INFORMED CONSENT

TITLE: **A Phase 3, Twelve-week, Multi-Center, Multinational, Randomized, Double-Blind, Double-Dummy, Parallel Group Study to Determine the Efficacy, Safety, and Tolerability of P2B001 Once Daily Compared to its Individual Components in Subjects With Early Parkinson's Disease and to a Calibration Arm of Pramipexole ER**

PROTOCOL NO.: **P2B001/003**

SPONSOR: **Pharma Two B**

INVESTIGATOR:

SITE ADDRESS:

24 HR. TELEPHONE #:

INTRODUCTION

Before agreeing to participate in this research study, it is important that you read and understand the following explanation of the proposed research study. This consent document describes the purpose, procedures, benefits, risks, discomforts and precautions of the study. It also describes the alternative procedures that are available to you and your right to withdraw from the study at any time. No guarantees or assurances can be made as to the results of the study. It is up to you to decide if you wish to participate. Your study doctor or member of the study staff will go through this Information Sheet with you and answer any questions you might have. Ask the study doctor or member of the study staff if there is anything you do not understand. Talk to others about the study if you wish. Once you understand the study, and if you agree to take part, you will be asked to sign the Consent Form. You will be given a copy to keep. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

If you are not completely truthful with your Investigator regarding your health history, you may harm yourself by participating in this study.

This study is being organized by a pharmaceutical company, Pharma Two B, located at 3 Pekeris St., Weizmann Science Park Rehovot 7670203 Israel.

BACKGROUND AND PURPOSE

You are being asked to participate in this research study because you have early Parkinson's disease (PD). This is a research study to test a new investigational drug

(P2B001). An investigational drug is one that is not approved by the United States Food and Drug Administration (FDA).

The purpose of this research study is to:

- test the safety and effectiveness of the study drug, P2B001, in treating patients with early Parkinson's disease

P2B001 is comprised of low doses of two drugs, pramipexole and rasagiline, which are both approved drugs in the United States and routinely used in standard therapy for Parkinson's disease. The two drugs work in two different mechanisms that help each other, so there is a reason to believe that their combined activity will be better than each individual drug, and that lower doses can be used without losing the therapeutic effect. Thus, the development of P2B001 is intended to provide a combination of low doses of these two drugs, in an improved formulation, that is hoped to be more effective in controlling Parkinson's disease symptoms and with less side effects than each of the drugs taken alone or the current available commercial drugs taken together.

The safety and efficacy of P2B001 will be assessed by comparing P2B001 to its individual components; pramipexole and rasagiline. This will be done by evaluating the responses participants provide on questionnaires relating to Parkinson's disease and quality of life that will be completed on every visit. In addition, this study will also compare P2B001 to another FDA approved extended-release version of pramipexole.

Because this is a research study, the study product will be given to you only during this study and not after the study is over.

NUMBER OF SUBJECTS / LENGTH OF PARTICIPATION

About 525 subjects will participate in this study. Your participation in this study will last approximately 14 to 18 weeks and include 7 study visits to the study center.

PROCEDURES

Before any study-related tests and procedures are performed, you will be asked to read and sign this consent document. The following tests and procedures will be performed to determine if you qualify to take part in this study:

Visit 1 Screening – performed up to 28 days before Visit 2 (Baseline)

- Interview regarding your Medical History and Personal Information (name, date of birth, gender, race/ethnicity, etc.)
- Complete Physical and Neurological Examination
- Laboratory blood and urine tests (including a pregnancy test if you are a woman of child-bearing potential). The study doctor or study staff will tell you if the pregnancy test results are positive. The results of the pregnancy testing must be negative in order for you to be in the study.

- Electrocardiogram (ECG) to evaluate heart function
- Completion of questionnaires relating to your disease and symptoms and your mental health (including thoughts of suicide)
- Vital Signs (blood pressure, pulse, respiration, body temperature, height and weight)
- Review of symptoms and medications taken

After completion of all the testing for the assessment of eligibility, it will be decided by the study doctor whether you are eligible for the study.

If your study doctor decides you are eligible for the study, you will be randomly assigned by chance (like the flip of a coin) to receive either P2B001, Rasagiline, Pramipexole or extended-release Pramipexole. You will have a 2 in 7 chance of being assigned to one of the three first groups and 1 in 7 chance of being assigned to the fourth group:

- Group 1 : P2B001 (Pramipexole dihydrochloride 0.6 mg/Rasagiline 0.75 mg) once daily + Placebo of extended-release Pramipexole
- Group 2 : Pramipexole dihydrochloride 0.6 mg once daily + Placebo of extended-release Pramipexole
- Group 3: Rasagiline 0.75 mg once daily + Placebo of extended-release Pramipexole
- Group 4: extended-release Pramipexole individually titrated to optimal dose (1.5 - 4.5 mg / day) + Placebo of P2B001

This is a double-blind study, which means neither you nor the Investigator will know to which of these study drug groups you are assigned. In case of an emergency, however, the Investigator can get this information. In order to ensure that no one knows which of the 4 groups you have been assigned to you will be asked to take one capsule and one to three tablets once daily. The capsule will contain either P2B001 0.6/0.75 mg, pramipexole 0.6 mg, rasagiline 0.75 mg or matching placebo. The tablet(s) will contain either extended release Pramipexole or matching placebo. If you are assigned to groups 1, 2 or 3, you will take the assigned capsule together with placebo tablets of extended-release Pramipexole. If you are assigned to group 4, you will take extended-release Pramipexole tablet(s) with one placebo capsule.

Visit 2 – Baseline – performed <u>within</u> the 4 weeks after Visit 1 (Screening)

- Randomization to study drug dosing group (as described above)
- Electrocardiogram (ECG)
- Receive study drug as well as dosing instructions and emergency contact cards
- Completion of questionnaires relating to your disease, symptoms and mental health
- Vital Signs (Heart rate, blood pressure and respiration and weight)
- Review of symptoms and medications taken
- Urine pregnancy test (for women of child-bearing potential)

Visit 3 – Week 3 (± 2 days)

At the end of week 3 ± 2 days, you will be required to visit the clinic so that the study doctor can evaluate how you tolerate the study drugs, at this time you will be taking the 1.5 mg dose of pramipexole ER (or matching placebo tablets). After this evaluation, the study doctor may decide to keep your dose of this medication at 1.5 mg or increase it to 3.0 mg depending on how you tolerate the study drugs and how they are affecting your Parkinson's symptoms. If you are unable to tolerate a dose of least 1.5 mg of Pramipexole ER (or placebo) per day you will be asked to stop taking all study medications.

The following activities will be performed:

- Evaluation of Pramipexole ER (or matching placebo tablets) dose
- Review of symptoms and medications taken
- Completion of questionnaires relating to your disease, symptoms and mental health

Phone Call - Week 4 (± 2 days)

At the end of week 4, you will receive a phone call from the study doctor so that the study doctor can again evaluate how you tolerate the study drugs and how they are affecting your Parkinson's symptoms. At this time you may be taking 1.5 mg or 3.0 mg of pramipexole ER (or matching placebo tablets). After this evaluation, the study doctor may decide to keep your dose of this medication unchanged or the study doctor may decide to increase or decrease your dose of this medication if you need it. During this phone call a review of symptoms and medications taken will also be done. If the study doctor deems it necessary, you may be asked to visit the clinic so that the study doctor can perform these evaluations in person.

Visit 4 – Week 5 (± 2 days)

At the end of week 5 (± 2 days) you will be required to visit the clinic so that the study doctor can evaluate how you tolerate the study drugs. At this time you may be taking 1.5 mg or 3.0 mg or 4.5 mg of Pramipexole ER (or matching placebo tablets). Again, the study doctor may adjust your dosage of this medication based on how you tolerate the study drugs and how they are affecting your Parkinson's symptoms. The study doctor can continue to evaluate your dosage of Pramipexole ER (or matching placebo tablets) up to the end of the following week (Week 6). At that point, you will stay at the same dose of this medication through to Week 12.

The following activities will be performed:

- Return bottles of study medication of the titration box (opened and unopened bottles)
- Completion of questionnaires relating to your disease, symptoms and mental health
- Vital Signs (Heart rate, blood pressure and respiration and weight)
- Review of symptoms and medications taken
- Laboratory test (only in specific cases when required by the study doctor; the study doctor will tell you if you need these blood tests)

Visit 5 – Week 8 (± 2 days)

The following activities will be performed:

- Return bottles of study medication of the first maintenance box (opened and unopened bottles)
- Completion of questionnaires relating to your disease, symptoms and mental health
- Vital Signs (Heart rate, blood pressure and respiration and weight)
- Review of symptoms and medications taken
- Laboratory test (only in specific cases when required by the study doctor; the study doctor will tell you if you need these blood tests)

Visit 6 – Week 12 (± 2 days) Treatment termination

The following activities will be performed:

- Return bottles of study medication of the second maintenance box (opened and unopened bottles)
- Completion of questionnaires relating to your disease, symptoms and mental health
- Vital Signs (Heart rate, blood pressure and respiration and weight)
- Review of symptoms and medications taken

Visit 7 – Dosing Follow-up – performed 2 weeks after termination visit

The following activities will be performed:

- Physical and Neurological Examination
- Completion of questionnaires relating to your disease, symptoms and mental health
- Vital Signs (Heart rate, blood pressure and respiration and weight)
- Return bottles of study medication of the down titration box (opened and unopened bottles)
- Electrocardiogram (ECG)
- Review of symptoms and medications taken
- Laboratory blood and urine tests (including a pregnancy test if you are a woman of child-bearing potential). The study doctor or study staff will tell you if the pregnancy test results are positive

Unscheduled Visits

If needed, your study doctor may request unscheduled visits:

- Unscheduled visit for titration follow-up:

During the titration phase (first 6 weeks) an unscheduled visit may be conducted to assess the need to raise or lower the dose of extended-release pramipexole or placebo. In addition to the dose evaluation, a review of symptoms and medications will also be conducted. No other study activities will be performed at this visit unless safety considerations arise (see next section).

- Unscheduled visit for other reasons:

An unscheduled visit may take place at any time during the study (for example new Parkinson's Disease symptoms or any symptom that warrant personal evaluation). The following activities will be performed:

- Vital signs (Heart rate, blood pressure and respiration and weight)
- Review of symptoms and medications taken
- Physical and Neurological Examination
- Completion of any uncompleted questionnaires, as needed

A summary of the visits and activities that will be performed are in the table below:

Visit Number	1	2	3	****	4	5	6	7
Visit Type	**Screening**	**Baseline**	**End of Week 3**	**End of Week 4**	**End of Week 5**	**End of Week 8**	**End of Week 12**	**End of Week 14**
ACTIVITIES								
Obtain your written informed consent	X							
Determine if you meet the study entry criteria	X	X						
Test your thinking abilities	X							
Obtain your medical history & demographic information	X							
Complete Physical and Neurological examination performed	X							
Physical and Neurological examination performed (only if you have symptoms)								X
Take blood and urine samples for safety laboratory tests (including pregnancy test if you are a woman of child bearing potential)	X							X
Urine pregnancy test (if you are a woman of child bearing potential)		X						
Heart Function Test (ECG)	X	X						X
Randomization to study drug		X						
Receive study drug and review dosing instructions		X						
Receive dosing instruction cards and emergency contact cards		X						
Obtain your vital signs/weight	X	X			X	X	X	X
Review medications you are taking	X	X	X	X	X	X	X	X
Review any symptoms you may be having	X	X	X	X	X	X	X	X
Assessment of your Parkinson's disease and symptoms	X	X			X	X	X	
Complete questionnaires regarding your thoughts and feelings including thoughts of suicide	X	X	X		X	X	X	X
Complete questionnaire regarding any changes in obsessive behaviors		X	X		X	X	X	X
Complete questionnaires regarding your blood pressure and your sleep		X			X	X	X	
Complete questionnaires regarding your health, mood and Parkinson's disease symptoms		X					X	
Evaluation of how well you are tolerating study drugs			X	X	X			
Return study drug and review your compliance					X	X	X	X
Trial Completion								X

STUDY RESTRICTIONS

There are certain medications you cannot take while you are in the study, including most medications to treat Parkinson's disease. The study doctor will review those medications with you, and you should let the study team know when any of your medications change.

You may not take the following medications during the study:

- Other investigational drugs (within 30 days before starting study drug)
- Anti-Parkinson's Disease drugs such as:
    - MAO-B inhibitors (selegiline (*Emsam, Eldepryl, Zelapar*) or rasagiline (*Azilect*)) (within 3 months before starting study drug);
    - Levodopa or other dopamine agonists (pramipexole (*Mirapex*), ropinerole (*Requip*), pergolide (*Permax*), apomorphine (*Apokyn*), piribedil (*Trivastal*), cabergoline (*Dostinex*), lisuride (*Dopergin*), bromocriptine (*Cycloset*)) (within 2 months before starting study drug).
    - Anticholinergic drugs such as benztropine (*Cogentin*), biperiden (*Akineton*), ethopropazine (*Parsitan*), orphenadrine hydrochloride, (*Disipal*), procyclidine (*Kemadrin*) and trihexyphenidyl (*Artane*) and amantadine (within 1 month before starting study drug).

Taking certain other drugs together with P2B001 may increase the chance of serious unwanted effects; therefore you may not take the following medications during the study:

- Ciprofloxacin (*Cipro*) or other CYP1A2 inhibitors
- Dextromethorphan (*Delsym*) cough suppressant
- Opioid based pain medications such as tramadol (*Ultram*), methadone, meperidine (*Demerol*) and propoxyphene (*Darvon*)
- St. John's Wort or cyclobenzaprine (*Flexeril* - muscle relaxant)
- Non selective MAO inhibitors, such as phenelzine (*Nardil*), tranylcypromine (*Parnate*)
- Dopamine antagonists, such as the neuroleptics (phenothiazines (eg. prochlorperazine (*Compro, Procomp*) or promethazine (*Promethegan*), butyrophenones (eg. haloperidol or droperidol), thioxanthenes (eg. thiothixene (*Navane*)) or metoclopramide (*Reglan*).
- Marijuana (within 30 days before starting study drug)

You can take peripheral anticholinergic drugs (such as oxybutynin (*Ditropan*), orphenadrine citrate (*Norflex*), tiotropium bromide (*Spiriva*) if you are stable on low dose for at least 4 weeks prior to study entry, and without (or with minor) effects on your thinking abilities; however, once enrolled into the study use of new peripheral anticholinergic drugs is not allowed. If you are taking one of these drugs, you will be followed very closely for possible side effects related to your thinking abilities.

Care should be taken to avoid or minimize use of sympathomimetic medications, including nasal, oral and ophthalmic decongestants and cold remedies and sedating medication (such as ephedrine, and tetrahydrozoline-ophthalmic (Clarif-Eye, Murine Plus, Opti-Clear, Visine)) due to possible hypertensive reactions.

Care should also be taken when taking sedating medications (e.g. Diphenhydramine, (Benadryl, Sominex) Doxylamine Succinate (Unisom) and other first generation antihistamines such as clemastine (Tavist), chlorpheniramine (Chlor-Trimeton), and brompheniramine (Dimetane)) as these may make you sleepy when combined with the study drugs. You should exercise special caution when driving or using machinery since the study drugs may cause drowsiness, lack of coordination or decreased reaction time. Finally, if you take antidepressant medication such as a selective-serotonin reuptake inhibitor (SSRI) like Prozac, Zoloft or Paxil, you will need to pay special attention for signs and symptoms of serotonin syndrome (for example, headache, agitation, hypomania, mental confusion, sweating, hyperthermia (high body temperature), hypertension, tachycardia (rapid heartbeat), nausea, diarrhea, myoclonus (muscle twitching), overactive reflexes (involuntary twitching), tremor, as the risk of experiencing this rare syndrome are increased when taking study drug with antidepressants.

Because of possible drug reactions, you cannot enter this study if you are allergic or sensitive to pramipexole or rasagiline. Notify your study doctor if you have had allergic reactions to components of other drugs.

Taking certain other drugs (described above) together with study drugs may increase the chance of unwanted effects. The risk will depend on how much of each drug you take every day, and on how long you take the drugs together. If your medical doctor directs you to take these drugs together on a regular basis, follow his or her directions carefully.

Alcohol may increase drowsiness or sleepiness that can be caused by taking the study drug. You will be requested to limit alcoholic consumption to one glass of wine or one shot a day, and not within three hours before or after taking the study drug.

You will be requested to take one capsule and 1-3 tablets of study drug by mouth with a glass of water. Study drugs can be taken with or without food. You should try to take study drug at about the same time each day.

You will need to limit yourself from eating certain aged cheeses, like stilton cheese, that contain very high amounts of a chemical called tyramine, which can potentially cause a hypertensive reaction (a sudden increase in blood pressure) in subjects taking study drug.

EXPECTATIONS

If you participate in this study, you will be expected to:

- Complete all required visits and procedures
- Bring your study drug with you for accountability

- Take the study drug as prescribed
- Follow the medication restrictions
- Report all side effects, changes in your health or the way you feel, and medical problems to the study personnel
- Complete all questionnaires
- If you miss or forget to answer questions on these questionnaires, study personnel may phone you to obtain answers to these questions
- Inform the study doctor or study staff if you decide to discontinue your participation. You will be asked to complete a treatment termination visit and continue with all study visits and activities as planned, for follow up, without taking any study medication.

RISKS, SIDE EFFECTS AND/OR DISCOMFORTS

Based on previous studies with P2B001 as well as past experience with the doses of rasagiline, pramipexole and extended-release pramipexole used in this study, possible side effects of the drugs used in this study include the following:

Common (more than 10% of people)

- Drowsiness
- Nausea

Uncommon (between 2 to 10% of people)

- Headache
- Fall
- Accidental injury
- Indigestion
- Diarrhea
- Dizziness, spinning sensation
- Loss of appetite
- Depression
- Weight loss
- Flu symptoms
- Loss of coordination
- Shortness of breath
- Muscle spasms
- Excessive daytime sleepiness
- Decrease in blood pressure when standing
- Constipation
- Hallucinations
- Vomiting
- Dry mouth, loss of appetite
- Involuntary movements
- Joint Pain
- Swelling of the limbs
- Fatigue
- Abdominal discomfort / pain
- Loss of balance,
- Skin rash
- Insomnia
- Problems with Impulse Control
- Compulsive Behaviors
- Erectile Dysfunction
- Behavioral/mental status changes
- Stooped Posture

Rare (between 1 to 2% of people)

- Pink Eye
- Fever
- Runny Nose
- Skin discolorations
- Abnormal dreams
- Involuntary muscle contractions
- Infection
- Sweating
- Weakness
- Muscle Weakness
- Tendon inflammation
- Cough
- Stomach Flu
- Tremor
- “Pins and Needles”
- Back pain
- Increased appetite
- Sleep disorder
- Arthritis
- Fatigue
- Neck Pain

Other less common side effects have been reported. The Investigator or staff can discuss these with you.

Please tell the study doctor or study staff right away if you have any side effects. Please tell them if you have any other problems with your health or the way you feel during the study, whether or not you think these problems are related to the study drug.

RISKS OF STUDY PROCEDURES

- Blood samples: possible side effects from blood drawing include faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. There is also a slight possibility of infection.
- ECG: skin irritation is rare but could occur during an ECG from the electrodes or gel that is used.
- Questionnaires: filling out the questionnaires or answering the study doctor or study staff’s questions could lead you to feel uncomfortable or upset. Please tell the study doctor or study staff if you feel uncomfortable or upset while filling out a questionnaire or answering questions. You have the right to refuse to answer any questions.

UNFORESEEN RISKS

Since the study drug is investigational when taken alone or in combination with other medications, there may be other risks that are unknown. You will be informed in a timely manner if new information about the study becomes available that may be relevant to continued participation in the trial. All drugs have a potential risk of an allergic reaction, which if not treated promptly, could become life-threatening. Some things that happen during an allergic reaction that could be a sign or symptom of a life-threatening allergic reaction (anaphylaxis) are:

- a rash
- a fast pulse
- sweating

- a feeling of dread
- swelling around the eyes and mouth
- swelling of the throat
- wheezing
- having a hard time breathing
- a sudden drop in blood pressure (making you feel dizzy or lightheaded)
- inability to breathe without assistance

You should get medical help and contact the study doctor or study staff if you have any of these or any other side effects during the study.

PREGNANCY / BIRTH CONTROL

Taking the study drug may involve unknown risks to a pregnant woman, an embryo, fetus (unborn baby) or nursing infant. Therefore, if you are pregnant, planning to become pregnant or are breastfeeding a child, you cannot participate in this study.

Females of child bearing potential must have a negative pregnancy test before the study starts and again just before receiving study drug. In order to reduce the risk of pregnancy, if you are a female of child bearing potential you must use an effective method of birth control while you are participating in this study. Acceptable methods of birth control include oral contraceptive or long-term injectable or implantable hormonal contraceptive, double-barrier methods such as condom plus diaphragm, condom plus spermicide foam, condom plus sponge, or intra-uterine devices or abstinence. Oral, implantable, or injectable contraceptives are only considered effective if used properly and started at least 30 days prior to the screening visit. Some drugs (e.g., antibiotics) may interact with hormonal contraceptives, making them not work properly. Please inform your study doctor of all other drugs you are taking.

If you suspect that you may have become pregnant during the study, you must contact the study doctor immediately and have a urine pregnancy test performed at the site. If the urine test is positive, study drug administration will be interrupted pending the results of a confirmatory blood/serum test. If the pregnancy is confirmed with a positive blood/serum test, then you will be permanently discontinued from study drug and be asked to return to the site for a study termination visit. Your study doctor will ask to follow you and the progress of your pregnancy until the baby is born. Information about your pregnancy and its outcome will be collected and used to learn more about the effects of the study drug on pregnancy.

ALTERNATIVE TREATMENT

You do not have to be in this study to get help for your Parkinson's Disease.

If you do not wish to participate in this study, you will continue to be treated by your regular doctor and your care will not be jeopardized in any way. Your regular doctor may continue with your current treatment regimen with modifications that you and your regular doctor agree are appropriate.

Other treatments available for Parkinson's Disease include: levodopa/carbidopa, pramipexole or other dopamine agonists, rasagiline, selegiline, amantadine or several anticholinergic drugs. There are benefits and risks associated with these medications that should be discussed with your study doctor. In addition, you may discuss your options with your regular health-care provider.

NEW FINDINGS

Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be made available to you.

BENEFITS

The study drug may result in an improvement in the mental and movement symptoms associated with early Parkinson's disease as well as your performance of daily activities. There is, however, no guarantee that you will benefit from your participation in this study. Results from this study may benefit others with Parkinson's disease in the future.

COMPENSATION FOR PARTICIPATION

You will not receive any monetary compensation for your participation in this study.

CONFIDENTIALITY

Records of your participation in this study will be held confidential except when sharing the information is required by law or as described in this informed consent. The Investigator, the sponsor or persons working on behalf of the sponsor, and under certain circumstances, the United States Food and Drug Administration (FDA) and the Institutional Review Board (IRB) will be able to inspect and copy confidential study-related records which identify you by name. This means that absolute confidentiality cannot be guaranteed. If the results of this study are published or presented at meetings, you will not be identified.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

COMPENSATION FOR INJURY

If you are injured as a result of taking the study drug(s) or from procedures done for the purpose of this study, the sponsor will pay for those medical expenses necessary to treat your injury that are not covered by your medical insurance or any other third party

coverage. There are no plans to provide other compensation beyond that which is listed in this informed consent document. You will not lose any of your legal rights or release the Sponsor, the Investigator, the study staff, or study site from liability for mistakes or intentional misconduct by signing this consent document.

If you are injured during this study, your Investigator will discuss with you the available medical treatment options.

COSTS

There will be no charge to you for your participation in this study. The study drug, study-related procedures, and study visits will be provided at no charge to you or your insurance company.

EMERGENCY CONTACT / IRB CONTACT

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on page 1 of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in a research study being conducted by the Investigator listed on page 1 of this document.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, you should write to Schulman IRB, 4445 Lake Forest Drive – Suite 300, Cincinnati, Ohio 45242, or call toll-free 1-888-557-2472 during business hours Monday - Friday 8:00 a.m. to 6:00 p.m. EST.

VOLUNTARY PARTICIPATION / WITHDRAWAL

Your decision to participate in this study is voluntary. You may choose to not participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care.

The Investigator or the sponsor can stop your participation at any time without your consent for the following reasons:

- If it appears to be medically harmful to you;
- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled; or
- For administrative reasons, including competitive enrollment - the target number of subjects has entered the study.

If you leave the study for any reason, the Investigator may ask you to have some end-of-study tests for your safety.

If for any reason you or your doctor decide you need to completely stop taking the study drug during the course of the study (prior to visit 6), you will need to undergo an early treatment termination visit.

This visit can be conducted as part of the next scheduled study visit if it is within 5 days of the day you stopped taking study medication. If the next scheduled visits is more than 5 days away your doctor may ask you to return to the clinic as soon as possible for an "unscheduled" visit. All efforts should be made to schedule the early treatment termination visit as close to the day when you stopped taking study medication as possible. All activities listed in the treatment termination (visit 6) and safety visits (visit 7) will be performed at this visit. The entire study medication kit with all boxes and opened and unopened bottles should be returned at this time.

After the early treatment termination visit is performed, you will be asked to continue with all study visits and activities as planned, for follow up, without taking any study medication. During this time, you will be allowed to take medications for your Parkinson's disease if needed.

Finally, if you decide to stop study participation for any reason before the end of week 12, including study treatment and study scheduled visits and activities, you will need to undergo an early study termination visit. Again, all efforts should be made to schedule the early study termination visit as close to the day when you decided to stop your participation in all study visits and activities. Again, all activities listed in the treatment termination (visit 6) and safety visits (visit 7) will be performed at this visit. If not already returned, the entire study medication kit with all boxes and opened and unopened bottles should be returned at this time.

PRIMARY CARE PHYSICIAN / SPECIALIST NOTIFICATION OPTION

Please indicate below whether you want us to notify your primary care physician or your specialist of your participation in this study.

_____ Yes, I want the Investigator to inform my primary care physician/specialist of my participation in this study.

_____ No, I do not want the Investigator to inform my primary care physician/specialist of my participation in this study.

_____ I do not have a primary care physician/specialist.

_____ The Investigator is my primary care physician/specialist.

CONSENT

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing this consent document. I will receive a copy of this signed consent document.

_____
Subject's Printed Name

_____ _____
Subject's Signature Date

_____
Printed Name of the Person Conducting the Consent Discussion

_____ _____
Signature of the Person Conducting the Consent Discussion Date

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

During your participation in this research study, the Investigator and study staff will collect or create personal health information about you (for example, medical histories and results of any tests, examinations or procedures you undergo while in the study) and record it on study documents. The Investigator will keep this personal health information in your study-related records (that we will refer to as "your study records"). In addition, the Investigator may obtain, and include in your records, information regarding your past, present and/or future physical or mental health and/or condition. Your Investigator may ask you to sign a separate authorization to obtain some or all of your medical records from your doctor. Your study records may include other personal information (such as social security number, medical record numbers, date of birth, etc.), which could be used to identify you. Health information that could identify you is called "Protected Health Information" (or "PHI").

Under federal law (the "Privacy Rule"), your PHI that is created or obtained during this research study cannot be "used" to conduct the research or "disclosed" (given to anyone) for research purposes without your permission. This permission is called an "Authorization". Therefore, you may not participate in this study unless you give your permission to use and disclose your PHI by signing this Authorization. By signing, you are agreeing to allow the Investigator and staff to use your PHI to conduct this study.

By signing this Authorization, you also are agreeing to allow the Investigator to disclose PHI as described below:

- The sponsor of this study and anyone working on behalf of the sponsor to conduct this study (referred to as "the sponsor"). The sponsor will analyze and evaluate the PHI and may use it to develop new tests, procedures and commercial products. The study staff will assign a code number and/or letters to your records, which means that you will not ordinarily be identified in the records sent to the sponsor. The sponsor may, however, look at your complete study records that identify you. In addition, the sponsor may visit the study site to oversee the way the study is being conducted and may review your PHI during these visits to

make sure the information is correct.

- The Institutional Review Board ("IRB") may have access to your PHI in relation to its responsibilities as an Institutional Review Board.
- Central Laboratory: Your blood and urine laboratory samples collected for this study will be temporarily stored and analyzed by a central laboratory. Your privacy is kept as only your study patient number will be written by the study personnel on the sample label beside the barcode number. All testing samples will be destroyed at the end of the testing process, which is estimated to take approximately 3 years.
- Data & Safety Monitoring Board (DSMB): will periodically review all data collected for this study in order to monitor safety for study patients. Again, the study staff will assign a code number and/or letters to your records, which means that you will not ordinarily be identified in the records reviewed by the DSMB.

The Investigator or sponsor may disclose your PHI to the United States Food and Drug Administration ("FDA") or similar regulatory agencies in the United States and/or foreign countries.

These disclosures also help ensure that the information related to the research is available to all parties who may need it for research purposes.

Except for the disclosures described above, your PHI will not be shared with others unless required by law. If your PHI is given to the parties listed above and/or to others who are not required to comply with the federal law, your PHI will no longer be protected by this law and could possibly be used or disclosed in ways other than those listed here.

You have a right to see and make copies of your PHI. You are agreeing, however, by signing this document, not to see or copy some or all of your PHI until the sponsor has completed all work related to this study. At that time, you may ask to see your records.

This Authorization will expire 50 years from the date you sign it unless you revoke (cancel or withdraw) it sooner.

You have a right to revoke your Authorization at any time. If you revoke it, your PHI will no longer be used for this study, except to the extent the parties to the research have already taken action based upon your

Authorization or need the information to complete analysis and reports for this research. To revoke your Authorization, you must write to the Investigator, stating that you are revoking your Authorization to Use and Disclose Protected Health Information. If you revoke this Authorization, you will not be allowed to continue to be in this study.

You will receive a copy of this Authorization after you have signed it.

_____
Printed Name of Subject

_____ _____
Signature of Subject Date

_____
Printed Name of the Person Obtaining the Authorization

_____ _____
Signature of the Person Obtaining the Authorization Date