eFigure 1

STEADY-PD III
Efficacy of Isradipine in early Parkinson Disease

Dear **[Health Care Provider NAME],**

[site name] has been selected as a clinical study site for the STEADY-PD III clinical trial for isradipine. The success of this study depends on clinicians like you referring your newly diagnosed Parkinson disease patients to the study.

[site name] is one of 56 Parkinson Study Group (PSG) sites funded by the National Institute of Neurological Disorders and Stroke (NINDS) of the National Institutes of Health. Collaboratively, the sites will recruit 336 early, untreated PD patients not receiving dopaminergic therapy and not projected to require PD symptomatic treatment for at least 3 months. STEADY-PD III is based on preclinical data demonstrating neuroprotective effects of isradipine in animal models of parkinsonism, positive epidemiological data, and results of a Phase II study that demonstrated acceptable safety and tolerability of isradipine.

STEADY PD III rate of enrollment has been successful, but we are now turning our focus toward reaching our goal of 10% minority enrollment. We would greatly appreciate any minority referrals you could provide. Please be assured that any patient you refer will remain in your practice.

You will find enclosed:

- STEADY-PD III Poster
- Study Pocket Card

Please place the STEADY-PD III Poster in a location visible to patients who may be interested in participating. The Study Pocket Card is a quick reference tool depicting the inclusion and exclusion (eligibility) criteria for identifying potential participants.

Additional information about STEADY-PD III may be found by visiting http://www.STEADYPD3.com or http://www.clinicaltrials.gov.

If you or any of your patients are interested in learning more about STEADY-PD III, please share my information or that of my study coordinator, **[coordinator's name],** who can be reached at **[coordinator's phone number]** or **[coordinator's e-mail address]**.

Thank you in advance for considering this request.

Best regards,
[Investigator's name]
[investigator's title]
[investigator's department and hospital]
[investigator's phone number] [Investigator's e-mail address]

eFigure 2

PSG PARKINSON STUDY GROUP

STEADY-PD III

Efficacy of isradipine in early Parkinson's Disease

What is the STEADY-PD III Trial?

- The purpose is to study whether isradipine (an investigational drug) is effective in slowing the progression of Parkinson's disease (PD)
- Isradipine is a calcium channel blocker approved for the treatment of high blood pressure since 1990, but is considered investigational in this study as it has not been approved for treatment of PD
- Isradipine has been shown to have a neuroprotective effect on pre-clinical models of parkinsonism

Who is eligible to participate in STEADY-PD III?

- Diagnosis of Parkinson's disease less than 3 years
- At least 30 years old at the time of diagnosis
- Not currently receiving dopaminergic therapy or not on symptomatic therapy

NIH National Institute of Neurological Disorders and Stroke

What are the study requirements?

- If you are interested in being in the STEADY-PD III study, you will have a Screening visit with the study doctor to determine if you are eligible to participate
- If you are determined to be eligible, you will complete at least 12 in-person visits and 4 follow-up phone calls over approximately 36 months
- At your study visit, you will complete paper questionnaires about your general health, mood, physical activity and your ability to complete daily activities

How to learn more and participate in the STEADY-PD III study ?

- To learn more –please visit **www.SteadyPD3.com** or **www.ClinicalTrials.gov**
- If you are interested in participating –please call our toll free study number at 1-855-825-3390

A clinical trial conducted by the PSG funded by **a grant from the National Institute of Neurological Disorders and Stroke. Biomarker and DNA sub-study is funded by the Michael J. Fox Foundation.**

eFigure 3

[Insert Date]

Dear Dr. [Insert Referring Physician Name],

I am writing to invite you to play a critical role in referring potential participants for a Parkinson Study Group (PSG) clinical research project funded by the National Institute of Neurological Disease and Stroke (NINDS) and the Michael J. Fox Foundation for Parkinson's Research.

This pivotal study is entitled: "*A randomized, double-blind, placebo-controlled trial of urate-elevating inosine treatment to slow clinical decline in early Parkinson's disease"* and is known as **SURE-PD3** (for **S**tudy of **UR**ate **E**levation in **P**arkinson's **D**isease, phase **3**). We are asking for your help identifying patients within your practice who may qualify for participation. Specifically, we are seeking newly diagnosed Parkinson's disease (PD) patients who are not currently taking any PD medications (unless it is an MAO-B inhibitor). The primary objective of this study is to determine whether oral inosine dosed to moderately elevate serum urate (from ≤5.7 mg/dL to 7.1-8.0 mg/dL) over 2 years slows clinical decline in early PD.

The SURE-PD3 study is enrolling 270 subjects at 60 centers across the United States. Study subjects who meet all eligibility criteria will be randomized 1:1 for treatment with inosine or placebo for two years. Please take a moment to look at the key eligibility criteria listed below to see if you may have appropriate patients to refer to this study.

Key Eligibility Criteria:

1. Fulfillment of diagnostic criteria for idiopathic PD with at least two of the cardinal signs of PD (resting tremor, bradykinesia, rigidity).
2. Absence of current or imminent (within 90 days of enrollment) PD disability requiring dopaminergic therapy.
3. Diagnosis of PD made within 3 years prior to 1st Screening Visit.
4. No history of chronic obstructive pulmonary disease, gout, uric acid, urate urolithiasis, myocardial infarction or stroke.

The success of this study in evaluating the effectiveness of inosine hinges entirely on the ability of sites to meet the study enrollment targets. Enclosed we have included a patient brochure that can be placed in your waiting room and shared with potential participants. We know that the appropriate participants for the study are out there, but can only be successful in this endeavor with your help identifying them.

We hope you see the value in the work we are doing and that you will join us as a clinical research partner. Please feel free to contact me for more information about this project or for additional materials to distribute to your patients. Thank you for your valuable support in this venture.

Warm regards,

{Site PI Signature}

[PI Name]

[Contact information]

Ver1.0
22 March 2016

eFigure 4

SURE-PD3 Study

A randomized, double-blind, placebo-controlled trial of urate-elevating inosine treatment to slow clinical decline in early Parkinson's disease

Do you have Parkinson's disease?

Have you been diagnosed within the past 3 years?

If yes to both, you may be a good candidate for a research study.

STUDY DETAILS

What is the goal of this study?

The SURE-PD3 study is looking for patients who have early largely untreated Parkinson's disease. We are doing this research study to see if increasing ones own levels of the antioxidant urate can slow the progression of Parkinson's disease (PD). We will increase blood urate levels with a natural supplement called inosine.

You may qualify for the study if you:

- Have been diagnosed with PD within the past 3 years.
- Are not taking any medication to treat PD (except for MAO-B inhibitors).
- Don't have a history of gout, recurrent kidney stones, heart attack or stroke.

What is involved if I participate?

- Volunteers will be in this study for about 28 months and will visit the clinic at least 14 times.
- If you choose to volunteer and pass several screening tests, you will be randomly assigned to either inosine (active drug) or a placebo (an inactive drug) with an equal chance of receiving either.

If you are interested in participating or want to learn more,
please contact [INSERT SITE CONATCT INFORMATION HERE].