



Accelerated Research Collaboration

Trailblazing for
Myelin Repair Treatments

NASA Space Life Sciences
Innovation Lecture Series
July 9, 2009

Agenda

1. Possible relevance to NASA
2. The status quo in medical research – a broken system
3. MRF's solution - the evolving ARC™ model
4. Summary
5. Q&A

Possible Relevance to NASA Space Life Sciences

- Begin with the end in mind
- Ignorance can be beneficial
- Science can be accelerated
- Innovation can be managed
- Creativity can be enhanced
- Add value to all participants
- Never ending flexibility and problem solving
- Convince and cajole not command and control

MS and Myelin

■ Multiple Sclerosis

- Damage in CNS
- Typical impacts
- Increasing incidence
- Complex disease
- No exact animal model
- Auto immune disease?
- Why 70% women?

■ Myelin

- “Insulation” on axons
- Key to MS, depression and many other diseases

Why is the MRF Necessary?

❖ The problem

- In 2001 the potential for myelin repair was underappreciated.
- The system is broken.

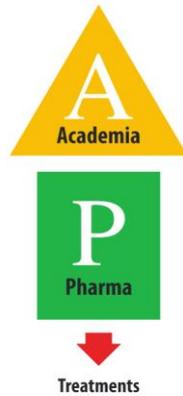
❖ The vision

- An entirely new approach to greatly accelerate getting treatments to patients.

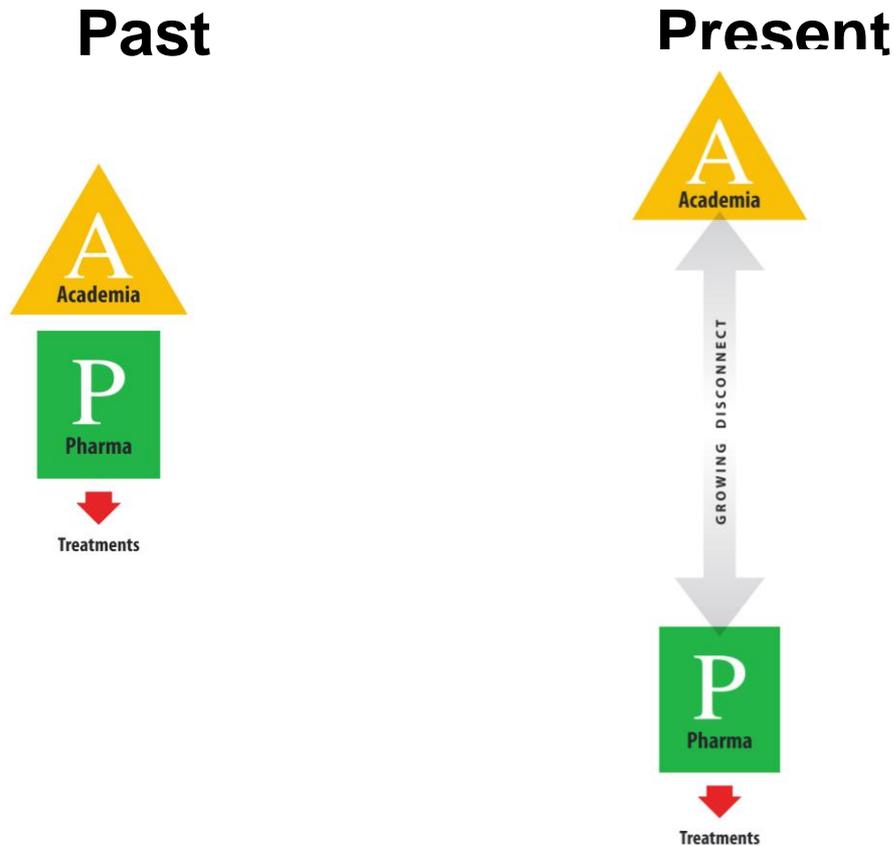
❖ The goal

- Develop and demonstrate a new model to accelerate new treatments for ALL diseases.
- License the first myelin repair target to biopharma within five years.

Traditional Model for Medical Research - Past

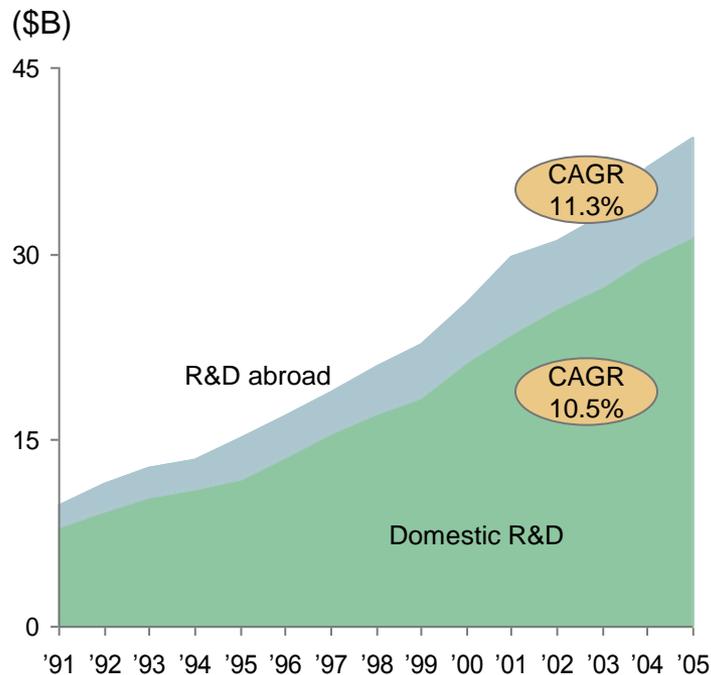


Traditional Model for Medical Research

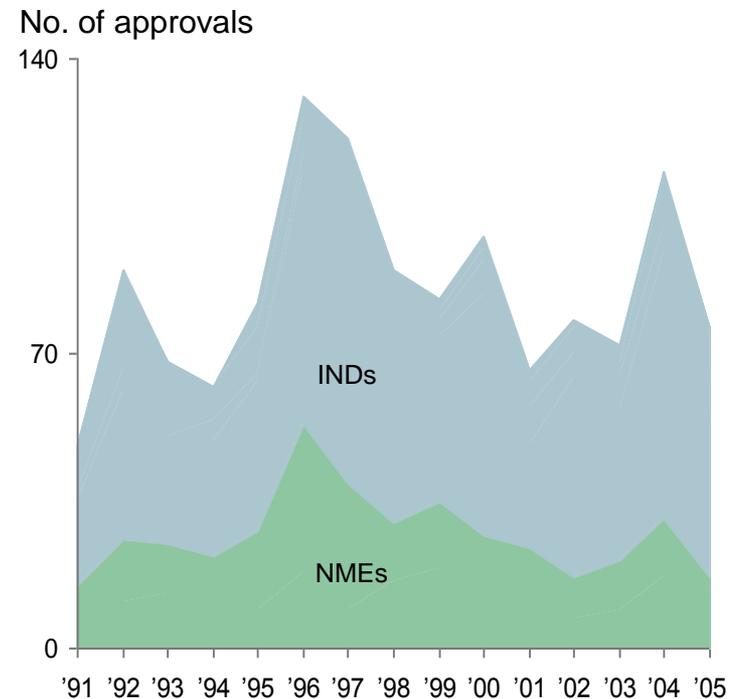


Pharmaceutical R&D output flat despite increasing spend...

R&D spending has grown steadily...

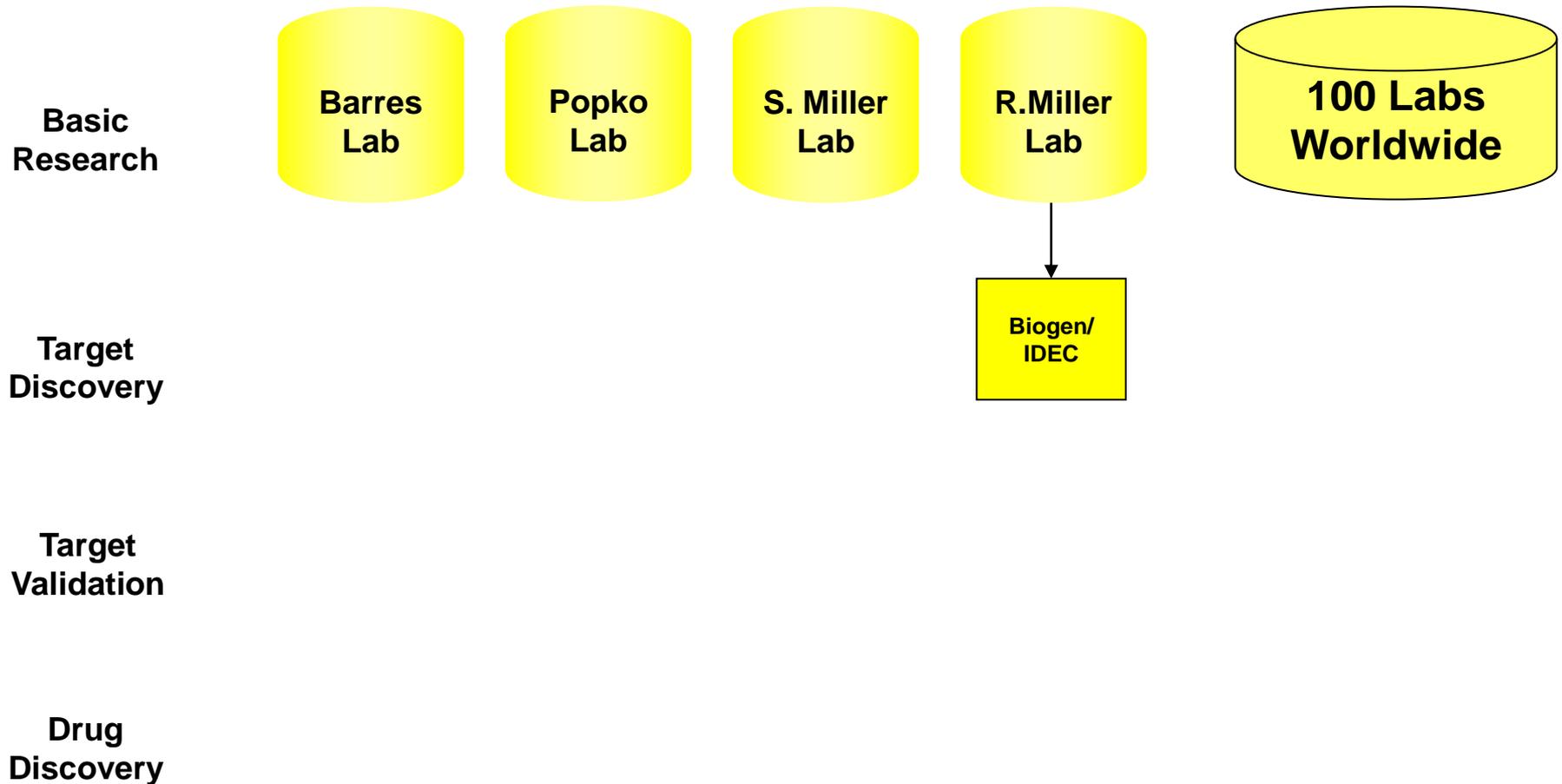


...but NME approvals relatively flat

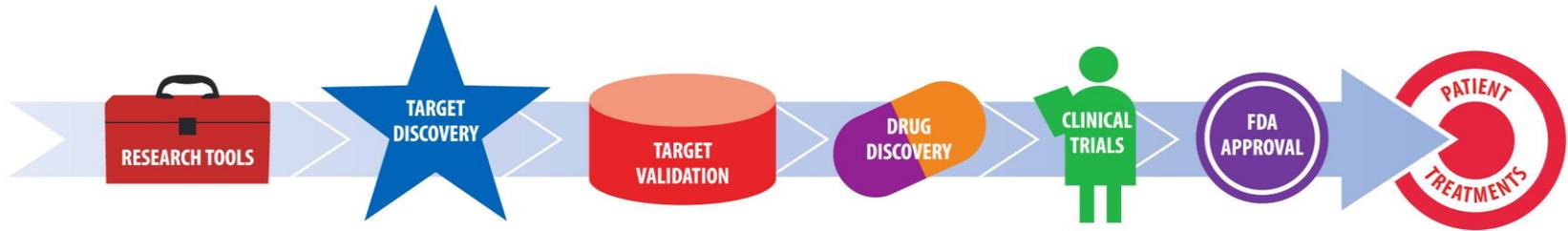


1. IMDs (Incrementally Modified Drugs) are new derivatives, formulations and combinations
 2. NME (New Molecular Entities) include both chemical and biological therapeutic agents, excludes contrast agents and diagnostics
 Source: FDA, PhRMA 2005 Yearbook

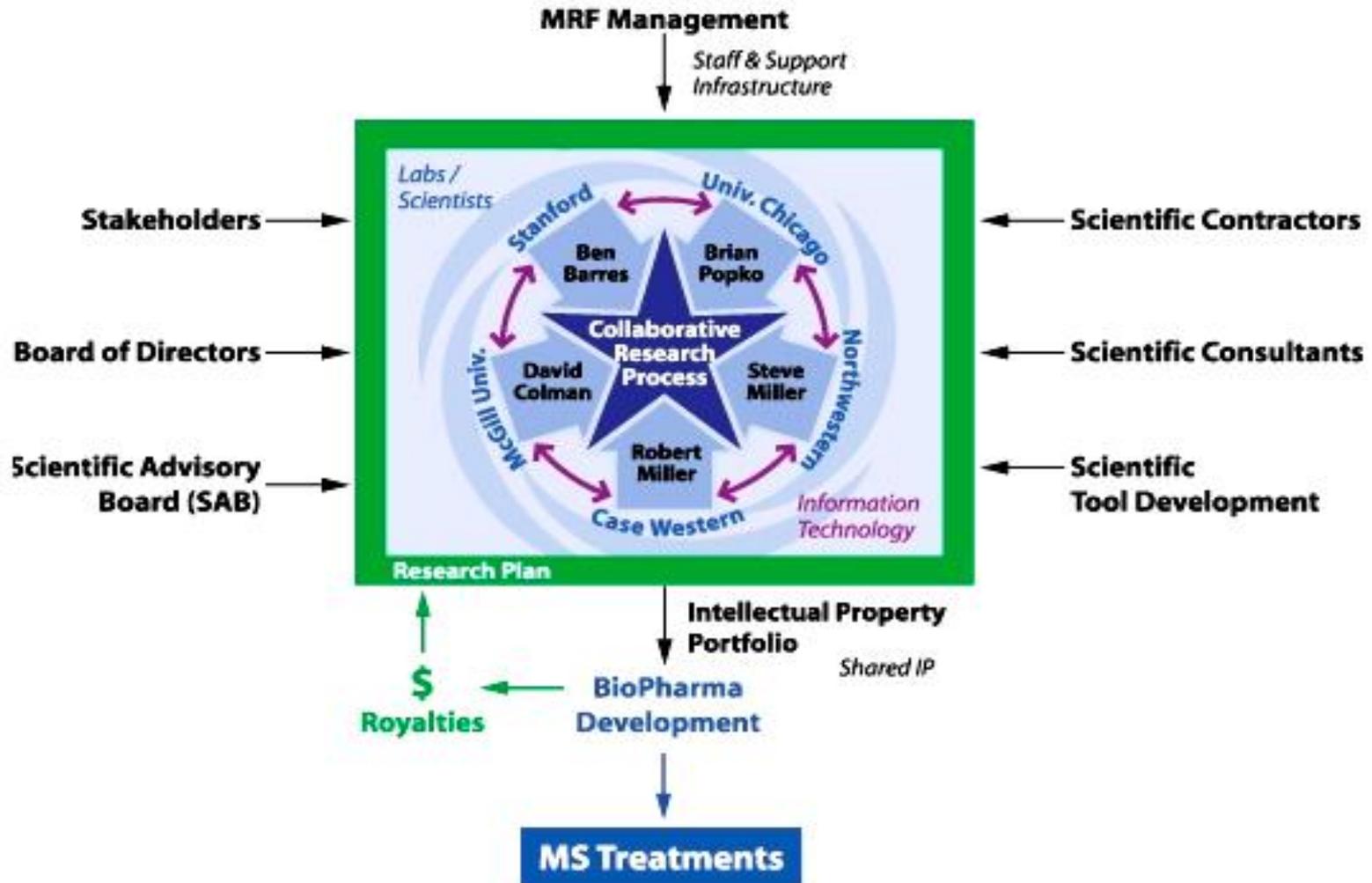
Myelin Repair Research Landscape - 2002



There are many steps required to get a new therapeutic to patients



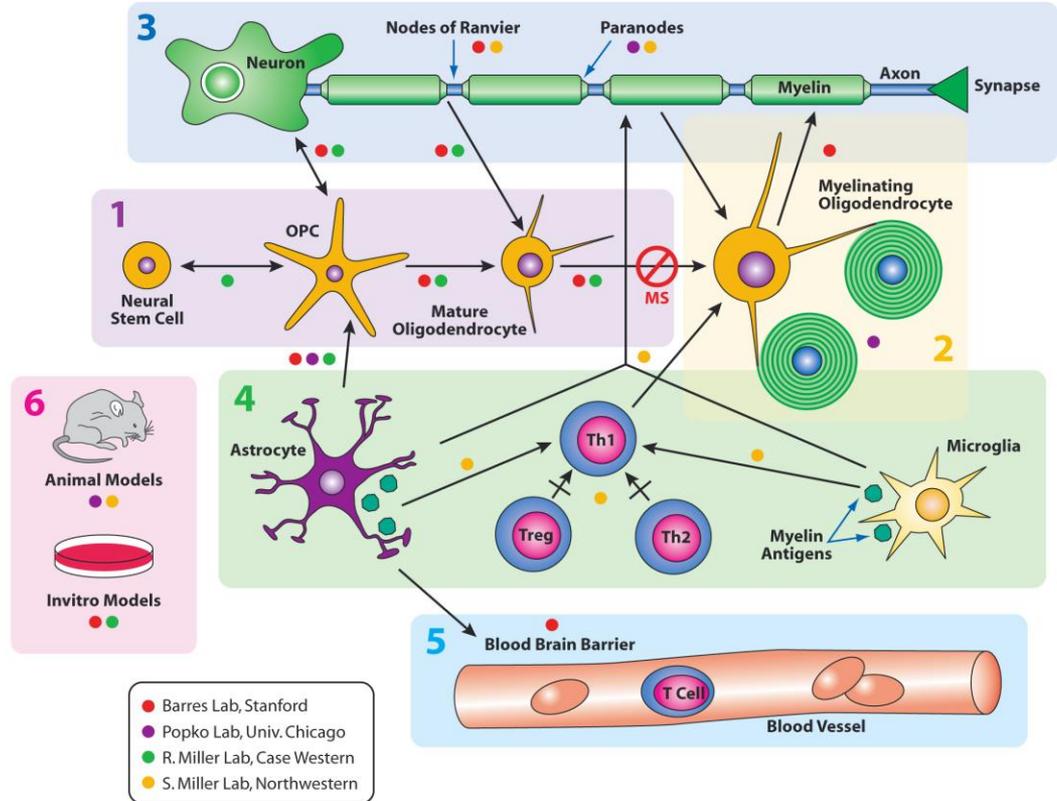
Accelerated Research Collaboration Model



Myelin Repair Discovery Biology

Six Areas of Research

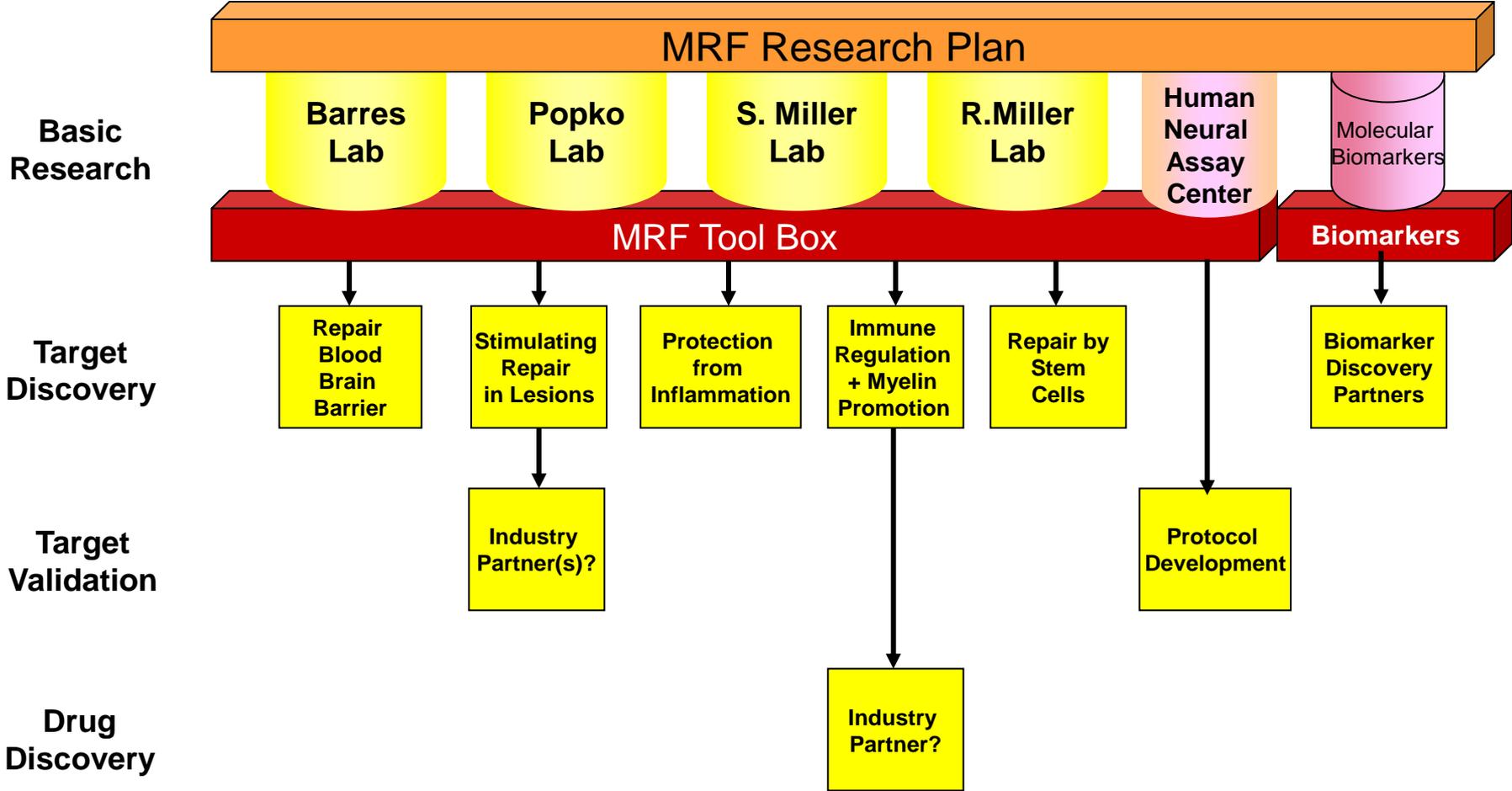
1. Understanding how oligodendrocytes are normally generated from neural stem cells and how MS perturbs this process
2. Understanding the underlying mechanism of myelination and how it is perturbed in MS
3. Understanding how nodes of Ranvier and paranodes are normally formed and how they are perturbed in MS
4. Understanding the immune response in MS and how inflammation affects myelin repair
5. Understanding how the Blood Brain Barrier is affected in MS and its role in the disease
6. Development of better animal models for study of MS and remyelination.



Major Milestones Achieved since 2004

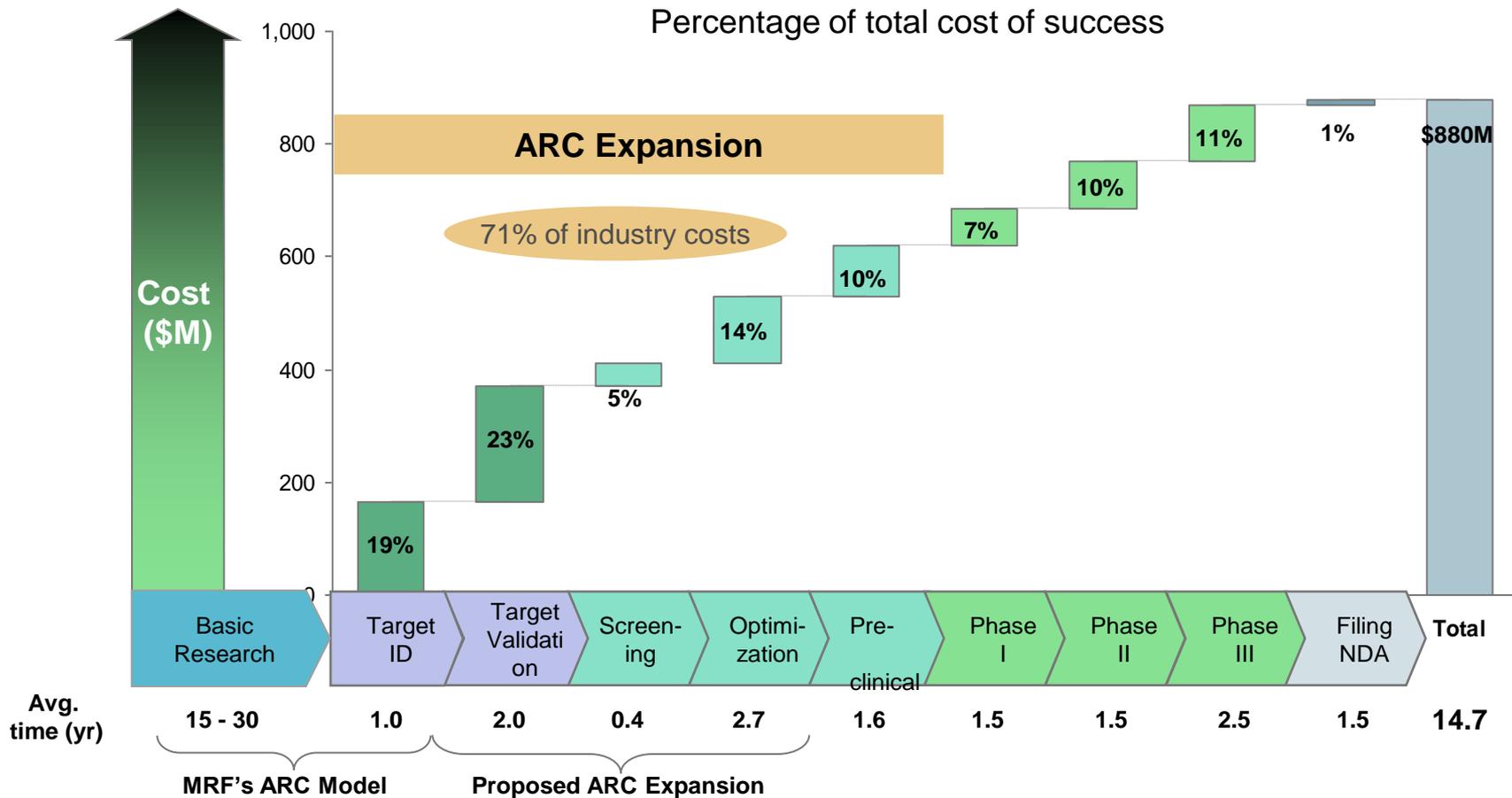
- ~ 19 new targets/pathways identified
- > 24 new research tools, assays and models developed
- 9 patent applications filed and 8 in prep (first patent awarded 2008)
- > 75 publications in peer-reviewed journals
- Recognized by the media, academics and non-profits for developing a breakthrough model for medical research
- Biopharma now views myelin repair as a viable therapeutic area

MRF Research Landscape - 2009



Crossing the Valley of Death –

Accelerating the transition from promising targets to clinical candidates



Source: BCG economic model study in Biomedical Industry Advisory Group, 2005; BCG clinical development model, 2007

Extending the MRF's Research Model into Drug Discovery

- The Drug Discovery process is essential for
 - The continued success of the MRF
 - The development of a therapeutic
- MRF's research model has efficiently produced many novel myelin repair targets
- The drug discovery process operates on a different set of requirements, skill sets, experience and scientific criteria than academic target identification.
- Because of the significant cost to develop a therapeutic, industry requires a very compelling and comprehensive data package prior to the investment of resources on a drug target.

Progress Toward Developing Myelin Repair Treatments

- Internal drug discovery team
- Drug Discovery Advisory Group (DDAG)
- Partnering/Licensing Strategy

Myelin Repair Foundation Pipeline 2009

Therapeutic Approach	Target/Pathway	Target Discovery	Drug Discovery	Preclinical	Phase 0/I	Phase IIa
Immunomodulation	Induced Cell Tolerance					
Immunomodulation	MSC					
Immunomodulation	Costimulatory Blockade					
Immunomodulation	MDC blockade					
Immunomodulation	Costimulatory Blockade					
Protect Myelinating OPCs	ISR Antagnoist					
Protect Myelinating OPCs	ISR gene					
Enhance OPC Migration and Lesion Penetration	Cytokine Receptor Antagonist					
Enhance OPC Migration and Lesion Penetration	Migration & Expansion Enhancer					
Enhance OPC Migration and Lesion Penetration	Migration Promoter					
Enhance OPC Migration and Lesion Penetration	Migration Enhancer					
OPC Differentiation/Enhance Remyelination	Differentiation Promoter					
OPC Differentiation/Enhance Remyelination	Differentiation Controller					
OPC Differentiation/Enhance Remyelination	Differentiation Controller					
OPC Differentiation/Enhance Remyelination	Differentiation Controller					
OPC Differentiation/Enhance Remyelination	Myelination Controller					
Repair Blood Brain Barrier	Tight Junction Formation					
Repair Blood Brain Barrier	Tight Junction Formation					

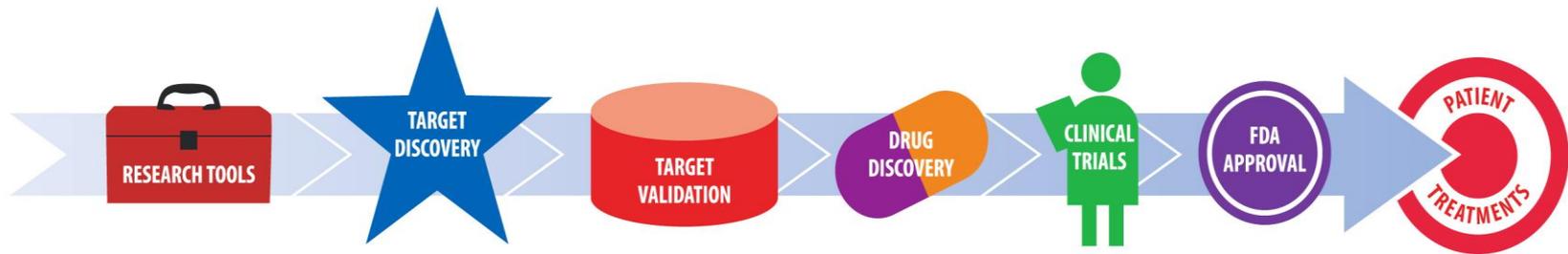
Strategies for Translating MRF Discoveries

- Support existing pharma company pipelines
 - Offer access to MRF Target Validation toolkit
 - Provide data for “repurposing” existing clinical candidates
- Contracting
 - Promote research collaborations with corporate entities
 - Fund Target Validation/Drug Discovery studies at CROs
- Partnering
 - Offer exclusive licensing options to MRF targets/tools
 - Create Joint IP with biotech/pharma partners
- Spinoffs
 - Create new corporate entities to develop innovative MRF programs

Relevance to NASA Space Life Sciences

- Collaboration is intellectually stimulating and very productive
- Many teams vs. single large team
- Creative problem solving
- The ARC model could be a starting point
- Encourage risk taking and entrepreneurship
- Set audacious goals
- Keep it fun

The only non-profit medical research foundation that participates in the entire continuum of drug discovery



Summary

- MRF began with a specific, narrow, measurable audacious goal
- MRF set out to accelerate all elements in the value chain
- MRF convenes experts to help solve problems as they become evident
- MRF uses its non-profit status to the fullest advantage
- MRF has made remarkable progress
- The second five years will require \$100M
- Networking is critical to achieving our goals

www.myelinrepair.org