

Promises Made, Promises Kept

# RESULTS

2004-2009



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*Myelin Repair Foundation supporter, Bob Gregory, coined the theme for this report. Bob has been waiting for a cure for MS since 1990.*

I'm a keeper of lists, a setter of goals, a manufacturer of timetables. I'm also impatient and have a chronic inability to accept the status quo. When I was diagnosed with MS in 1990, I decided I was going to return to my marathon running ways by 1995. Then, it was by the time my daughter went to school. Then, by the new millennium. Each time I pushed back my arbitrary timetable I became more discouraged.

Then one day in December 2004 I had dinner with Scott Johnson and Rusty Bromley. They talked about pulling together the top researchers in some of our most valued universities, who didn't know each other except by reputation, and have them collaborate and thereby sacrifice their most valuable asset: the proprietary use of their ideas. And by the way, Scott and Rusty said, we're going to raise \$25 million, identify and validate new myelin repair drug targets and license one of them, all in five years.

My heart said yes. My brain said no way. But, they had a plan!

And as you can see from this report, it's working. **Promises made, promises kept.**

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# That was then. An audacious promise.

In 2004, a little-known group called the Myelin Repair Foundation made a bold promise: it would accelerate the pace of basic research leading to the next generation of multiple sclerosis treatments — myelin repair. It would keep this promise by bringing the best minds in science and industry together and managing a unique collaboration focused on a strategic research plan. It would keep this promise with a relentless effort to break down the barriers, one by one, until myelin repair treatments are finally found.

These untried strategies challenged a status quo in academia and industry that has guided medical research for decades. Today, five years later, we offer proof of what happens when you think and work together.

In 2009, this small organization intent on change has kept its promise and is sharing its extraordinary results. The implications are vast, not only for those living with MS, but for millions of others with diseases that have few, if any, effective treatments or cures. Indeed, there is promise for the future.

“ We’re changing the research process to one that is faster and more focused on producing treatments. I believe this will improve the lives of billions of people by the time it’s done. It will change the world. ”

— *Scott Cook*  
*Myelin Repair Foundation Donor*  
*Intuit Co-Founder*

# This is now. Promise kept.

From the beginning in 2004 we did things differently. We developed an entrepreneurial business-style research model, the Accelerated Research Collaboration™ (ARC™) model. Then we picked a team of the world's leading neuroscientists and asked them to do something truly groundbreaking — share their research, ideas and data with each other in real time.

By all accounts, the results are impressive. Our MRF team has uncovered five promising approaches to myelin repair, each focusing on different biological processes with multiple therapeutic targets. The discoveries include 19 new potential myelin repair targets, two of which are currently undergoing validation and early-stage drug discovery studies. We have also developed 24 new tools, assays and models that have potential application to all neurological research.

## CHANGING THE MS LANDSCAPE

Five years ago, myelin repair was not on the radar screen as a potential MS treatment. Not anymore. Our results are gaining attention and many biotech and pharmaceutical companies are now familiar with our work and the potential for advancing our targets into the development pipeline.

Bottom line? It's clear that cooperation beats competition in MS research. Teamwork, integration and the ARC business model are speeding up the process and producing remarkable results. We're not stopping. We have a comprehensive plan in place and more promises to keep.

“ I haven't taken a step in five years. Fortunately, the MRF has. ”

— Myelin Repair Foundation volunteer and donor, Fred Schwartz. Waiting for a cure since 1994.

## MONEY WELL SPENT

Two more promises we made were to raise \$25 million and to ensure that at least 80% of our expenses would be dedicated to research and development. Done and done.

### Five-Year Income Statement as of June 30, 2009

	Five-Year Total
<b>TOTAL REVENUE</b> .....	<b>\$28,220,000</b>
<b>TOTAL EXPENDITURES</b> .....	<b>\$19,540,000</b>
Research and Development	\$15,790,000
General and Administrative	\$1,960,000
Fundraising and Communications	\$1,780,000
<b>RESEARCH AND DEVELOPMENT AS A PERCENTAGE OF TOTAL EXPENDITURES</b> .....	<b>81%</b>

### Among our discoveries

- How cell signaling via the chemokine receptor CXCR2 retards myelin repair.
- How controlling the integrated stress response can protect myelinating cells from inflammation.
- How the blood brain barrier is formed and the previously unknown role of pericytes.
- How myeloid dendritic cells locally activate T cells within the brain in animal models and human MS lesions.
- New methods for inducing immune tolerance using myelin-specific antigens.
- Three triggers for initiating myelination at the cellular level.
- Three new, non-immune animal models, using different methods of inducible demyelination.

# This is how. Milestones of our success.

Our success is grounded in four key components.

## 1. FUNDING

### Fiscal accountability

From our inception, we have taken great care to manage and spend our resources in a way that would produce the best outcomes for a patient treatment. Our goal was to spend at least 80% of every dollar on the pursuit of myelin repair treatments. We surpassed that mark. Research thus far has accounted for 81% of total expenditures.

### Funding innovation and risk

Since 2004, we have funded more than 40 research projects. Many of these would have been viewed by the National Institutes of Health and others who fund medical research as too high risk. We viewed these experiments as high risk/high reward and they have borne considerable fruit.

## 2. RESEARCH

### Targeted research plan

Funding decisions are based on a carefully designed, collaborative research plan with results measured against desired goals. Resources are allocated to achieve the greatest results.

### Leading minds in science and business

We handpicked a world-class team of MS scientists and a research management team with know-how in drug development. Joining them are scientific advisors, industry consultants, and visionary business leaders who bring fast-track expertise to the research process. All data is shared and integrated across our entire network to accelerate results.

### New tools and technologies

Myelin Repair Foundation has supported the development of more than 24 new research tools, including gene expression databases, methods for evaluating myelin repair therapies at the cellular level, and new animal models of demyelinating disease.

### Advancing myelin repair science

Since 2004, through the publication of more than 75 articles in peer-reviewed scientific journals, our research team has contributed their discoveries to the larger community of scientists investigating MS treatments.

### 3. VALIDATION

#### Data for new drug programs

We are funding essential target validation and early-stage drug discovery studies designed to provide data required for new commercial drug development programs. Today, we are supporting these studies on two of our most promising treatment targets. No other research organization is advancing discoveries made in academic laboratories in this way.

#### Patents for discoveries

Since 2004, MRF scientists have created 18 patentable inventions, the first of which was awarded a patent in 2008. Without patent protection, few discoveries move forward toward patient treatments.

#### Engage biopharma

In the past four years, we have engaged the expertise and interest of more than 30 biotech and pharmaceutical companies as we explored the parameters of commercial target validation and early-stage drug discovery in preparation for commercial partnerships.

### 4. GROWTH

#### Committed network of supporters

We began our work with a small seed fund from a handful of entrepreneurs who saw value in our proposition. Support for our efforts has grown to include a broad base of individuals, foundations and corporations, including the Robert Wood Johnson Foundation, the Donaghue Foundation, the Penates Foundation, Omidyar Network and Biogen Idec. This support continues to grow daily.

#### Gaining national attention

News is spreading of the success of our Accelerated Research Collaboration model and our advances toward MS treatments. From the *Wall Street Journal* to *BusinessWeek*, *Newsweek* and *Scientific American*, our work is drawing attention. In addition, more than 60 research and funding organizations have expressed an interest in our model. Many believe it could change the way all medical research is done.

# This is next. Promise for 2009-2014.



*President and Founder, Scott Johnson.  
Waiting for a cure since 1976.*

Our team's work has yielded landmark results for our proof-of-concept for target discovery, IP protection, tool development, target validation and commercial partnerships. Your support will enable us to underwrite several critical ongoing initiatives:

## **Identify more high-quality potential therapeutic targets.**

According to a recent analysis by the Boston Consulting Group, on average within commercial research and development, it requires as many as 360 potential therapeutic targets entering the drug development pipeline to bring a single treatment to market! We believe the quality of our targets could cut that number by 80%. Still, it would require more than 50 targets to ensure that one treatment reaches patients. By 2014, our goal is to at least double the number of targets in our portfolio.

## **Validate therapeutic targets to meet industry standards.**

We have designed a number of validation protocols that are now being used to validate our first two therapeutic targets. By 2014, we anticipate developing new models and advanced protocols to validate as many as 10 additional targets.

### Build industry partnerships leading to clinical trials.

As our portfolio of high-quality therapeutic targets continues to grow, we plan to establish partnerships with at least four companies with the goal of bringing at least one therapeutic target to Phase 1 clinical trials by 2014.

### Identify new approaches to measuring clinical outcomes to speed clinical trials.

We will invest in the discovery and development of biomarkers, imaging tools and other techniques that will improve our rate of target identification, the development of new drugs and early diagnoses, as well as speed clinical trials by providing more concrete measurements of the relative impact of new treatment options.

Achieving these outcomes will demonstrate the value of the ARC model and provide a new avenue of hope for those living with MS and other debilitating diseases. Together, we are changing the world!

A handwritten signature in black ink that reads "Scott Johnson". The signature is fluid and cursive, with the first letter of "S" being particularly large and stylized.

Scott Johnson, President and Founder, Myelin Repair Foundation

# Commitment without compromise.

Our success is a combined effort of many different people and organizations, all focused on one common goal: finding a treatment for MS as soon as possible.

## PRINCIPAL INVESTIGATORS

**Ben Barres, M.D., Ph.D.**  
Stanford University

**David Colman, Ph.D.**  
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McGill University \*

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Consultant and Chairman, MRF Drug Discovery  
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**Mark Scheideler, Ph.D.**  
Program Director, National Institute of Neurological  
Disorders and Stroke

\* *past participants*

## SPONSORED RESEARCH

**Carlos Pardo, M.D., Ph.D.**  
Johns Hopkins University \*

**Center for Stem Cell & Regenerative Medicine**

**Wensheng Lin, Ph.D.**  
University of South Alabama

## CONTRACT RESEARCH ORGANIZATIONS

**Blue Dolphin Lead Discovery LLC**

**Bolder Biopath, Inc.**

**Charles River Laboratories, Pathology Associates, Inc.**

**Collaborative Drug Discovery**

**Dalton Pharma Services**

**Datacloud SPLtrak**

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**Russell Rydel, Ph.D.**  
Consultant, Discovery Biology and  
Target Validation

**Carol Menaker**  
Director of Communications

# Join our cause.

Please help us continue our work. We promise to use your donation wisely.

**Donate today at [myelinrepair.org](http://myelinrepair.org) or call 1-877-ToFixMS**



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For a detailed report of scientific progress, visit [www.myelinrepair.org](http://www.myelinrepair.org)