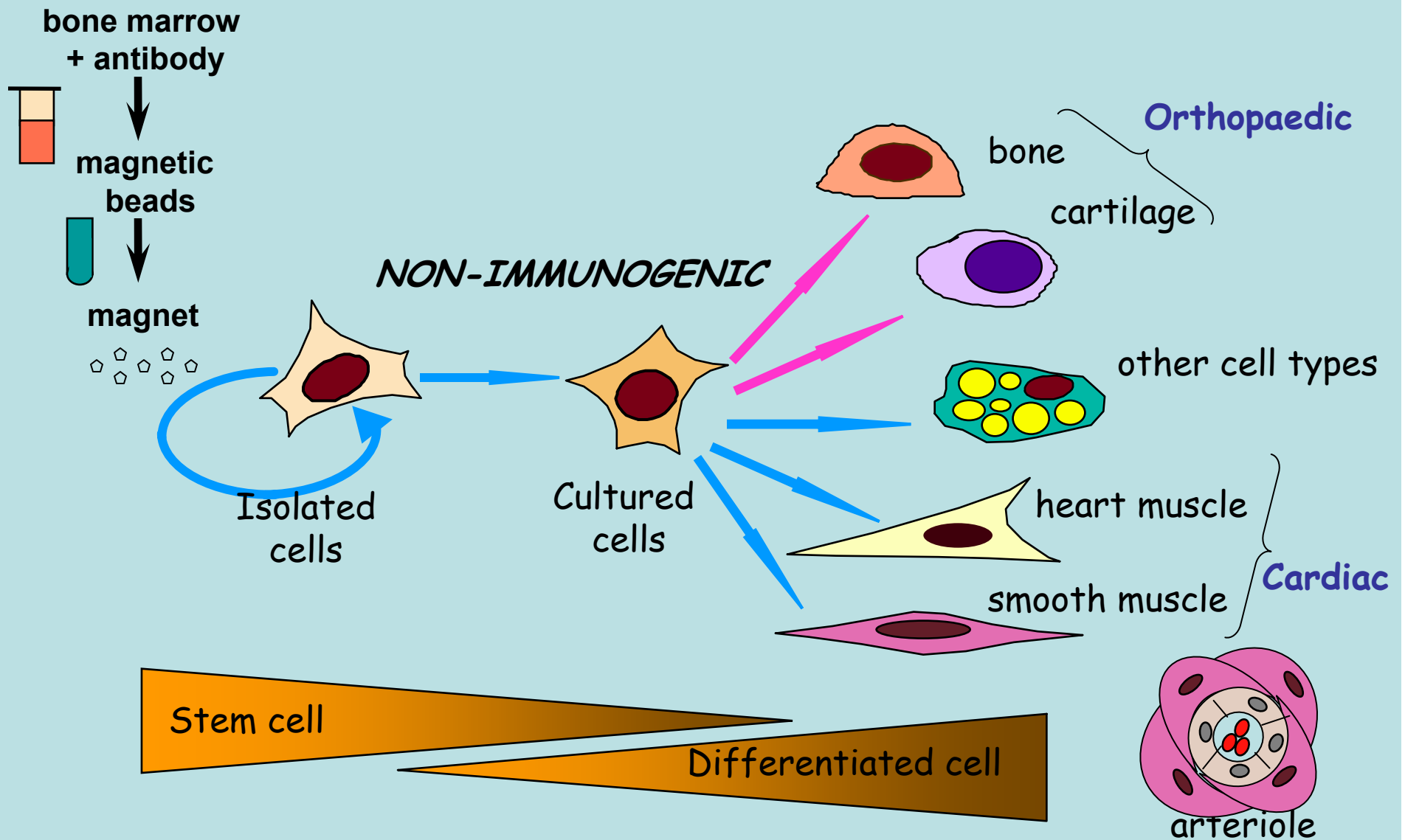


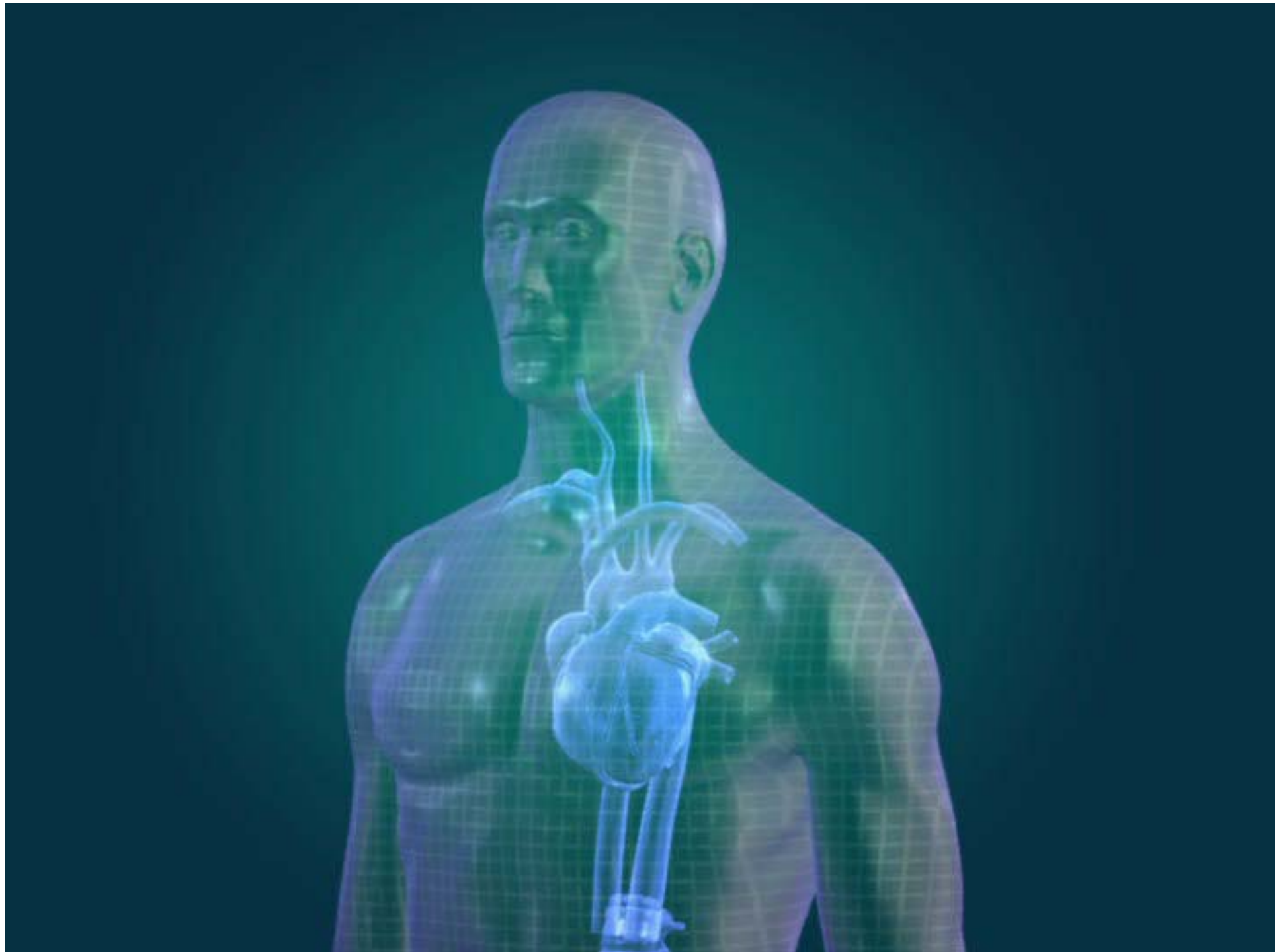
### *Competitive Advantages:*

*Precise identification,  
ease of isolation and scale-up*

- purer initial stem cell pool
- homogeneous population
- efficient large-scale expansion
- lower costs of cell culture process
- batch-to-batch consistency
- stringent release criteria
- greater potency of expanded product

# Our Experience Proves Efficient Commercial Stem Cell Production, With High Safety Profile







## Road To FDA Approvals For An Allogeneic Stem Cell Product

### *Preclinical*

- characterize stem cell population
- proof-of-principle small animal studies
- optimize *ex vivo* culture process in GMP facility
- safety/dose-ranging studies in appropriate large animal model (e.g sheep)

### *Clinical*

- phase 2 trials to identify safe, effective dose
- phase 3 trials to establish efficacy for product registration

## ***Lead Clinical Programs***

### **1. Non-union long bone fracture repair**

**Phase 1b clinical trial completed,  
IND submission for Phase 2a clinical trial early 2008**

### **2. Spinal Fusion**

**Phase 2a clinical trial IND cleared by FDA <30 days,  
patient implantation commenced at Hospital for Special  
Surgery in New York**

### **3. Knee Osteoarthritis**

**IND submission for Phase 2a clinical trial in 2008**

## Treatment Of Non-Union Long Bone Fractures\_\_

- pilot trial at Royal Melbourne Hospital
- 10 patients with non-union of long bone fractures
- safety of own (autologous) culture-expanded MPC
- evaluate manufacturing process in a clinical environment

### *experience to date*

- all 10 patients have been implanted
- good safety profile, no acute or mid term reaction to stem cells
- positive interim efficacy data
- complete union in 5/5 patients followed out to 12 months (primary study endpoint)

## **MPCs Induce New Bone Growth And Union In A Patient With Femoral Fracture And Non-Union After 9 Months**



baseline



6 wks post-MPC  
implantation



12 wks post-MPC  
implantation

## MPC repair of distal tibia fracture non-union

**Pre-Implant**



**12 weeks  
Post-Implant**





# Knee Osteoarthritis



Compression / traction

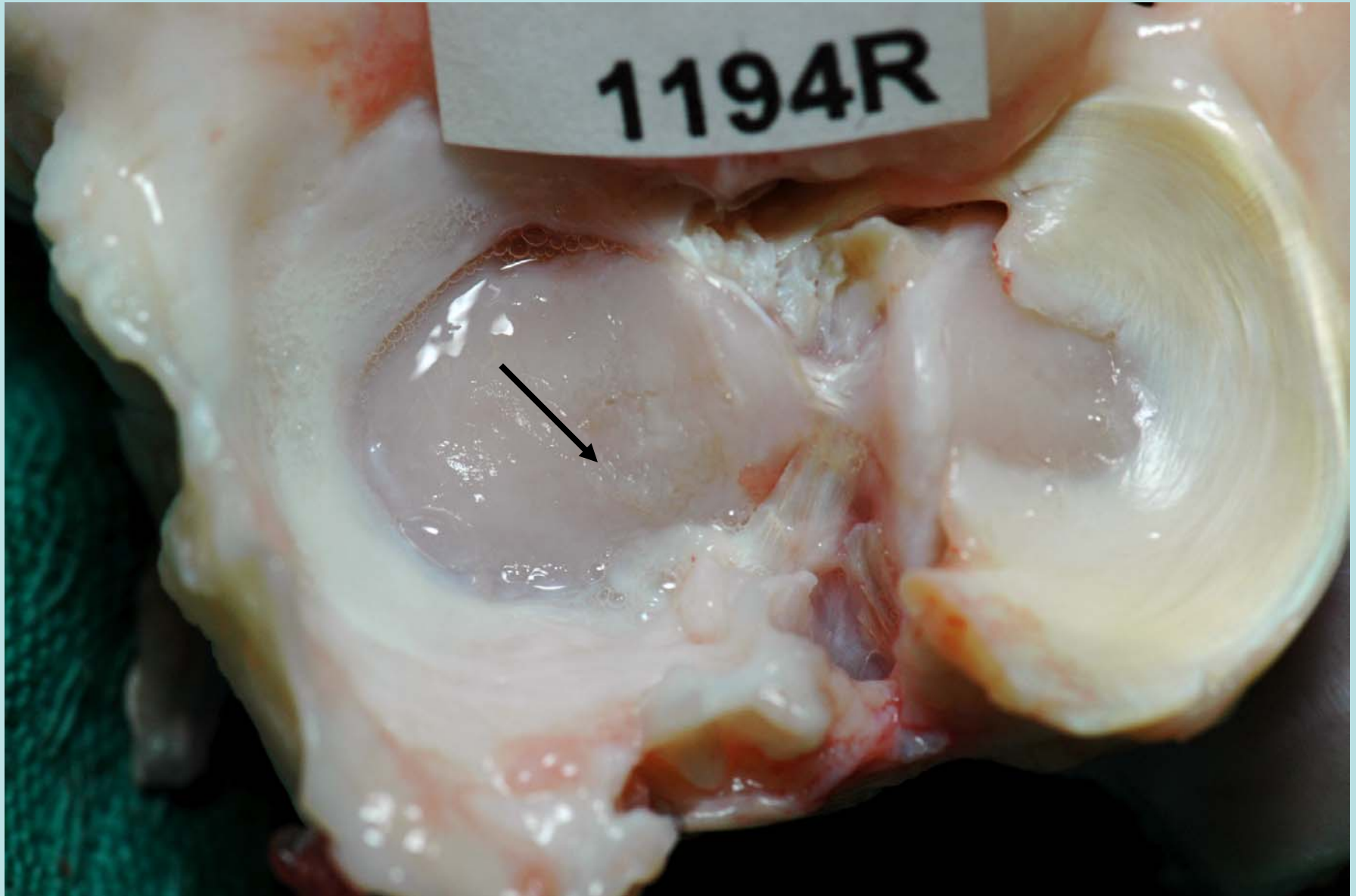
Lateral instability

Osteophyte formation

High impact stresses

Focal erosion



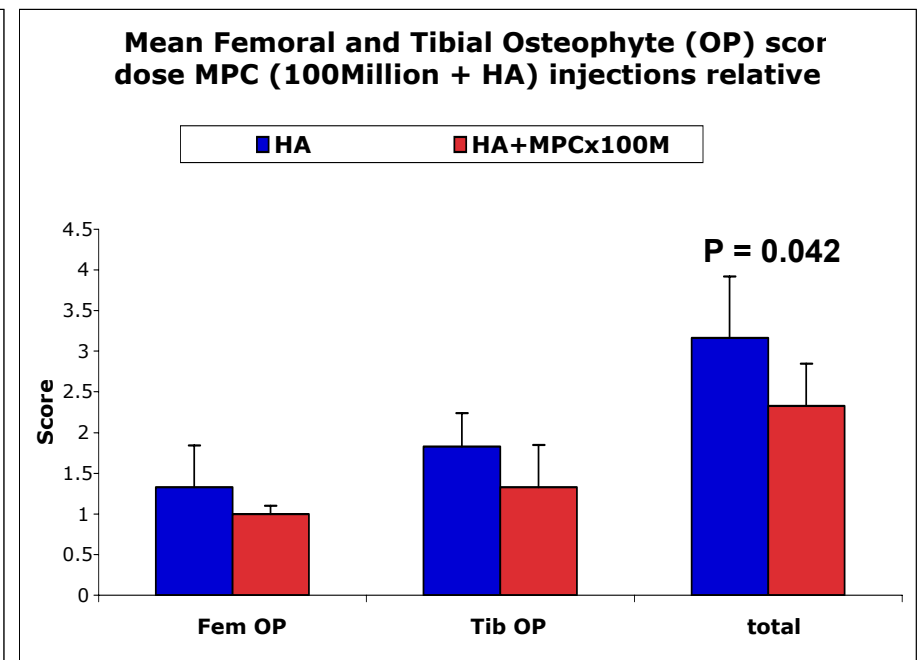
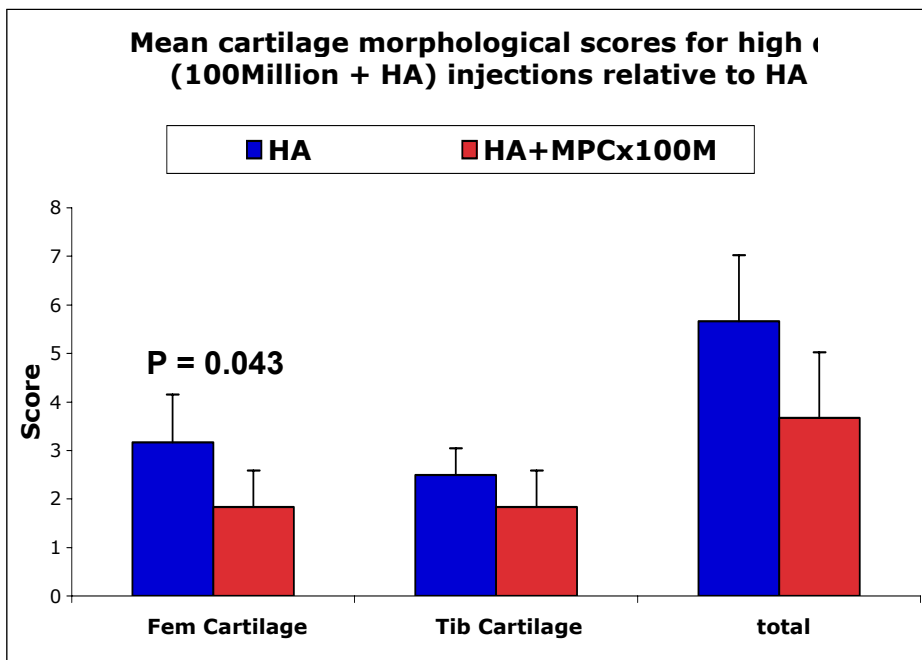


**Ovine Meniscectomy Model and Progressive Osteoarthritis**

# MPC Protect Femoral Condyle Against Cartilage Erosion



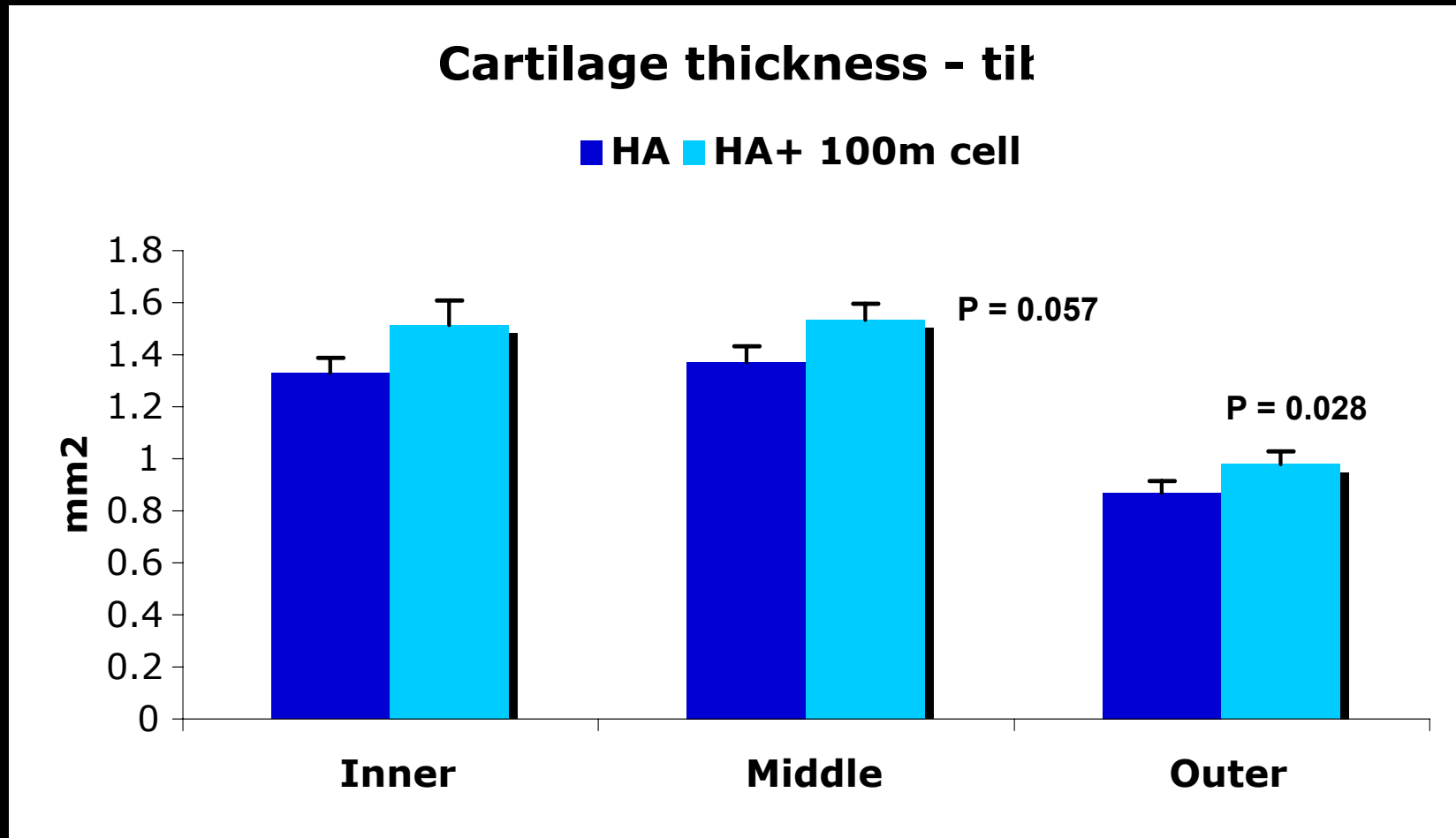
# MPC Protect Hyaline Cartilage Against Degradation And Prevent Osteophyte Formation



CARTILAGE

OSTEOPHYTES

# MPC Increase Thickness Of Tibial Cartilage



***Cardiac Programs In Partnership With Angioblast Systems, Inc.***

**1. Congestive Heart Failure (CHF):**

**Phase 1b clinical trial completed**

**Phase 2a clinical trial to commence 2008**

**2. Acute Myocardial Infarction (AMI)**

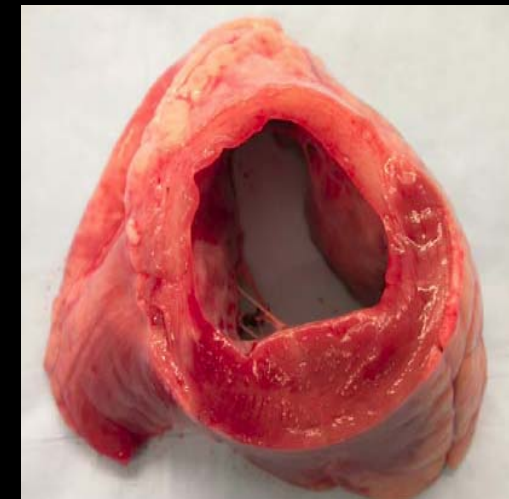
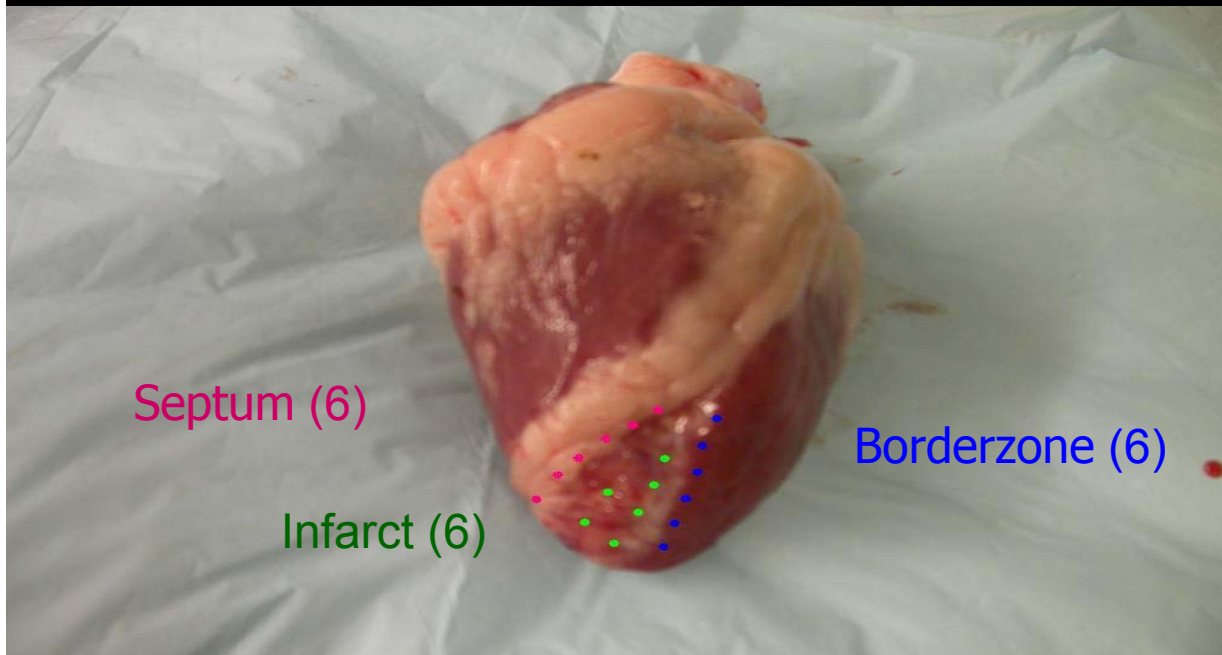
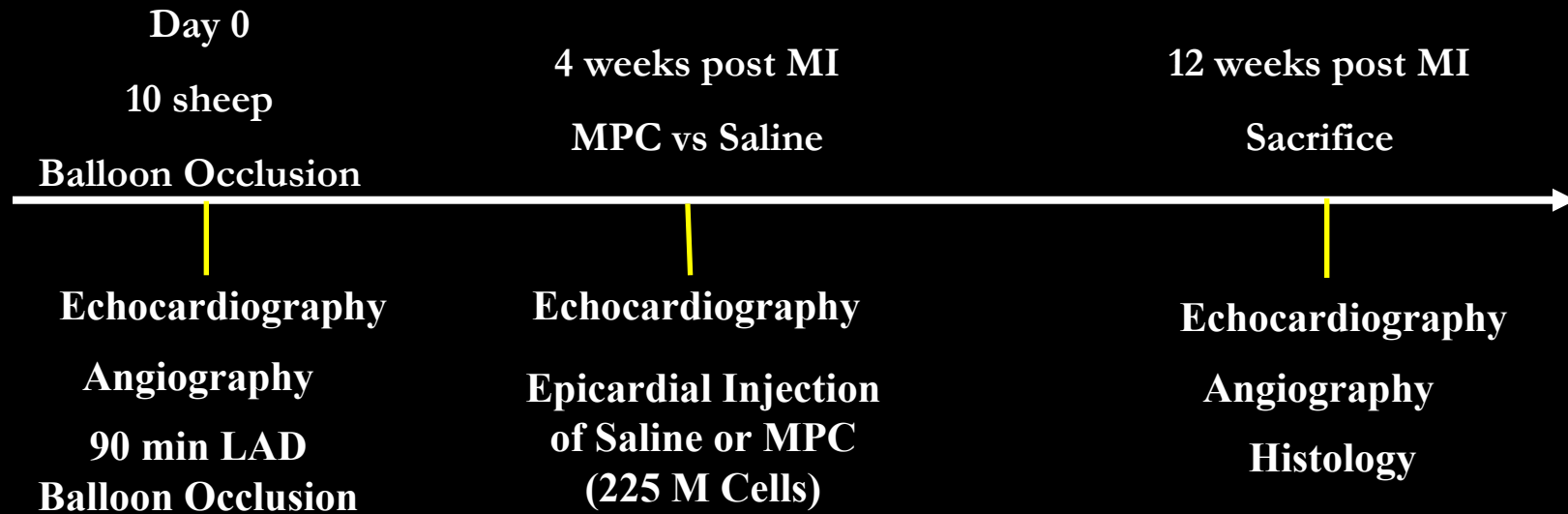
**Phase 2a clinical trial IND cleared by FDA**

**recruitment commenced at Texas Heart Institute**

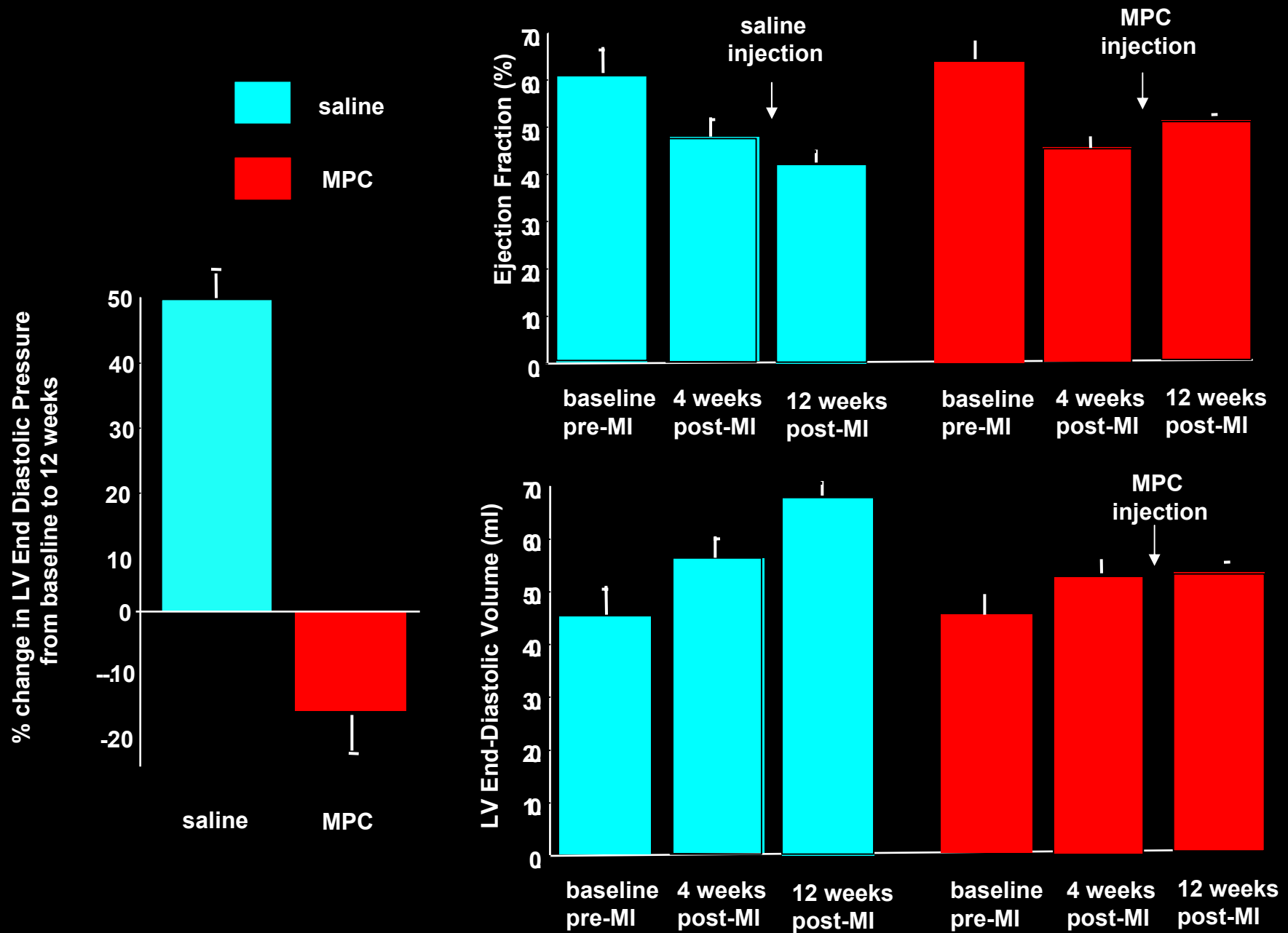
**3. Age-Related Macular Degeneration (AMD), and  
Diabetic Retinopathy**

**Phase 2a clinical trial to commence 2008**

# Allogeneic Sheep MPC For Heart Failure



# Allogeneic MPC Reverse Established Heart Failure





## Treatment Of Chronic Angina/Heart Failure

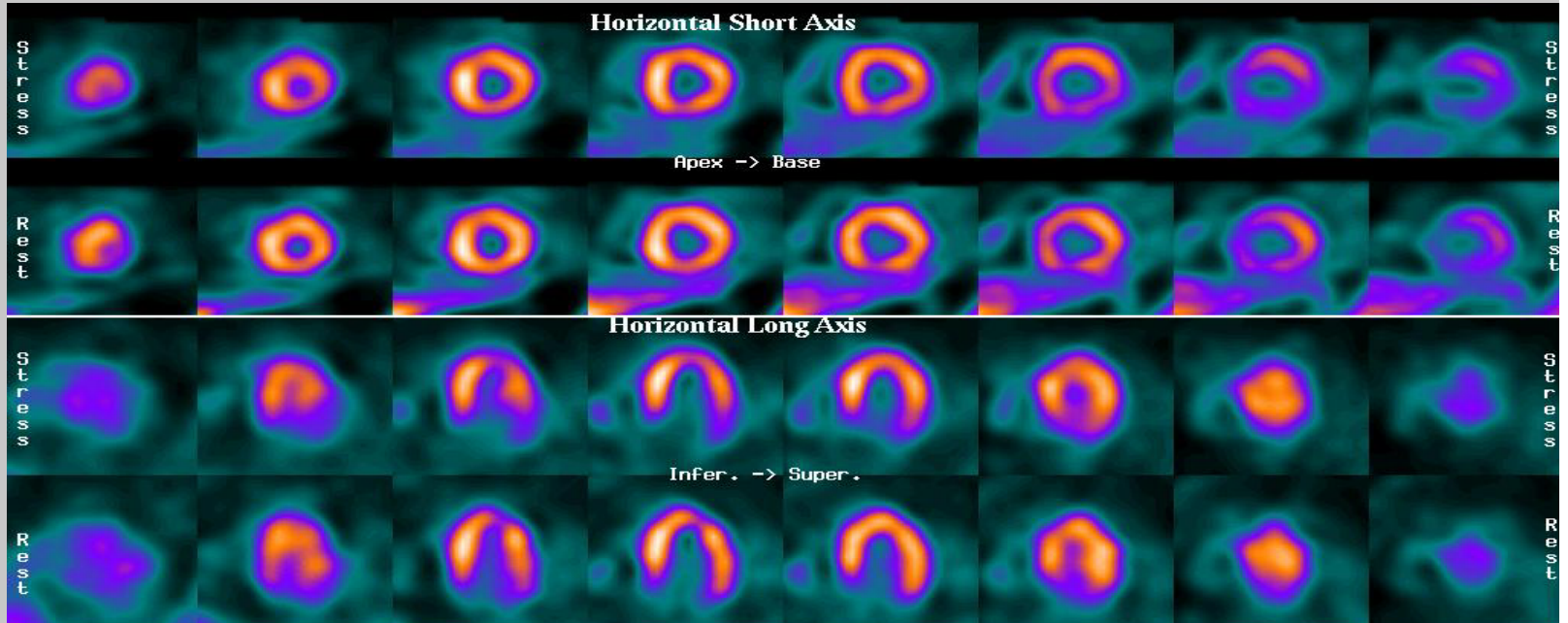
- pilot trial at John Hunter Hospital
- 6 patients with coronary artery disease, angina, heart failure
- safety of own (autologous) culture-expanded MPC
- evaluate manufacturing process in a clinical environment

### *experience to date*

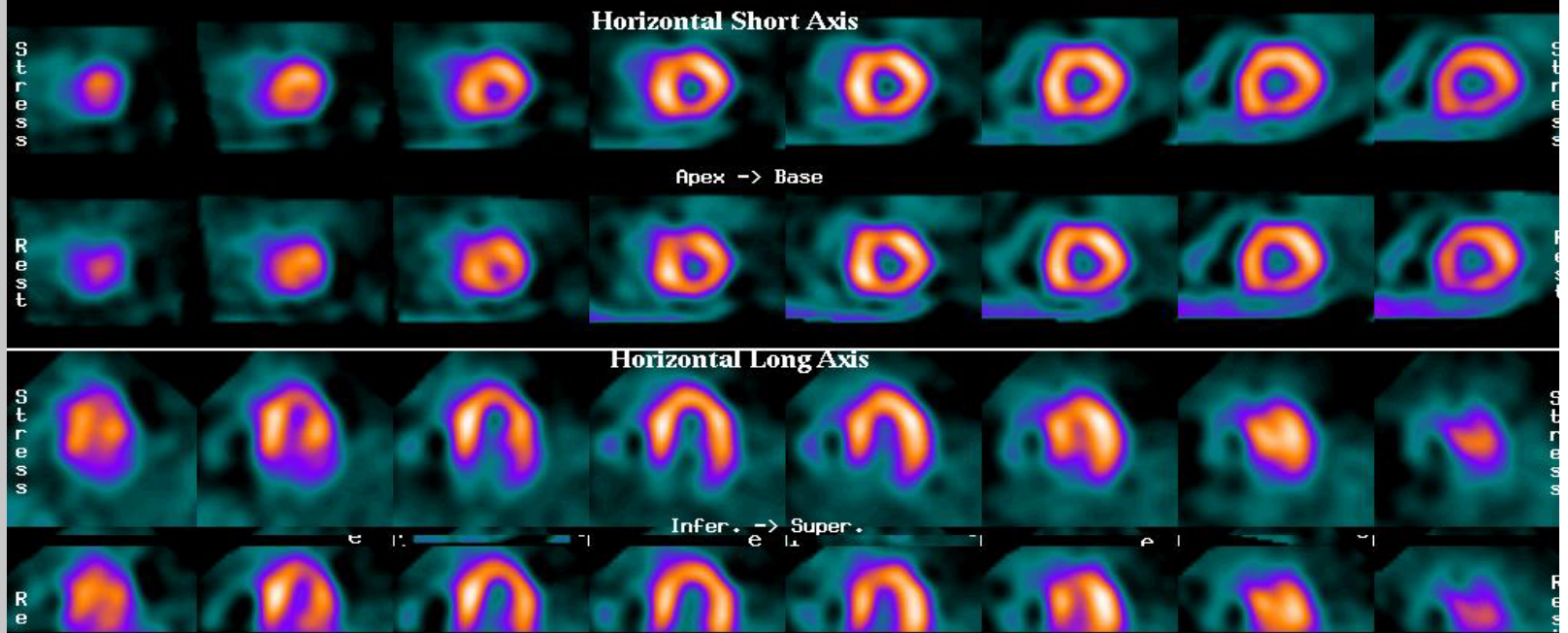
- all 6 patients have been safely implanted using J&J NOGA catheter
- good safety profile, no acute or mid term reaction to stem cells
- positive interim efficacy data
- improvement in anginal symptoms and heart muscle function in complete union in 6/6 patients

# MPC Increase Perfusion In A Patient With Chronic Ischemia

baseline

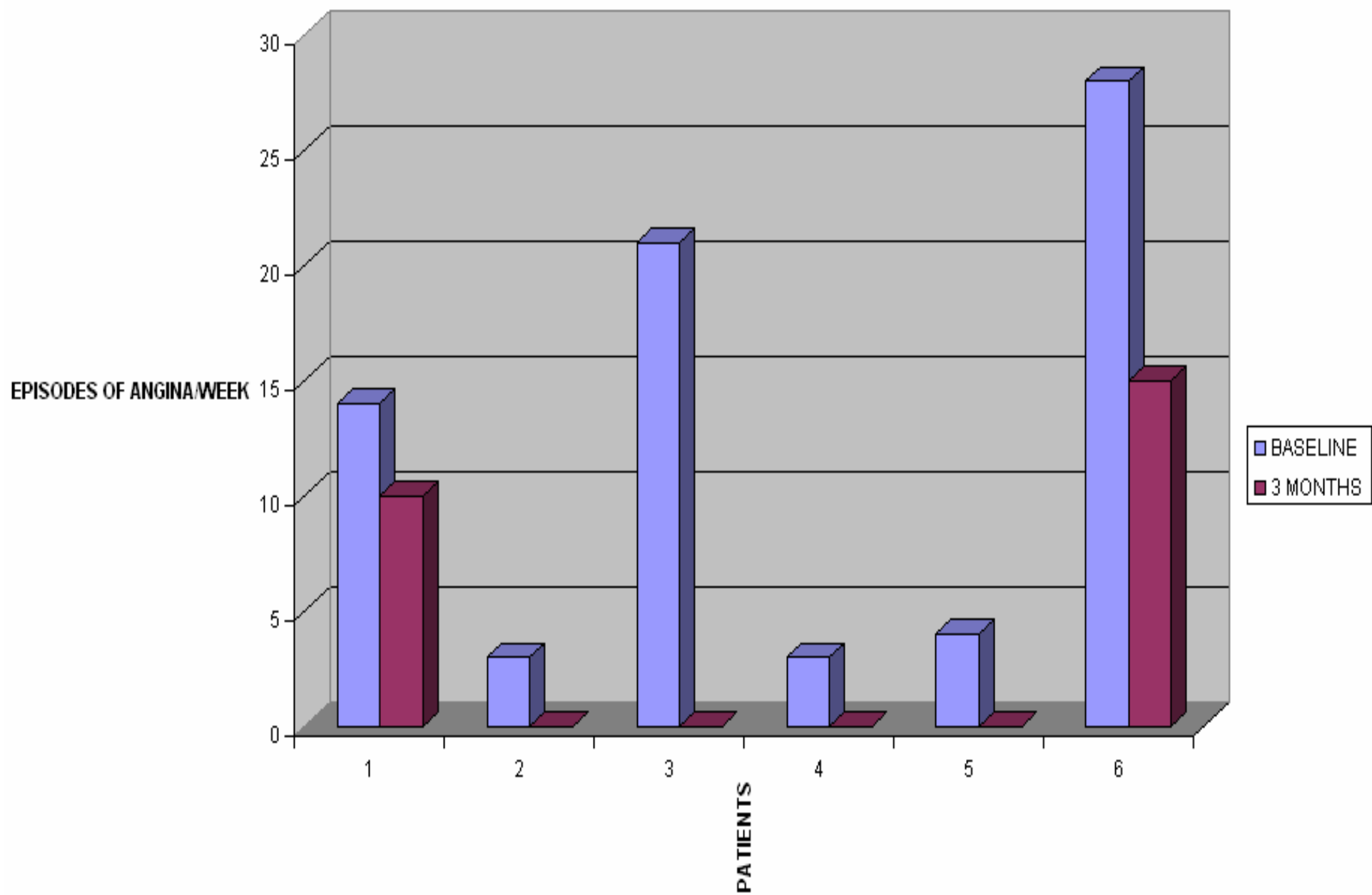


Six months  
post-MPC  
injection

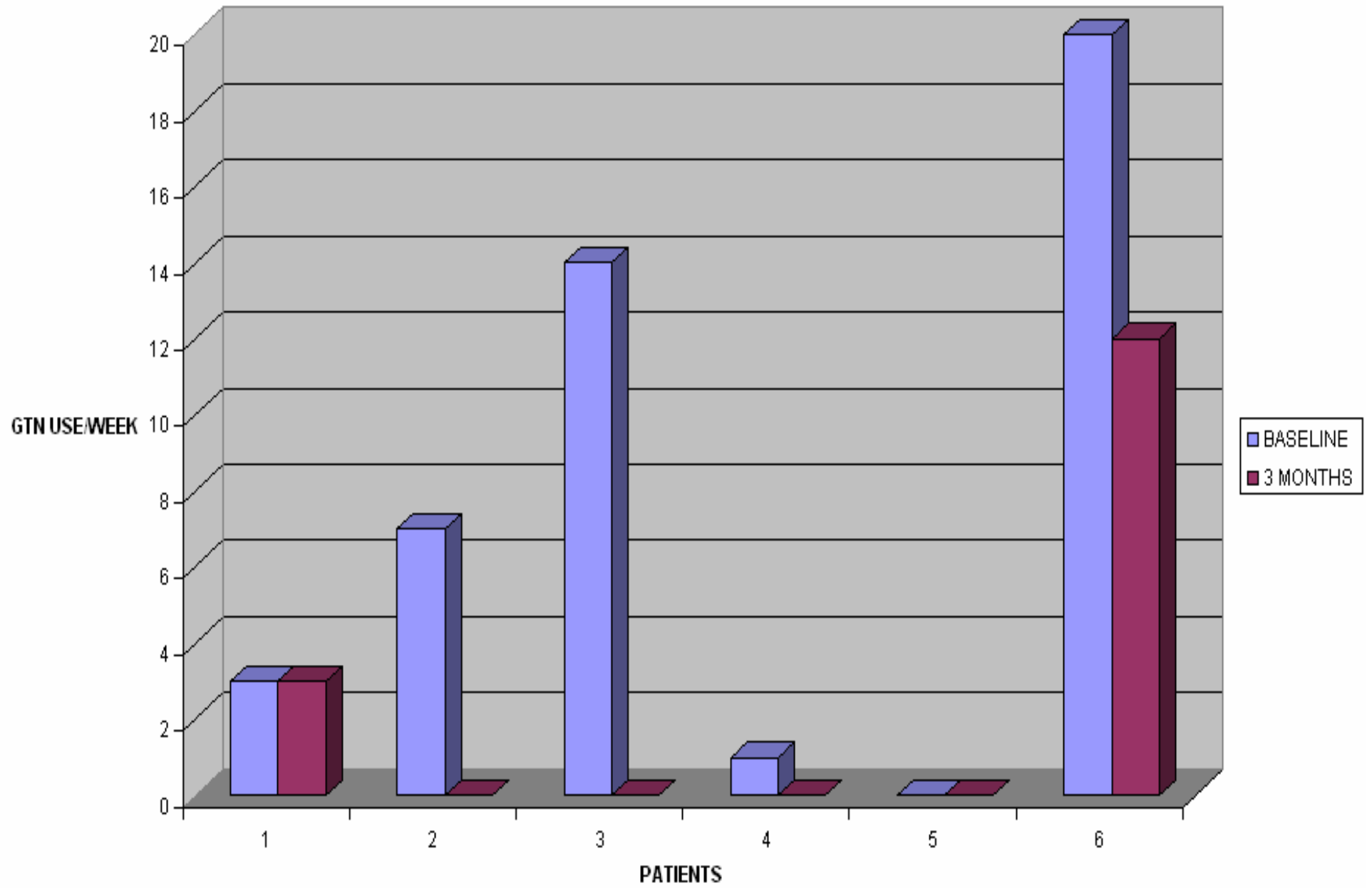


CONFIDENTIAL

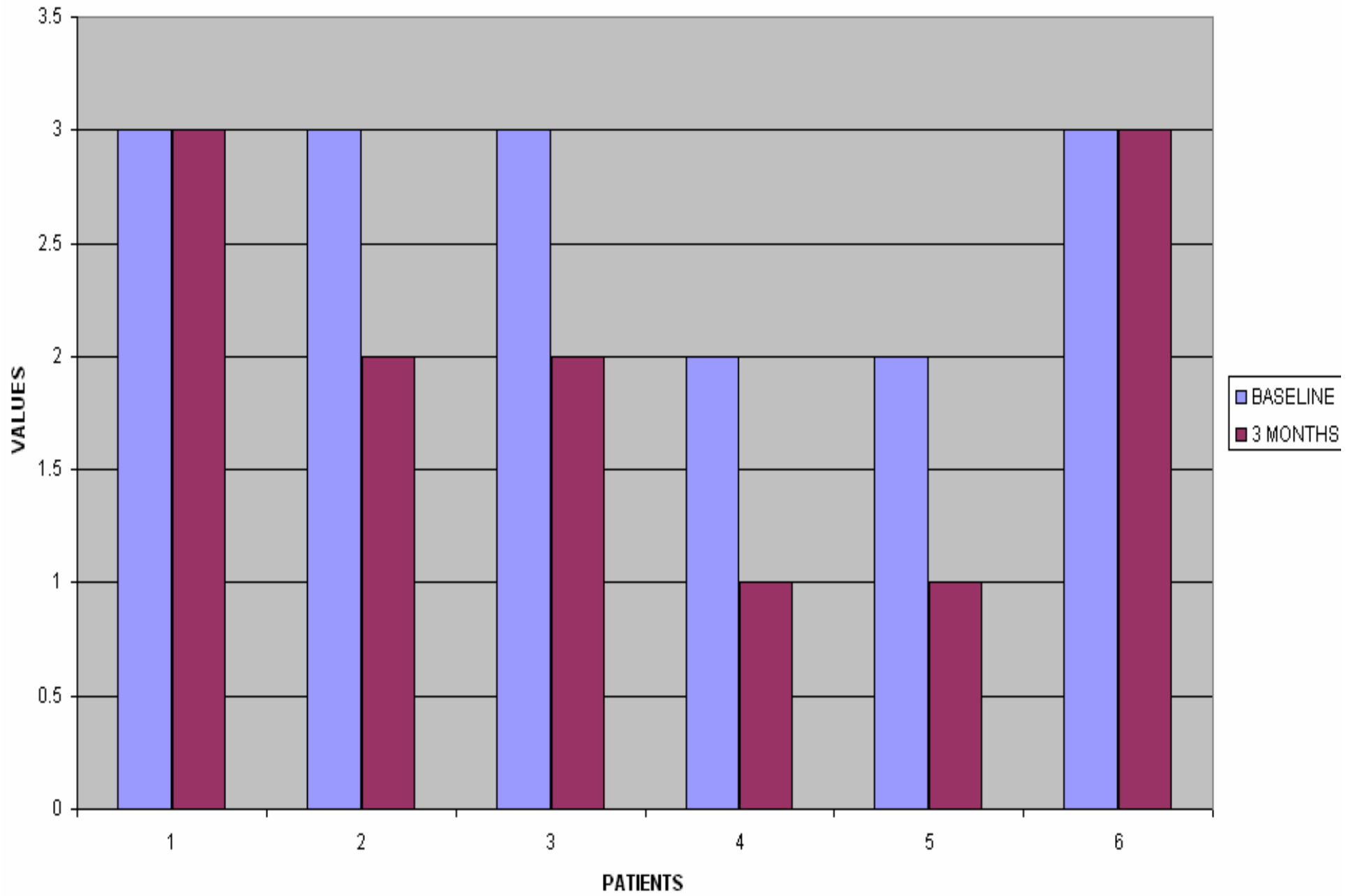
# ANGINA



# GTN USE



# NYHA



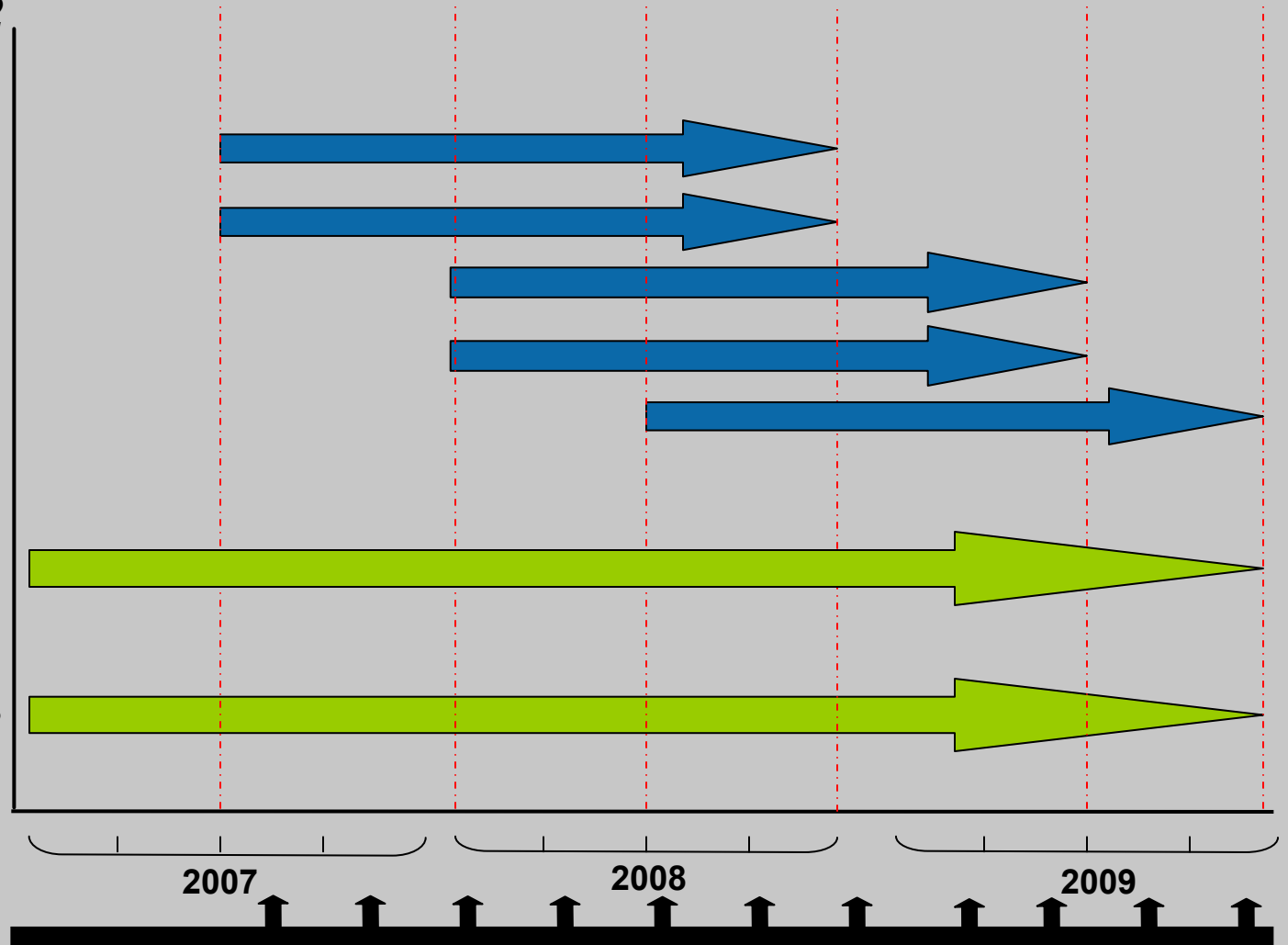
## Tracking Clear Value Drivers

### *Allogeneic Phase 2 Clinical Trials*

- spinal fusion
- heart attack
- tibial fractures
- heart failure
- knee osteoarthritis

IP Devt/ Pre-Clin R&D

Corporate Partnerships





## **Stem cells can deliver market leadership:** **opportunities for strategic partnerships**

- major pharmaceutical and medical device companies with market share of orthopaedic and cardiovascular fields proactively seeking transforming technologies
- Biologicals can convert generic devices to proprietary market leading products
- Mesoblast's adult stem cells ideal technology to enable market leadership --- opportunity for value-creating strategic partnership
- *major device companies*
  - Medtronic
  - J&J
  - Abbott
  - Smith and Nephew
  - Biomet
  - others
- *major pharma companies*
  - Merck
  - Lily
  - Pfizer
  - AstraZeneca
  - others