TRANSLATING BASIC DISCOVERIES INTO BETTER TREATMENTS AND A CURE

2006 PROGRESS REPORT

The Michael J. Fox Foundation funded over $23 million in research in 2006. It was a year in which we continued to expand our emphasis on translational and clinical research,

with over 90 percent of our funding earmarked for projects in this category (see chart, other side). Today we remain the single largest research funder solely focused on Parkinson's disease.

But even as we approach and surpass the $100-million mark in research funded directly or through partnerships since 2001, we continue to work vigilantly to ensure that our contribution to the field goes far beyond writing checks.

THE MJFF APPROACH

The Foundation's goal is not merely to fund research. Rather, we proactively partner with scientists and the PD community at large to conceive and implement new strategies for how *best* to fund research. To us, that means identifying and driving work with realistic potential to yield patient-relevant results: improved diagnosis and treatment of Parkinson's disease.

The business of translating early-stage discovery research into new and better therapies is not a simple one. It is work that requires a great deal of thoughtful, coordinated input from a wide range of players; and it is work that is essential if we are to maximize the potential of every research dollar to impact this generation of patients. Succeeding in delivering better therapies means that the Foundation's capital must behave differently from either of the major funding pools working at opposite ends of the drug development pipeline *(see illustration below)*.

MJFF delivers resources to the underfunded middle stages of the pipeline. But funding alone is not enough. To accelerate translation requires that we creatively leverage our intellectual, financial and scientific resources to influence and bridge academia and industry — making sure they are in the same conversations, both literally and figuratively.

This progress report details some of our activities to speed translation in 2006, all of which were evaluated — as are all potential MJFF investments — against their promise to return meaningful progress in critical areas of the pipeline.

The investments we make typically fall into one of two categories:

- Research exploring **specific therapeutic approaches**, where our input is likely to push prospective targets or therapies to the next stage of development.
- Research to develop **tools and resources**, where our input can provide clarity or information required to speed the creation of new treatments and/or advance the field.

HIGHLIGHTS OF 2006 MJFF INVESTMENTS IN SPECIFIC THERAPEUTIC APPROACHES

A novel strategy for alleviating levodopa-induced dyskinesias. Angela Cenci-Nilsson, MD, PhD, of Lund University in Sweden received funding under the Foundation's *Target Validation* initiative to test a novel compound that may prevent and/or reduce dyskinesias — disruptive, debilitating movements that are a common side effect of long-term levodopa therapy. At the midpoint assessment of her grant, Dr. Cenci-Nilsson confirmed that the compound had prevented dyskinesia-like abnormal movements in a rodent model of Parkinson's. If the results are validated, this work will advance to the next stages of the drug development pipeline, continuing toward clinical testing.

A partnership to keep promising drug targets moving forward. In 2006 MJFF partnered with biotech firm Elan, Inc., to launch *Novel Approaches to Drug Discovery for Parkinson's Disease,* a $2-million initiative that picks up where *Target*

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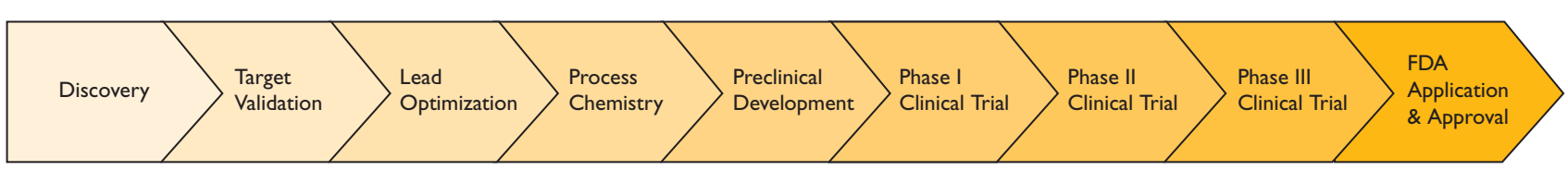
SPEEDING PROGRESS ALONG THE THERAPEUTICS DEVELOPMENT PIPELINE IS A MAJOR GOAL OF THE MICHAEL J. FOX FOUNDATION



The federal government annually funds millions in PD research, the vast majority of it early-stage basic science conducted in academic labs. At the opposite end of the pipeline, the pharmaceutical industry spends even more, primarily for late-stage drug discovery. Currently it takes 10 to 20 years, on average, for a symptomatic treatment for a central nervous system disorder to advance from discovery to FDA approval — and this timeline is likely even longer for a disease-modifying therapy.

Validation leaves off. *Novel Approaches* focuses exclusively on therapeutic targets whose potential benefit has already been demonstrated in an animal model of Parkinson's. The program holds unique potential to rapidly advance promising leads: If therapeutic approaches identified through this program warrant further development, Elan will be poised to work with grant recipients to quickly carry the work forward, one critical step closer to the clinic and patients.

Catalyzing and expanding industry investment in preclinical Parkinson's research. In 2006 MJFF awarded $4.6 million total to 10 industry research teams under the *Therapeutics Development Initiative*, our first industry-exclusive funding program, designed to catalyze and expand industry investment in preclinical research for Parkinson's disease. The program adds MJFF resources to companies' own — making industry investment in PD, specifically, more likely — thereby helping to advance Parkinson's research toward the clinic and patients. The majority of awardees are pursuing the "Holy Grail" of Parkinson's treatments: a disease-modifying therapy that could slow or stop neuron degeneration rather than simply masking symptoms while the underlying disease continues to progress. "MJFF funding has been key to bringing my project from the idea stage to the action stage," said awardee Steve Zhang, PhD, of Sangamo BioSciences.

Funding for the Phase II clinical trial of a new gene therapy approach. The Foundation provided $1.9 million to support Ceregene Inc.'s Phase II study of CERE-120, a novel gene therapy product that uses a vector to deliver neurturin, a potent nervous system trophic factor. Neurturin is a member of the same family as GDNF, and like GDNF it has shown potential in preclinical studies to slow or stop Parkinson's disease progression. The Phase II funding followed on the announcement of promising early results from Ceregene's open-label Phase I trial of CERE-120, which also received Foundation support.

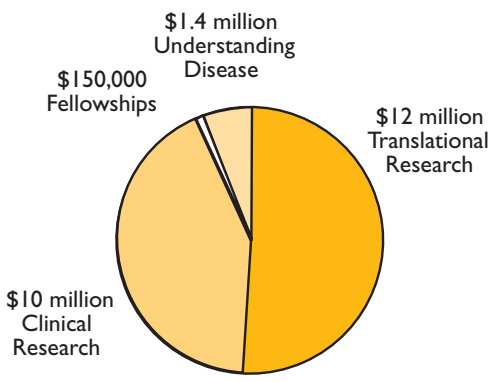
HIGHLIGHTS OF 2006 MJFF INVESTMENTS IN TOOLS AND RESOURCES

A potential biomarker breakthrough. With over $4 million in biomarker research funded to date, the Foundation continues to marshal the search for a PD biomarker. The field recently received a considerable boost when MJFF-funded researchers found a specific expression pattern of eight genes that might someday be used to spot people at high risk of developing Parkinson's disease. The work is an early but vital step toward a simple blood test for Parkinson's disease. Additionally, the results could improve clinical trials by allowing researchers to better track disease progression in the presence of a given therapy.

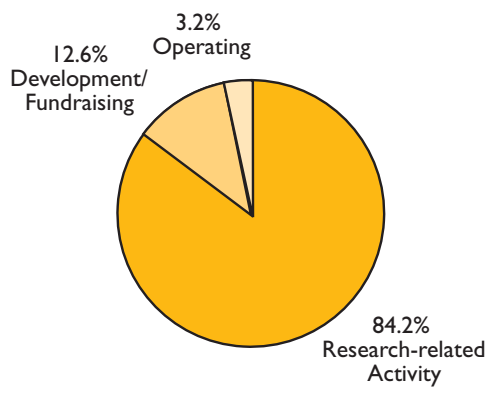
Maximizing the potential of a unique resource. In fall 2006 the Foundation announced a $2.8-million collaboration with the Arizona Parkinson's Disease Consortium (APDC). *The Prescott Family Initiative at the Arizona Parkinson's Disease Consortium* will expand APDC's Brain and Body Donation Program, a unique resource that conducts in-depth clinical and post-mortem studies of normal-aging adults as well as PD patients. The MJFF collaboration will maximize the program's potential to advance PD research by tying clinical evidence to pathological underpinnings of onset and progression — information that could contribute to earlier detection and diagnosis of PD.

A first-of-its-kind PD genetics database. Given the rapid pace of the field of genetics, a centralized information source for genetic discoveries is critical to their translation into treatments. Yet until recently, the field lacked such a tool. Last fall the Foundation, together with collaborators at Harvard Medical School and the Alzheimer Research Forum, announced the launch of *PDGene* (www.pdgene.org), an online inventory of studies on genes implicated in Parkinson's disease. This regularly updated Web portal provides scientists with the most current information, in one place, about every gene that previous research has shown may play a role in Parkinson's.

RESEARCH GRANT ALLOCATION 2006

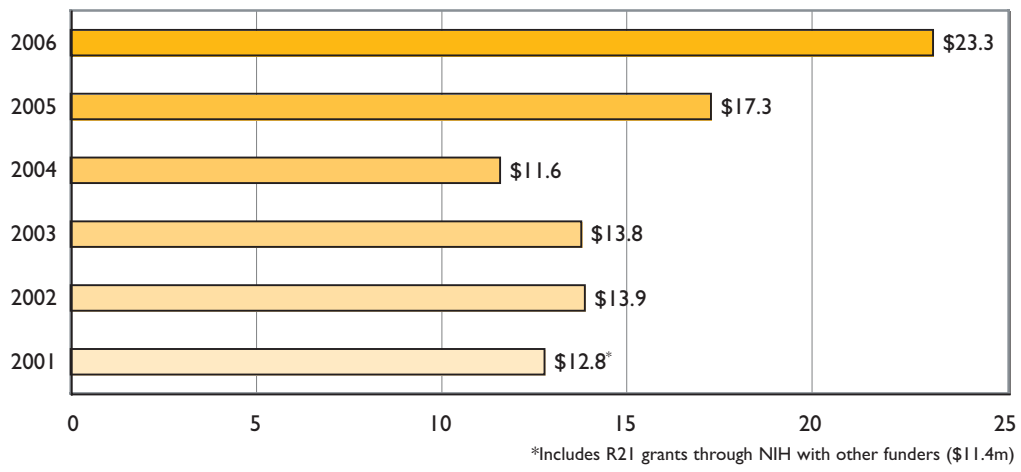


OUR EFFICIENCY 2000–2005



RESEARCH FUNDED 2001–2006

Dollar amounts in millions



*Includes R21 grants through NIH with other funders ($11.4m)

For more information about any of the projects highlighted in this report, including lay abstracts and researcher bios, please visit the Foundation's Web site at www.michaeljfox.org.