

Whatever It Takes

2007 PROGRESS REPORT



In 2007 The Michael J. Fox Foundation funded over \$25 million in new grants, nearly 90 percent toward translational or clinical projects, putting us over the \$100-million mark in research funded since inception. While we're proud of that milestone, we know that our ultimate goal — transformative treatments for PD — requires much more than money.

That's why the past year saw MJFF strengthen its commitment to what we increasingly deem "disruptive philanthropy" — a focused, proactive strategy to do whatever it takes to speed transformative treatments to the nearly five million people living with Parkinson's disease worldwide. We are working to maximize impact by pushing basic discoveries toward the clinic and strategically targeting resources toward critical research hurdles that other funders cannot or will not prioritize. We stand ready to forge a new model of what a research funding organization can be — stepping up to deliver Parkinson's solutions and, in the process, transforming a flawed biomedical research system in ways that ultimately could impact every life touched by illness or injury.

We embraced every opportunity to make ourselves — and our determination to drive change in this broken system — known to influential audiences and constituents. In May, Michael J. Fox addressed 4,000 pharmaceutical industry leaders at the BIO Global Convention with a keynote on the urgent need for creative new approaches to translation: "I truly believe that if we spur innovation, work together to reduce the risk of early-stage ideas, and seed the drug development pipeline with the next generation of therapies, we can assure every stakeholder of transformative results."

This annual progress report provides a brief overview of 12 months of activities to get us closer to our goal — **setting the agenda** to drive innovative research and prioritize translation of therapeutic targets; ensuring **a seat at the table** for the Foundation, and patients' interests, in critical drug development decisions; **solving problems** to keep vitally needed tools and resources moving forward and to increase clinical trial activity in PD; and **setting the standard** for accountability, urgency and effective use of donors' dollars.

SETTING THE AGENDA

Reforming a flawed system starts with having an opinion — and using it to inform and set an agenda that will yield results. The Michael J. Fox Foundation has established a world-class, in-house scientific team that engages with researchers worldwide and has gained respect for its combination of tough standards, integrity and impartiality, clear direction and comprehensive

knowledge of the field. Having our own team allows us to bring our own priorities to bear in a wide field of seemingly equally important research opportunities — to direct and prioritize scientific activities toward transformative treatments.

DRIVING INNOVATIVE RESEARCH

Following an overwhelming response from the scientific community, the Foundation funded about \$2 million total for 28 novel research projects under its inaugural *Rapid Response Innovation Awards* initiative. Unique among MJFF programs, *Rapid Response* accepts applications on a rolling basis with no deadline. Researchers may submit proposals for grants of up to \$75,000 to fund new ideas as they arise; funding decisions are made within six weeks.

Scientific journal *Chemical and Engineering News* called *Rapid Response* an example of "a trend among nonprofits of finding creative ways to finance cutting-edge research in disease areas that big pharma has traditionally ignored. The nonprofit support is particularly useful to scientists whose research is in the difficult-to-fund idea stage."

One awardee, D. James Surmeier, PhD, of Northwestern University, received approval to advance early research suggesting that an already FDA-approved high-blood-pressure drug, isradipine, administered at high dosages, could protect dopamine neurons from death in animal models of Parkinson's disease.

"It's exciting that an FDA-approved drug with a long history of safe human use has such great potential for slowing the progression of PD," said Dr. Surmeier. "The *Rapid Response* funding my team received has allowed us to quickly gather dosage information on isradipine — data that's vital to designing the most efficient neuroprotection clinical trial for PD."

PRIORITIZING TARGETS FOR THERAPEUTIC TRANSLATION

MJFF resources have driven testing of over 100 therapeutic targets for Parkinson's to date, in areas as diverse as inflammation, dyskinesia and genetics. Much of this work was funded under the Foundation's annual *Target Validation* (TV) initiative, which pushes therapeutic targets

closer to the clinic by determining whether and how they affect the symptoms and progression of Parkinson's. Not all previous TV awardees have had capacity to carry out the highly specialized studies needed to obtain critical information, such as dosing amounts and brain bioavailability, for fully validating a target. Recognizing the importance of these studies, in 2007 MJFF enlisted contract research organizations (CROs) — independent labs with the staff and equipment to carry out any project element an awardee cannot complete within his or her own institution.

In spring the Foundation launched *Critical Challenges in Parkinson's Disease Research* to define and answer pivotal questions about targets that are consistently the locus of the field's most intense investigation. With input from a panel of the world's foremost Parkinson's academic and industry researchers, the Foundation allocated \$2 million for four research projects to decisively address specific, MJFF-prioritized questions as to how the PD-implicated genes alpha-synuclein and LRRK2 (respectively) trigger the death of dopamine neurons.

In a story titled "The Michael J. Fox Foundation Gets It and Gets It Done," *Thomson Center-Watch*, a journal for the clinical trial industry, wrote: "Fox... is willing to put its money where it is needed to move along the drug development process."

A SEAT AT THE TABLE

The Michael J. Fox Foundation recognizes that directing research toward transformative treatments increasingly requires cooperation and multidisciplinary efforts. In 2007 we brought together nearly 400 researchers from academic and industry labs all over the world for conferences, workshops and new collaborations to move the field forward faster.

SHARING RISK WITH INDUSTRY PARTNERS TO INCREASE OVERALL ACTIVITY

In 2007 MJFF expanded strategic risk-sharing partnerships to catalyze greater biotechnology and pharmaceutical company investment in PD drug development.

Continued on other side

In December the Foundation launched the \$2-million *Cognitive Deficits and Mood Disorders in Parkinson's Disease* initiative with generous leadership funding from Merck Serono (EMD Serono in North America), affiliates of Merck KGaA, Darmstadt, Germany. Recognizing the urgent need for new therapies to alleviate PD-related mood disorders and cognitive dysfunction, a mutual partnership between Merck Serono and MJFF was formed to invigorate research in this underaddressed area. MJFF and Merck Serono hope to encourage collaborations between PD scientists and researchers from other areas, including psychiatry.

MJFF also awarded a total \$1.2 million to four research teams under *Novel Approaches to Drug Discovery for Parkinson's Disease*, made possible by generous leadership funding from Elan Corporation, plc. *Novel Approaches* furthers the development of therapeutic targets that already have some promising initial data behind them. If projects funded under *Novel Approaches* warrant further development, Elan has the option to participate more actively and help further the progress made by the awardees.

Awardee Peter Jenner, PhD, of London's Proximagen Neuroscience, plc, received funding to investigate a gene therapy approach to deliver protein osteopontin, which has shown potential to protect dopamine neurons, to the brains of rodent PD models. Dr. Jenner said: "MJFF provided critical funding for our next step. And the award structure means that Elan could increase its involvement, should our results show promise. From our company's point of view, it's a win-win situation."

The potential results of partnerships like these were evident in June, when Ceregene, Inc., announced that it had entered a partnership with Genzyme that could provide up to \$150 million for the timely development and commercialization of CERE-120, Ceregene's gene therapy approach for delivery of trophic factor neurturin. MJFF has provided a total of about \$2.6 million in support for parts of the Phase 1 and 2 clinical trials of CERE-120. (The Phase 2 trial completed enrollment late in 2007; efficacy results are expected in 2009.)

"Assuming positive findings on efficacy, Genzyme's investment would let us take CERE-120 worldwide," said Jeffrey Ostrove, PhD, president and CEO of Ceregene. "The significant support we received from The Michael J. Fox Foundation was certainly a contributing factor in our ability to put this partnership together."

FORGING COLLABORATIONS TO ACCELERATE PATIENT IMPACT

Under its signature *LEAPS (Linked Efforts to Accelerate Parkinson's Solutions)* initiative, MJFF partners with multidisciplinary research teams who create comprehensive blueprints to answer seminal questions about PD and advance critical work toward clinical testing. In December MJFF awarded a total of \$8.2 million for two *LEAPS* projects aiming to establish entirely new classes of drugs to treat Parkinson's.

The Foundation also took increasing advantage of its position at the hub of Parkinson's research activity to convene scientists for the fruitful exchange of ideas. In October MJFF and The New York Academy of Sciences co-hosted the *PD Therapeutics Conference*, the first and only major scientific symposium exclusively focused on drug development in Parkinson's disease. Acting as "matchmaker," the Foundation brought together nearly 200 academic and industry researchers to showcase latest advances in PD science and assess tactical next steps for using these advances to accelerate drug development.

"The *PD Therapeutics Conference* exceeded my expectations for creating leads to potentially meaningful partnerships," said Charles Adler, MD, PhD, co-principal investigator of the Foundation's *Prescott Family Initiative at the Arizona Parkinson's Disease Consortium*. "After my talk, many attendees came to me interested in finding ways to leverage their resources and our data and resources to create collaborations that could further all of our work."

Additionally, the Foundation "convened" top experts in the pages of scientific journal *Experimental Neurology*, where the MJFF research staff was invited to guest-edit a special section focusing on the state of gene therapy for PD.

SOLVING PROBLEMS

The Michael J. Fox Foundation's independent viewpoint, centralized expertise and commitment to patients' interests make us relentless problem-solvers. Our programs and activities are precision-engineered to overcome institutional roadblocks and advance solutions. We're working urgently to effect critical tools and resources needed for the development of new treatments — including developing biomarkers and laying the groundwork to increase clinical research activity.

DEVELOPING CRITICAL RESEARCH TOOLS AND RESOURCES

Progress continues to be challenged by a system that fails to orchestrate and align the efforts of disparate stakeholders toward the development of research tools and resources. In a world where each entity must aggressively prioritize its resources, investments in tools that would benefit the entire field too often fall to the bottom of the list. As a neutral party interested exclusively in patient-relevant outcomes, the Foundation is uniquely poised to stimulate collaboration and forward progress in this arena — both by funding targeted research and by creating realistic channels for disparate players to share best practices and know-how.

In 2007 our overall investment in perhaps the single most needed tool, a Parkinson's biomarker of PD, reached \$8.5 million following awards totaling \$2 million for five projects under the *Biomarkers 2007* initiative.

MJFF also awarded over \$700,000 for seven projects under its *PD Subtypes* initiative to analyze data gathered through prior longitudinal studies of Parkinson's disease. The analysis could yield valuable information on different forms of the disease, opening avenues to potential new treatments or improving clinicians'

ability to treat patients with existing therapies. Results of the *PD Subtypes* initiative also could contribute to improved design of future clinical trials.

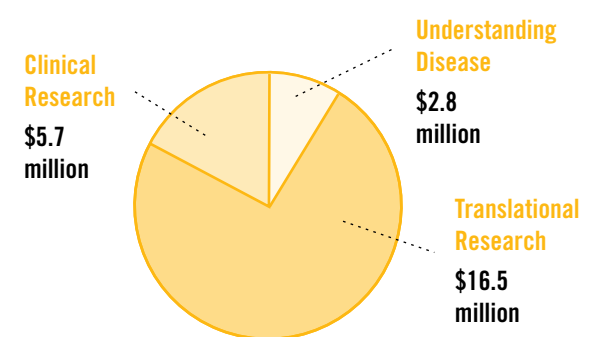
KEEPING PD RESEARCH MOVING TOWARD THE CLINIC

The Foundation maintained its focus on increasing clinical research activity in Parkinson's disease in 2007. In December we awarded \$2.5 million total for five clinical studies addressing debilitating aspects of PD such as dyskinesia and sleep disorders. And anticipating increased clinical activity in future years, the Foundation appointed SAB member Irene Hegeman Richard, MD, associate professor of neurology and psychiatry at the University of Rochester School of Medicine and Dentistry, to the newly created role of MJFF Senior Medical Advisor. The appointment formalizes Dr. Richard's role in helping to ensure that the Foundation's increasing involvement in clinical trials, including trial design and regulatory issues, is as efficient and targeted as possible.

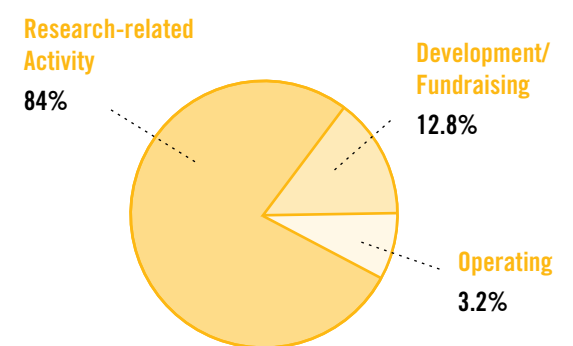
SETTING THE STANDARD

Our donors have the right to look for real, measurable returns on their investment. So we are determined to operate according to best practices and remain accountable to our supporters and the PD community at large for ensuring the highest possible degree of effectiveness. We bring a unique business model to the task — an entrepreneurial spirit and a fast-paced, high-urgency approach focused on performance and outcomes.

We ended 2007 with great optimism and enthusiasm for what lies ahead. The MJFF team is confident in its mission, committed to its strategy, and stronger than ever. While we are far from complacent and continue to learn and adjust as we go, we believe without fail that our efforts — and the efforts of those who support us — are truly making a difference in the fight to end Parkinson's disease.



RESEARCH GRANT ALLOCATION 2007



OUR EFFICIENCY 2000-2006