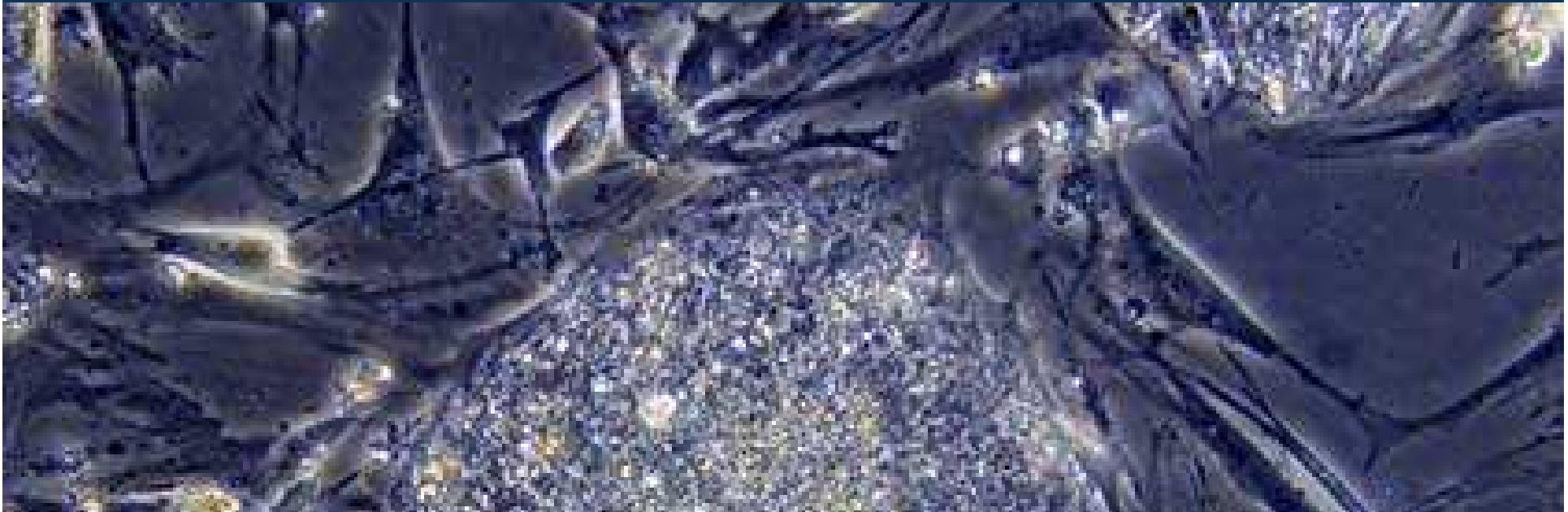


STEM CELLS and REGENERATIVE MEDICINE: SUCCESSES and CHALLENGES

Gregory A. Bonfiglio
Proteus Venture Partners

UC System-Wide Technology Transfer Forum – April 15, 2009

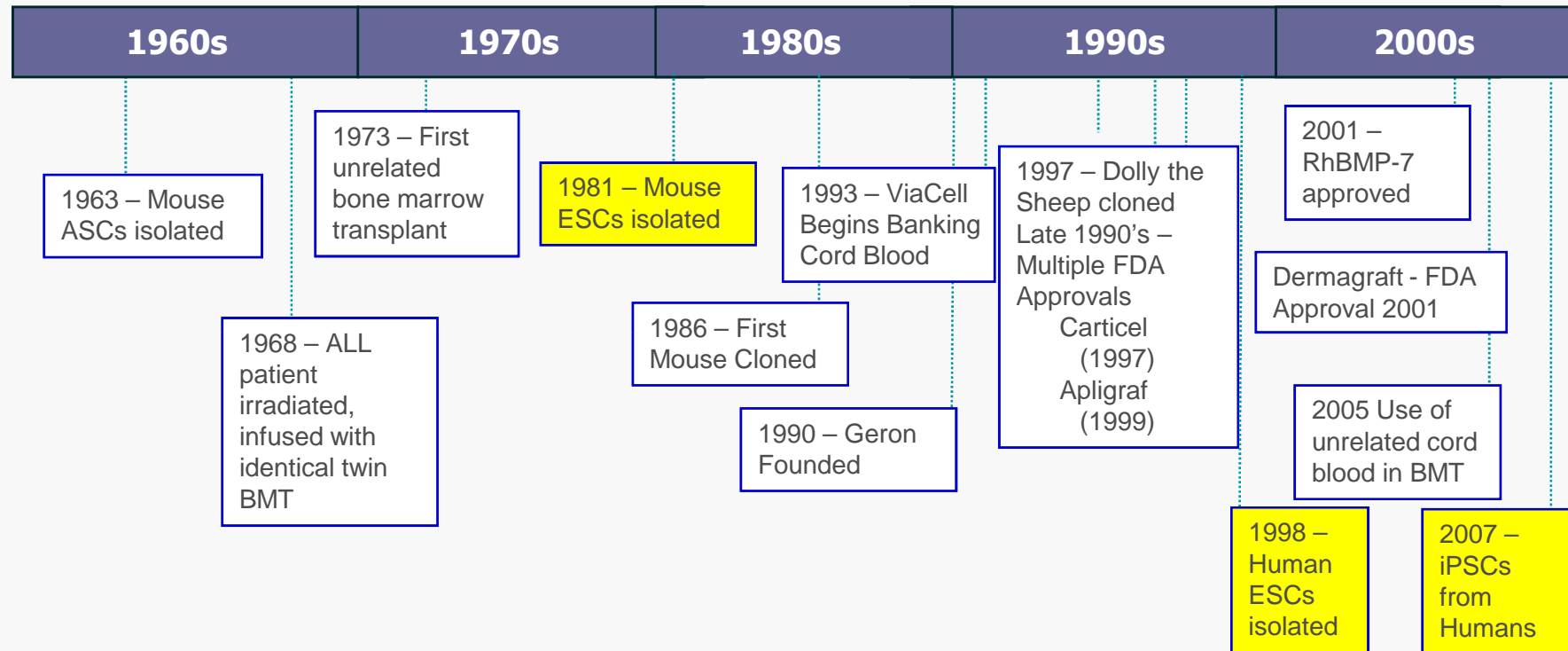


Panel Participants

- **Jane Lebkowski: SVP of Regenerative Medicine, Geron**
- **Pat Olson: Director of Scientific Activities, CIRM**
- **Paul Kemp: Founder, CSO and Executive Director, Intercytex, UK**
- **Frank Gleeson: CEO, Verio Therapeutics, Canada**

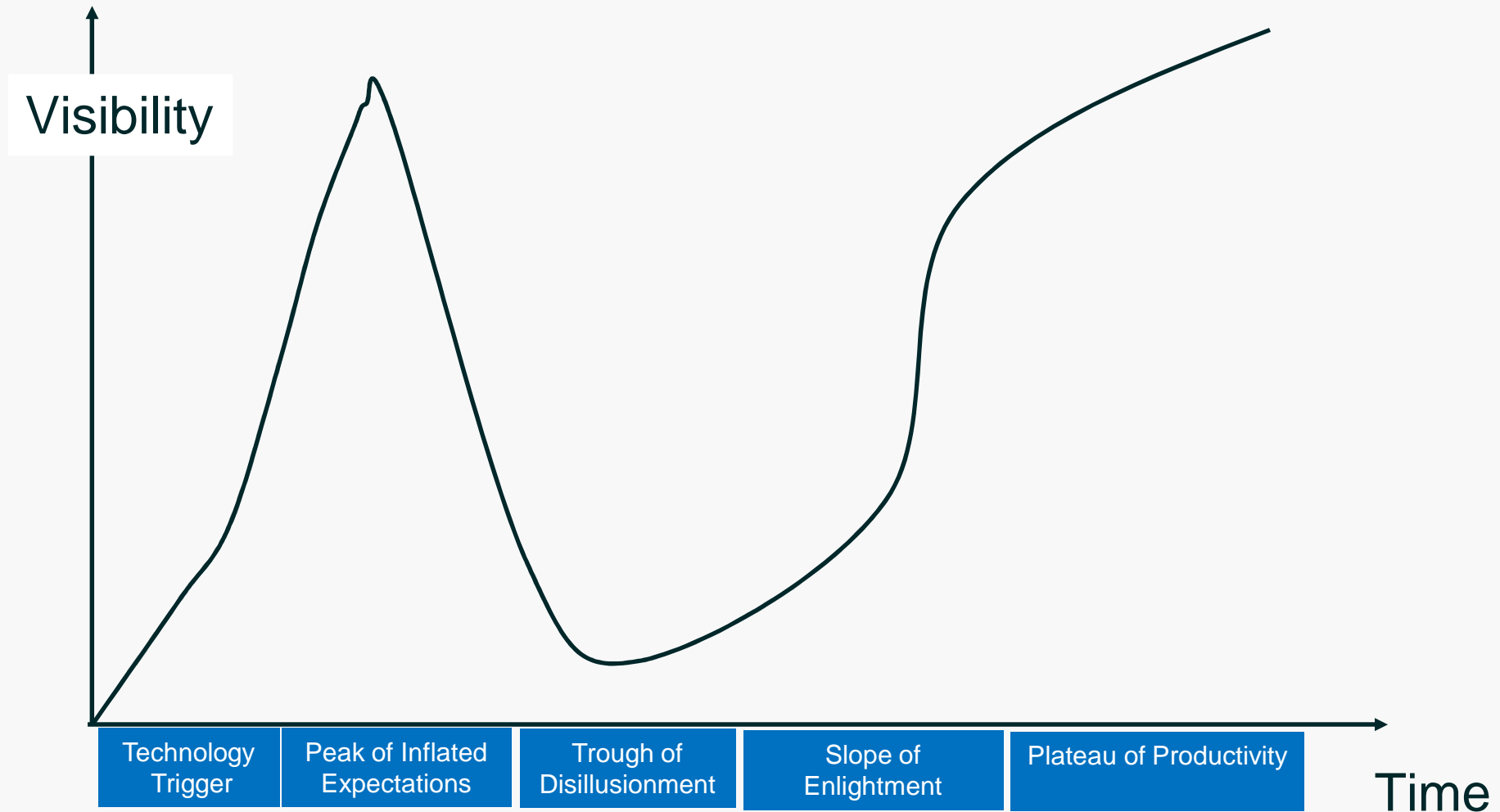
Development of Regenerative Medicine

Current technologies build on 40 years of research

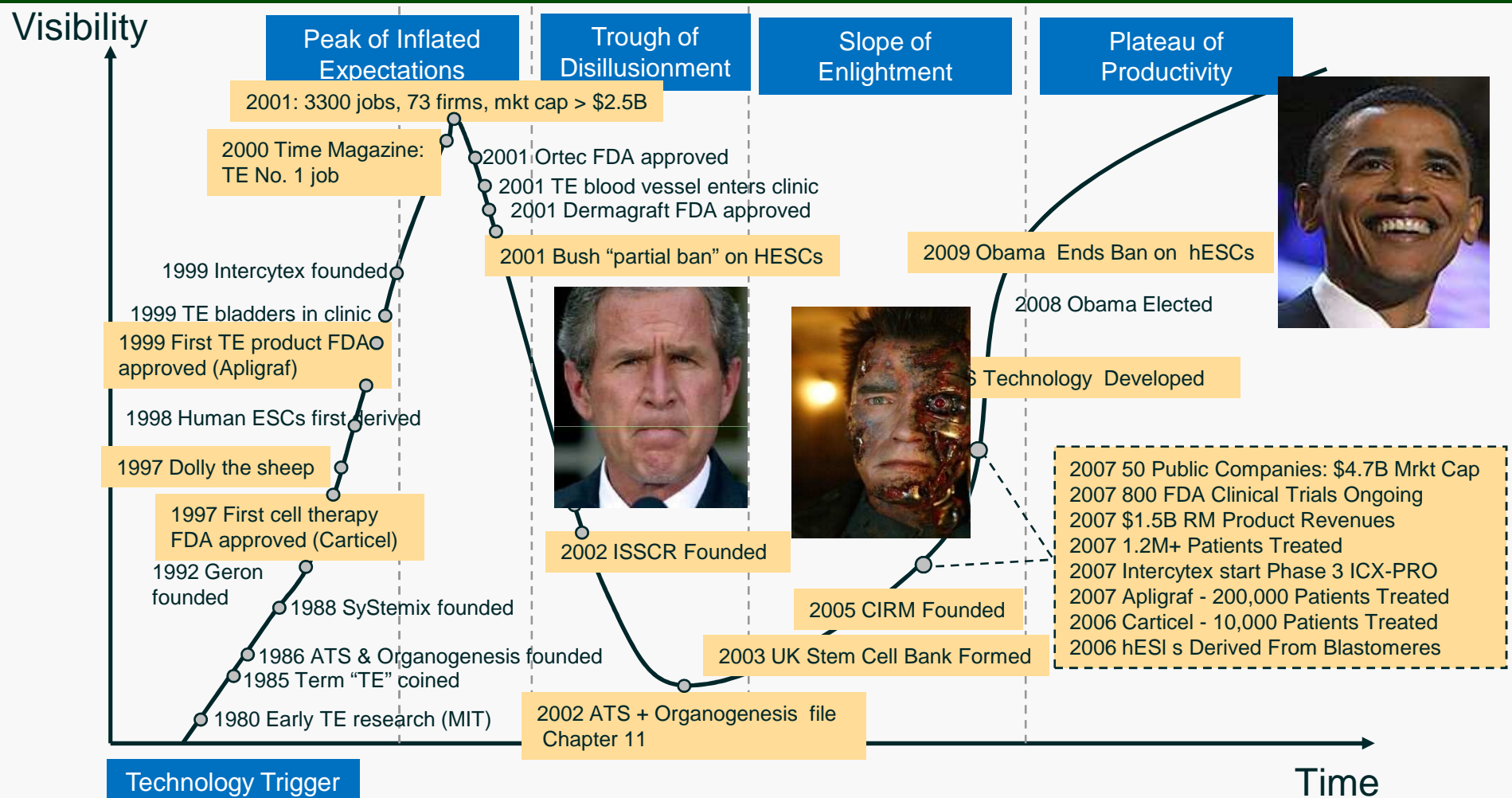


Source: Company websites, NIH, Pubmed

Gartner's Hype Cycle of Emerging Technologies



RM Market: On the 2nd Half of the Gartner Curve



RM Is Entering A New ERA

RM Market is Maturing: Key Metrics

▪ Rapidly Expanding Market:

- **\$3.6B** in 2008
- **\$118B** in 2013
- CAGR of **16%**

▪ Dramatic Revenue Growth

- **\$130M** in 2001
- **\$1.5B+** in 2008

▪ Worldwide funding for research Increasing

- **\$1.5B** Now
- **\$14B** in 10 Years

▪ Clinical Programs

- Over **900** Clinical Trials
- Over **200** ex-Oncology

▪ Commercial Products

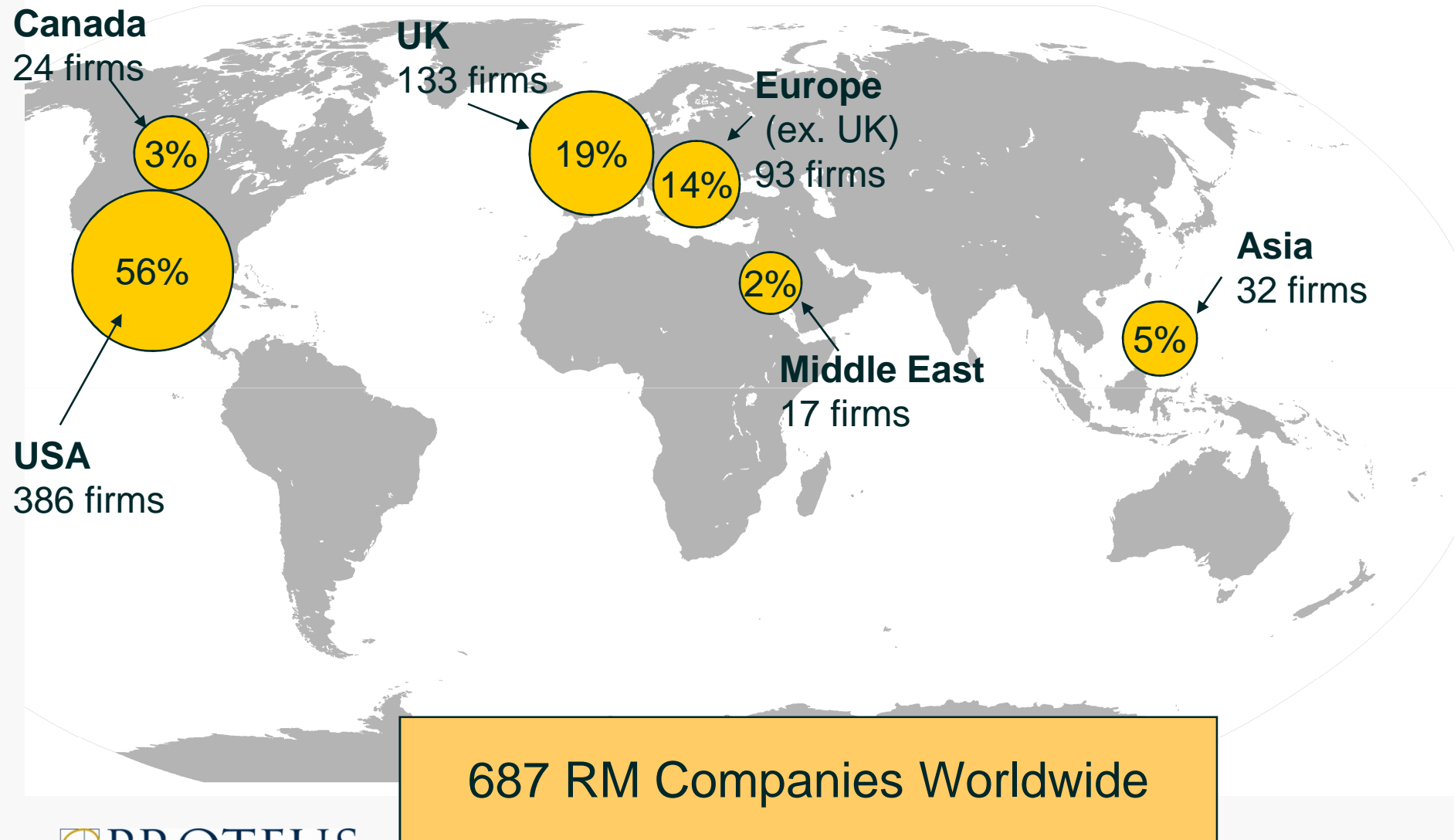
- **400** on Market (Mostly Skin, Tools & Devices)
- **600** in Development

▪ Patients Treated with RM Products: **1.2M+**

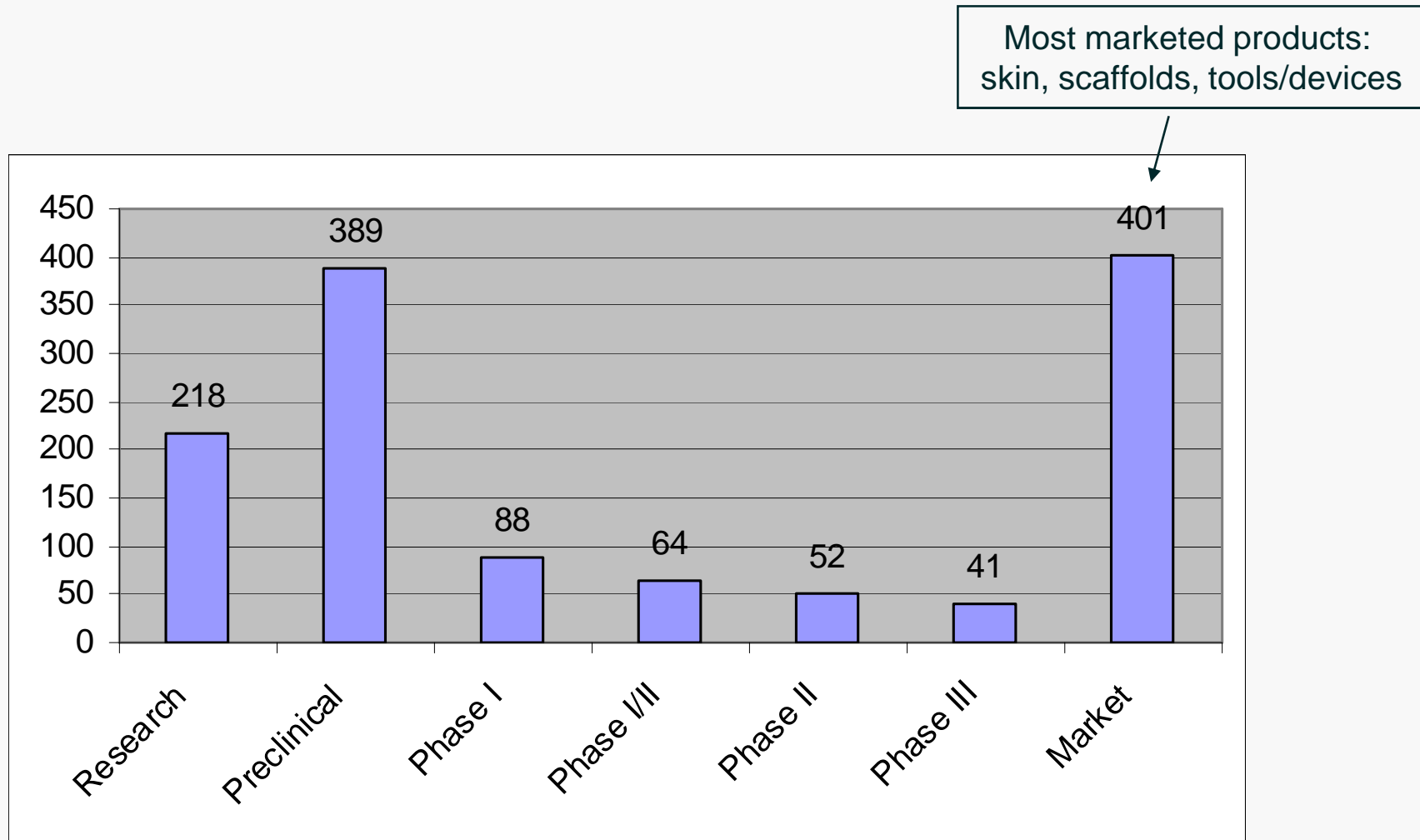
▪ Public Companies

- **40+** Public Companies
- **\$2.5B** Total Market Cap (down @18% YTD)

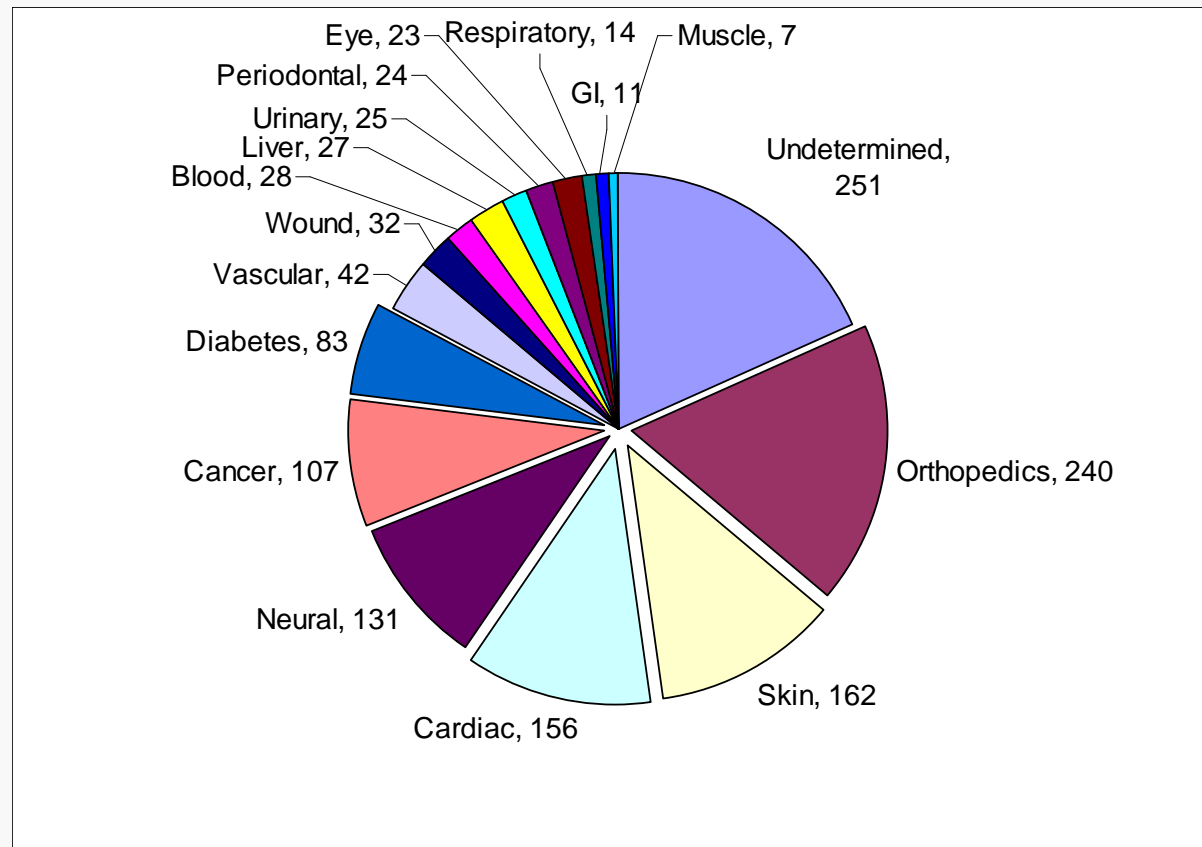
Global Company Distribution



Products In Development: Clinical Activity



Products in Development: Target Indications



Top Ten Regenerative Medicine Products

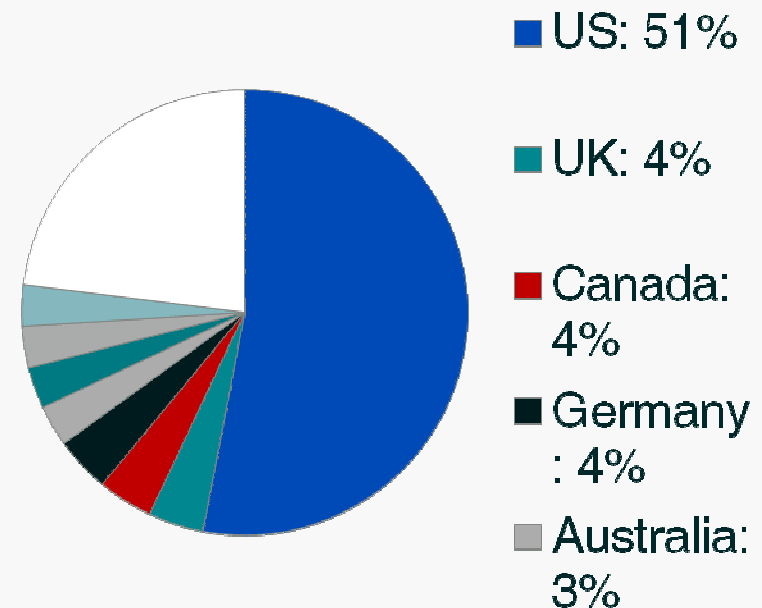
Company	Product	Product Type	Therapeutic Area	Indication	Launch	2007 WW Revenue	'06-'07 Rev Growth
Medtronic	Infuse	Growth factor w/matrix	Bone	Spinal fractures, orofacial fractures, open tibial fractures	2002	~\$700ME	18%
LifeCell	Alloderm	Allogeneic acellular matrix	Skin	Skin replacement / hernia repair	1994	\$167.1M	40%
Genzyme	Carticel	Autologous cell based	Cartilage	Knee repair	1995	~\$88ME	~30%
Stryker	OP-1	Growth factor w/matrix	Bone	Humanitarian Device Exemption for spine fusion & long bone fractures	2005	~\$80ME	60%
RTI	Spinal Implants	Allogeneic Acellular matrix	Bone	Spinal fractures	1991	\$41.1M	17%
Organogenesis	Apligraf	Allogeneic Neonatal cells w/matrix	Skin	Diabetic skin ulcers	1998	~\$30ME	10%+
Advanced Biohealing	Dermagraft	Allogeneic Neonatal cells w/matrix	Skin	Diabetic skin ulcers	1997	~\$20ME	10%+
Integra Lifesciences	Various	Allogeneic acellular matrix	Skin	Skin repair / replacement	2001	~\$20ME each	25%
Osiris/ Nuvasive	Osteocell	Allogeneic cell based	Bone	Fracture repair	2005	\$15.2M	83%
Cytori	Celution	Autologous cell based	Soft Tissue (adipose)	Reconstructive Breast Surgery	2008 (ex-US)	~\$10-12M*	N/A

RM IP Landscape: A Patent Thicket

Key Patent Metrics (1980-2005)

- **Substantial Activity**
 - Patent Applications: 10,000+
 - Patents Granted: 2,200+
- **Dramatic Increase in Filings Since 2000**
 - Over 25% Annual Growth Rate
- **Geographic Patent Distribution: US Dominates**
 - US: Over 50% of Patents
 - UK, Canada, Germany: @4% Each
 - Australia, Japan, China, Israel: @3% Each
- **Top 50 Patents Cover Core Technologies**
 - Cell Lines; Media; Differentiation

RM Patents Granted



Big Pharma Getting Interested



R&D: Regenerative Medicine Research Unit (UK+US)



Investments in Tengion (PA) and Novocell (CA)



R&D: Strong Interest in RM
Enlarged R&D facility in China



Investment in Cellerix (Spain)



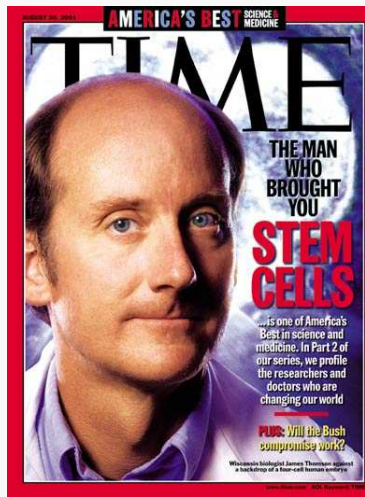
Partnership: Genzyme+Osiris Deal



Partnership: GSK + Harvard Deal



The Power of RM Is Capturing the Public's Imagination



2001



2006

Forbes Cover 2009:
Stem Cells Get Real



01/30/2009

BUT....

Worst Financial Crisis in 50+ years



RM Commercialization Challenges

- Technology & Business Issues
- Regulatory & IP Issues

Commercialization Challenges: Technology

R&D

- Creation and characterization of optimal cells for therapy
- Contaminant free cell lines
- Development of scaffolds & matrices for tissue engineering
- Safe & reliable expansion
- Controlling differentiation
- Track cell migration & engraftment
 - Imaging technology and biological markers
- Immune modulation

Manufacturing

- Technologies for scale-up
 - Commercial quantities of product
 - Pathogen free
 - Consistent lots
- Centralized vs. point of care
- Reliable preservation methods
- Logistics of shipping live cells
- Control COGS
- QC/ GMP
- Standardization in the field

Commercialization Challenges: Business

Regulatory & IP Landscape

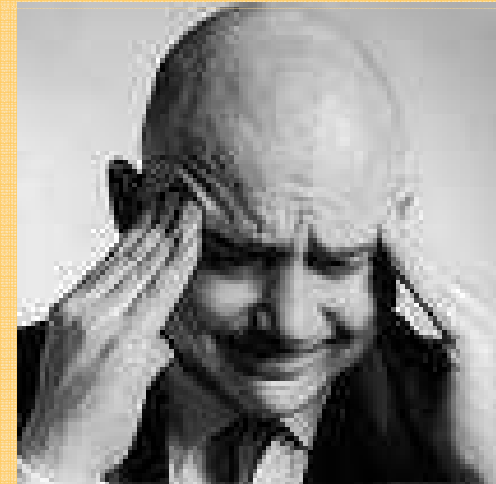
- Regulatory Environment Needs Clarity
 - Standards & guidelines are evolving
 - Characterization
 - Safety / Efficacy / Consistency
 - Cross border inconsistencies
- IP Landscape Is Treacherous
 - Fragmented Ownership;
 - Patents Proliferating Rapidly
 - Inconsistent & Competing patents: invites litigation
 - Need “Freedom To Operate” opinions

Business Issues

- Business Model Questions
 - Product v. service models
- Reimbursement Path Issues
 - Cost justification
- Sales & Marketing
 - Complex channel arrangements
 - Define marketable “product”
 - Educate consumers re: new treatment paradigms

RM Success & Challenges

- Field Has Achieved Many Success
 - Technology is Advancing at an Incredible Rate
 - Political Risks Declining
 - Market is Maturing - Enormous Opportunity
 - Significant Commercial Activity
- But Many Challenges Remain:
 - Funding
 - IP Issues
 - Business Models
 - Regulatory Pathway
 - Manufacturing & Scale UP



Fund Summary

▪ Regenerative Medicine Fund

- Global reach
- Stage agnostic
- Top tier venture returns
- 1st mover advantage

▪ Technology Focus

- Cell Therapies
- Regenerative Compounds
- Tissue Engineering
- Tools & Enabling Devices
- Aesthetic Medicine

▪ Addressing Large Markets

- Large unmet medical needs
- Aging population

▪ World Class Team

- Core team with complementary skills
- Deep domain expertise
- Outstanding SAB & strategic partners
- Industry leadership

▪ Disciplined Investment Approach

- Proprietary deal flow
- Rigorous due diligence
- Build value thru active management
- Timely exits

▪ Target Investments

- Outstanding technology & team
- Defensible IP
- Viable business model
- Near term path to clinic or revenues

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