SP0919, 2011-000056-42

CLINICAL STUDY REPORT SYNOPSIS

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This synopsis may include approved and non-approved uses, formulations or treatment regimens. The results from a single study may not reflect the overall results for the specific product. Prescribing decisions should be made by healthcare professionals based on the approved labeling information for the specific product in the respective country.

Personal information has been removed to protect the privacy of patients and the individuals named in the synopsis.

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Sponsor:

UCB Celltech

UK Registered Branch of UCB Pharma S.A.

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UNITED KINGDOM

Official study title:

Randomized Evaluation For Rotigotine's Efficacy in Sleep in idiopatHic PD patients: A multi-centre, randomized, double-blind, placebo controlled study to evaluate the effects of rotigotine on sleep efficiency in patients with advanced Parkinson's disease

SYNOPTIC CLINICAL STUDY REPORT: SP0919

Name of company: UCB Pharma	**Individual study table referring to part of the dossier:** Not applicable	*(For National Authority Use Only)*
Name of finished product: Neupro®	**Volume:** Not applicable	
Name of active ingredient: Rotigotine	**Page:** Not applicable	

Title of study: REFRESH-PD

Randomized Evaluation For Rotigotine's Efficacy in Sleep in idiopatHic PD patients

A multi-centre, randomized, double-blind, placebo controlled study to evaluate the effects of rotigotine on sleep efficiency in patients with advanced Parkinson's disease*

Investigators: Two investigators (Dr [redacted] and Dr [redacted]) enrolled a total of 3 subjects in the study; 2 were considered screen failures and 1 was randomized and completed the study.

Dr [redacted] was replaced by Dr [redacted] as the Principal Investigator during the study.

Study sites: The study was conducted at 2 sites in the [redacted] (Dr [redacted]'s site) and [redacted] (Dr [redacted]'s site)

Publications (references): None

Studied period: approximately 10 months **First subject enrolled:** 07 Mar 2012 **Last subject completed:** 14 Jan 2013 SP0919 was terminated due to recruitment issues on 14 Jan 2013. Three subjects were enrolled in the study; 2 were considered screen failures and 1 was randomized to placebo and completed the study (from Screening to the Safety Follow-Up [SFU] Visit). This synoptic clinical study report presents the raw data from the Oracle Clinical database for the 3 enrolled subjects.	**Phase of development:** Phase 4

Study administrative structure:

Clinical Program Director: [redacted], PharmD, UCB

Global Medical Affairs Medical Director: [redacted], MD, UCB

Clinical Trial Biostatistician: [redacted], PhD, UCB

Senior Clinical Program Manager: [redacted], UCB

*The study was registered on EudraCT without the additional abbreviated title: 'Randomized Evaluation For Rotigotine's Efficacy in Sleep in idiopatHic PD patients' (this note was added for clarification purposes afterwards)

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Study Physician: [redacted], MD, UCB

Contract research organization responsible for investigator recruitment, monitoring and regulatory activities: PRA International, [redacted]

Central laboratory for polysomnography (PSG) readings: [redacted]

Interactive Voice Response System: [redacted]

Clinical Trial Supply: UCB

Network involved in the study (protocol guidance and facilitation of investigator contracts): [redacted]

Objectives: The primary objective of this study was to evaluate the efficacy of rotigotine in improving sleep efficiency measured by PSG in subjects with advanced Parkinson's disease as compared to placebo.

Secondary objectives were to assess the effects of rotigotine on sleep maintenance, insomnia, nocturnal akinesia, and night-time movement in bed, as determined by objective and subjective measures in subjects with advanced Parkinson's disease as compared to placebo.

Other objectives were to evaluate the effect of rotigotine on cognitive performance and global cognitive function, the number of nocturias, and changes in the subject's health-related quality of life.

An exploratory objective was to study the relationship between objective sleep measures of PSG and subjective clinical measures and subject reported outcomes.

The safety objective was to assess the safety and tolerability of the rotigotine transdermal patch in a defined subject population.

These planned objectives were not met as only 3 subjects were enrolled in the study. Raw data from the Oracle Clinical database for the enrolled subjects are presented in listings.

Methodology: This was a parallel-group, double-blind, randomized, placebo-controlled, multicenter study to evaluate the effect of rotigotine on sleep maintenance in subjects with advanced Parkinson's disease.

A total of 60 subjects were planned to be randomized in a 1:1 ratio to rotigotine or placebo. The maximum dose of rotigotine was to be 16mg/24h.

The study consisted of a Screening Period (up to 28 days), Titration Period (up to 7 weeks),

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Maintenance Period (4 weeks), De-Escalation Period (up to 12 days), and the SFU Period (30 days excluding the De-Escalation Period). The study duration for all subjects was up to a maximum of 21 weeks, depending on the individual duration of the Screening Period and the individual optimal dose (rotigotine or matching placebo).

Subject's eligibility was to be assessed during the Screening Period (up to 28 days prior to the Baseline Visit [Visit 2], Day 1). At the Screening Visit (Visit 1), patch application and removal procedures were to be rehearsed with the subject using placebo training patches (smallest size). Eligible subjects were to come for a Baseline Visit (Visit 2), during which, all Baseline assessments were to be performed. The Baseline Visit could last from 3 to 5 days (Day -4, Day -3, Day -2, Day -1, and Day 1). Polysomnography was to be started in the evening of Day -4, Day -3, or Day -2 and run over 2 consecutive nights, with the first night of the PSG considered an adaptation night. Subjects were not allowed to sleep during the daytime on the day of a PSG reading. All questionnaires (Parkinson's Disease Sleep Scale [version 2] [PDSS2], Epworth Sleepiness Scale [ESS], etc) were to be completed prior to the first night of the PSG. On the final day of the Baseline Visit (Visit 2, Day 1), all other assessments were to be performed and then subjects were to be randomized in a 1:1 ratio, stratified by center, to receive rotigotine or placebo and begin the Titration Period. Subjects who were randomized to rotigotine were to start on a dose of 4mg/24h for 1 week. Thereafter, the dose was to be increased by 2mg/24h each week until the optimal or maximal dose of 16mg/24h was reached. For subjects who were randomized to placebo, study medication was to be titrated to the optimal or maximal dose, using placebo patches matching the respective rotigotine patches in size and appearance. The dose of study medication was to be regarded as optimal if both the investigator and the subject consider the symptoms adequately controlled. Subjects were to return to the clinic every week during the Titration Period.

If an adverse event (AE) occurred during the Titration Period that was considered by the investigator to be the result of excessive dopaminergic stimulation (eg, intolerable nausea/vomiting), then the subject's dose could have been back-titrated once to the previous dose level. Subjects who required back-titration and subjects who had reached the optimal dose were to proceed immediately to the Maintenance Period.

The Maintenance Period was to start once a subject attained the optimal or maximal dose (Visit 9, Day 1 of the Maintenance Period). Subjects had to stay on a stable dose of study medication throughout the 4-week Maintenance Period. At the end of the Maintenance Period, the subject was to return to the clinic and PSG was to be performed during the 2 consecutive nights starting either on Day 26, Day 27, or Day 28 after Visit 9 (start of the Maintenance Period). Prior to PSG, the questionnaires were to be completed. Visit 10 could last from 3 to 5 days (between Day 26 and Day 33). On the final day of Visit 10 (at the earliest on

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Name of finished product: Neupro®	**Volume:** Not applicable	
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Day 28 and at the latest on Day 33), all other assessments were to be performed. No PSG was to be performed for subjects who had prematurely withdrawn from the study. The end of the Maintenance Period was defined as the time point when a subject received a stable dose of rotigotine or placebo for a period of 4 weeks and PSG was performed.

Following the Maintenance Period, subjects were to be de-escalated by 2mg/24h every other day to 4mg/24h, and then to 0mg (no dose) after 2 days. Depending on the optimal dose, the De-Escalation Period could last up to 12 days.

The subject was to return to the clinic for a SFU Visit 30 days after the final removal of study medication.

A complete description of the study design, as well as a schematic diagram of the study and schedule of assessments, are provided in SP0919 Protocol Amendment 2. Instructions on the use of the patches, including the application and removal processes, are also provided in SP0919 Protocol Amendment 2.

The original protocol (dated 03 Mar 2011) was amended twice; Protocol Amendment 1 (dated 29 Jun 2011) and Protocol Amendment 2 (dated 03 Nov 2011). No subjects were enrolled in the study prior to the implementation of these amendments. Details of each amendment are presented in SP0919 Protocol Amendment 2.

Despite many attempts by the study sites to recruit subjects, only 3 subjects were enrolled in the study, with only 1 subject randomized, by [redacted] The study was put on hold. Following internal discussions, UCB decided that the required changes to the protocol to increase recruitment potential would alter the study design considerably, necessitating the closure of SP0919 and the initiation of a new study. Thus, UCB announced to the study sites on 29 Nov 2012 that the study was terminated. The randomized subject completed the study (defined as completing the SFU Visit) on [redacted].

Polysomnography: Polysomnography was to be performed for the 2 consecutive nights prior to Baseline Visit (Visit 2, Day 1) and the 2 consecutive nights prior to Visit 10 (Day 28 of the Maintenance Period). Readings from the first night of the PSG were not used for analysis as this was considered an adaptation night. Readings from the second night of the PSG were to be used for analysis.

Subjects were not allowed to sleep during the daytime on the day of a PSG reading. The PSG was to be recorded for a minimum of 6h and a maximum of 8h. All PSGs were to be recorded at the sleep laboratory following Standard Operating Procedures (American Academy of Sleep Medicine, 2007). The electronic recording was to be transferred to the central reading sleep laboratory for standardized assessment and evaluation.

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The following variables were to be determined based on PSG recordings:

- Rapid eye movement (REM)/stage 3 nonREM: derived from the hypnogram based on electroencephalogram (EEG), electromyography (EMG), electro-oculogram (EOG), and electrocardiogram (ECG).
- Time in bed: period between "lights off" and "lights on" (ie, period from analysis start to analysis stop).
- Sleep time: derived from the hypnogram based on EEG, EMG, EOG, and ECG.
- Arousals: derived from the hypnogram based on EEG, EMG, EOG, and ECG.
- Total number of turnings in bed: subjects' body positions were to be assessed in 5 distinct categories: standing/sitting, supine, prone, left, and right. A complete turn in bed was defined as a minimum turn of 90°.
- Total number of nocturias: information from video telemetry recording provided by the sleep laboratory technician (number of occasions and corresponding time a subject gets up to go to the bathroom will be recorded). Video data were not to be sent to the central reader.

Additional information on the measurements recorded during the PSG is provided in SP0919 Protocol Amendment 2.

Number of subjects (planned and analyzed): No exact determination of sample size was performed. It was estimated that 30 evaluable subjects per treatment group were sufficient to obtain a clinically distinct difference between rotigotine and placebo subjects for the primary efficacy variable. Therefore, a total of 60 subjects were planned to be randomized for the study at approximately 15 sites in the [redacted].

Finally, only 3 subjects were enrolled in the study. Two of the subjects were screen failures and the third subject who was randomized to placebo completed the study.

Diagnosis and main criteria for inclusion and exclusion: Subjects with advanced Parkinson's disease who were at least 18 years of age and had sleep maintenance insomnia were to be enrolled in the study.

Main inclusion criteria for subjects included the following:

- Female subjects must have been either postmenopausal for at least 1 year, surgically incapable of childbearing, or effectively practicing an acceptable method of contraception (either oral/parenteral/implantable hormonal contraceptives, intrauterine device, or barrier

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Name of finished product: Neupro®	**Volume:** Not applicable	
Name of active ingredient: Rotigotine	**Page:** Not applicable	

and spermicide). Abstinence only was not an acceptable method. Subjects must have agreed to use adequate contraception during the study and for 4 weeks after their final dose of rotigotine (or longer, if required by local regulations).

- Subject had advanced Parkinson's disease (ie, takes levodopa) and had been on a stable dose of levodopa (in combination with benserazide or carbidopa) for at least 28 days prior to the Baseline Visit.
- Subject had a Hoehn and Yahr stage score of 2 to 4.
- Subject had sleep maintenance insomnia (PDSS2 item 3="often" or 4="very often").
- If the subject was receiving an [redacted] (eg, benztropine, trihexyphenidyl, parsitan, procyclidine, biperiden), a [redacted] (eg, selegiline), or an [redacted] (eg, amantadine), he/she must have been on a stable dose for at least 28 days prior to the Baseline Visit and must have been maintained on that dose for the duration of the study.

Main exclusion criteria for subjects included the following**:**

- Subject had participated in another study of an investigational medicinal product (IMP) or a medical device within the previous 30 days, or was currently participating in another study of an IMP or a medical device.
- Subject received therapy with controlled-release levodopa, entacapone, or Stalevo® within 28 days prior to the Baseline Visit or had ever received therapy with tolcapone.
- Subject discontinued from previous therapy with a dopamine agonist after an adequate length of treatment, at an adequate dose, due to lack of efficacy as assessed by the investigator.
- Subject had prior therapy with a dopamine agonist within 28 days prior to the Baseline Visit.
- Subject was receiving therapy with 1 of the following drugs, either concurrently or within 28 days prior to the Baseline Visit: alpha-methyl dopa, metoclopramide, reserpine, [redacted] (except [redacted]; olanzapine, ziprasidone, aripiprazole, clozapine, and quetiapine), [redacted], methylphenidate, or amphetamine.
- Subject was receiving central nervous system therapy (eg, [redacted] [eg, modafinil]), unless dose had been stable daily for at least 28 days prior to the Baseline

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Name of finished product: Neupro®	**Volume:** Not applicable	
Name of active ingredient: Rotigotine	**Page:** Not applicable	

Visit and was likely to remain stable for the duration of the study.

- Subject has atypical Parkinsonian syndromes (including drug-induced Parkinsonian syndromes).
- Subject had a history of seizures or stroke within 1 year or a history of myocardial infarction within 6 months prior to enrollment (ie, the date of signing the Informed Consent form).
- Subject had evidence of significant cognitive impairment with a Mini Mental State Examination (MMSE) score of less than 25 at Screening (Visit 1).
- Subject's condition had previously been diagnosed as narcolepsy, sleep apnea syndrome, significant REM sleep behavior disorder, moderate to severe Restless Legs Syndrome as assessed by the International Restless Legs Scale, or periodic limb movement disorder.

All inclusion and exclusion criteria are presented in SP0919 Protocol Amendment 2.

Test product, doses and mode of administration, kit numbers: A silicone-based transdermal patch containing rotigotine in an adhesive matrix was provided in 3 different patch sizes and drug strengths; 20cm^2 (drug content 9mg, nominal dose 4mg/24h), 30cm^2 (drug content 13.5mg, nominal dose 6mg/24h), and 40cm^2 (drug content 18mg, nominal dose 8mg/24h). For doses above 8mg/24h, a combination of patches (ie, more than 1) had to be applied.

Rotigotine patch(es) was (were) to be administered transdermally once daily. The maximum dose of rotigotine was 16mg/24h.

No subject was randomized to receive rotigotine (Listing 35).

Duration of treatment: The duration of treatment for each subject was up to a maximum of 13 weeks and included a Titration Period (up to 7 weeks), Maintenance Period (4 weeks), and a De-Escalation Period (up to 12 days).

Reference therapy, doses and mode of administration, kit numbers: A silicone-based transdermal patch containing no drug (placebo) was provided in 3 different patches identical in size (20cm^2, 30cm^2, and 40cm^2) and appearance to the rotigotine patches. A combination of patches were required if the matching rotigotine dose was above 8mg/24h.

Placebo patch(es) was (were) to be administered transdermally once daily.

Subject [redacted] was randomized to receive placebo (Listing 35). The kit numbers for the placebo patches provided to Subject [redacted] are presented in Listing 7. For clarification, the

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Name of finished product: Neupro®	**Volume:** Not applicable	
Name of active ingredient: Rotigotine	**Page:** Not applicable	

drug name "rotigotine" in Listing 7 refers to the general name of the study and not the randomized treatment.

The treatment for Subject [redacted] was identified (ie, the blind was broken) after the sponsor had notified the sites that the study was terminated and after the subject had completed the Maintenance Period of the study (Listing 31 and Listing 30). No De-Escalation Period was required.

Criteria for evaluation: None of the planned efficacy or safety analyses were performed for this study since only 3 subjects enrolled in the study, 1 of whom received placebo and completed the study.

Planned efficacy: Efficacy of study medication was to be assessed by improvement in sleep efficiency (measured by PSG, stage 3 nonREM sleep, wake time after sleep onset [WASO], number of turnings in bed, number of nocturias) as well as by PDSS2; ESS; Nocturnal Akinesia, Dystonia, and Cramps Score (NADCS); and improvement in other assessments (Addenbrooke's Cognitive Examination-Revised [ACE-R], 39-item Parkinson's disease questionnaire [PDQ-39]).

Primary efficacy variable was:

- Change from Baseline to the end of Maintenance in Sleep Efficiency Index (SEI) (%)

Secondary efficacy variables were:

- Change from Baseline in the score of the PDSS2 by Day 1 of the Maintenance Period and Week 4 of the Maintenance Period
- Change from Baseline in the score of the ESS by Day 1 of the Maintenance Period and Week 4 of the Maintenance Period
- Change from Baseline to Week 4 of the Maintenance Period in the sleep period time in stage 3 nonREM (%) sleep (slow wave sleep time)
- Change from Baseline in the NADCS by Day 1 of the Maintenance Period and Week 4 of the Maintenance Period
- Change from Baseline to Week 4 of the Maintenance Period in the total WASO
- Change from Baseline to Week 4 of the Maintenance Period in the total number of turnings in bed

Name of company: UCB Pharma	**Individual study table referring to part of the dossier:** Not applicable	*(For National Authority Use Only)*
Name of finished product: Neupro®	**Volume:** Not applicable	
Name of active ingredient: Rotigotine	**Page:** Not applicable	

Other efficacy variables were:

- Change from Baseline in the total number of nocturias to Week 4 of the Maintenance Period
- Change from Baseline to Week 4 of the Maintenance Period on the ACE-R
- Change from Baseline in the score of the PDQ-39 by Day 1 of the Maintenance Period and Week 4 of the Maintenance Period and Week 4 of the Maintenance Period

Planned safety:

The safety variables were:

- Incidence of AEs
- Change from Baseline to Day 1 of the Maintenance Period and Week 4 of the Maintenance Period in vital signs (blood pressure [BP] and pulse rate)
- Change from Baseline to Week 4 of the Maintenance Period in ECG

Statistical methods: The statistical methods for the planned efficacy and safety analyses are presented in SP0919 Protocol Amendment 2. None of the planned efficacy or safety analyses were performed due to the low number of enrolled subjects.

Raw data from the Oracle Clinical database for the 3 enrolled subjects are presented in listings. Raw data for the efficacy assessments are listed for Subject [redacted] only; this subject was randomized to placebo and completed the study.

In the listings, AEs and medical history are coded using the Medical Dictionary for Regulatory Activities (MedDRA®), version 9.1 and are presented by system organ class, high level term, preferred term (PT), and reported term.

Treatment-emergent adverse events (TEAEs) were defined as AEs that occurred while study medication was applied up to 24h after the final patch application. Drug-related TEAEs were defined as TEAEs in the categories related, possibly related, unlikely related, and those with missing information.

In the listings, concomitant medications are coded using the World Health Organization Drug Reference List (version Q2/2004). Concomitant medications are presented by Anatomical Therapeutic Chemical main group, therapeutic subgroup, generic drug name, and reported term.

In general, Baseline value was the final nonmissing data collected prior to the first dose of study medication, unless otherwise stated.

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Name of finished product: Neupro®	**Volume:** Not applicable	
Name of active ingredient: Rotigotine	**Page:** Not applicable	

Summary and conclusions:

Subject disposition: Three subjects were enrolled in the study (Listing 5). Two of these subjects were considered screen failures; Subject [redacted] withdrew consent and Subject [redacted] was considered ineligible based on evidence of significant cognitive impairment with an MMSE score of less than [redacted] at Screening (Visit 1) (Listing 31 and Listing 10). Subject [redacted] was randomized to placebo and completed the study (defined as completing the SFU Visit [Visit 11]) (Listing 35 and Listing 31). A list of all subject visits is presented in Listing 30.

Subject demographics: Demographic characteristics of age and sex were collected at the Screening Visit (Visit 1) (Listing 5). The 3 subjects enrolled in the study were [redacted]. Two subjects were female and 1 was male. Subject [redacted], who was randomized to placebo, was [redacted] and female.

Baseline characteristics: Baseline characteristics collected at Screening (Visit 1) are presented for Subject [redacted]. This subject entered the study with a Hoehn and Yahr stage score of [redacted] (bilateral disease without impairment of balance ["on state"]) and had an MMSE score of [redacted] (Listing 9 and Listing 17). Based on the Unified Parkinson's Disease Rating Scale (Part IV), few complications of long-term dopaminergic treatment were reported for Subject [redacted]; predictable "off" periods averaging 1% to 25% each day and sleep disturbances (Listing 32).

Past and concomitant diseases (including Parkinson's disease) are presented in Listing 13. Of note, on entering the study, Subject [redacted] had [redacted] (on [redacted] treatment) and [redacted] (Listing 14). Past and concomitant medical procedures are presented for Subject [redacted] in Listing 25 and Listing 15, respectively. No medical procedures were performed during the study.

Concomitant medications are presented in Listing 14. Subject [redacted] did not take any prohibited medications during the study. A list of prohibited medications is presented in SP0919 Protocol Amendment 2.

Efficacy results: Raw data for the efficacy assessments are listed only for Subject [redacted]; this subject received placebo and completed the study.

Although PSGs were done on 2 consecutive nights prior to the Baseline Visit (Visit 2) and prior to the end of Maintenance Period (Visit 10), only the second PSG at each visit is presented since the first night was considered an adaptation night (Listing 34). At the Baseline Visit (Visit 2), the PSG for Subject [redacted] revealed a normal pattern of sleep architecture with no excess of limb movements and no abnormalities in the breathing parameters. There was a mild degree of [redacted]. At the end of the Maintenance

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Name of finished product: Neupro®	**Volume:** Not applicable	
Name of active ingredient: Rotigotine	**Page:** Not applicable	

Period (Visit 10), the PSG revealed a very similar (normal) pattern of sleep architecture with mild [redacted] as the only minor abnormality with [redacted]. At the Baseline Visit (Visit 2), Subject [redacted] had an SEI of [redacted]% and the sleep time period in stage 3 nonREM sleep was [redacted] minutes. At the end of the Maintenance Period (Visit 10), the subject's SEI was [redacted]% and the sleep time period in stage 3 nonREM sleep was [redacted] minutes. The number of nocturias on the 2 consecutive nights prior to the Baseline Visit (Visit 2) and the end of Maintenance Period (Visit 10) are presented for Subject [redacted] in Listing 20. Documentation of the dates and times of the PGS readings and the duration of lights "off" are provided for Subject [redacted] in Listing 26. Investigator comments are provided in Listing 11.

The start date for each sleep assessment log is recorded for Subject [redacted] in Listing 27. Daily assessment of sleep, both during the day and night, was collected by Subject [redacted] from the Screening Visit (Visit 1) to the Baseline Visit (Visit 2) and during the Maintenance Period (4-week data collection) (Listing 28). Changes in sleep during the day and night were minimal.

Subject [redacted] reported improved sleep and less nocturnal disability during the study (Listing 22). The total PDSS2 score was [redacted] at the Screening Visit (Visit 1), [redacted] at the Baseline Visit (Visit 2), [redacted] at the start of the Maintenance Period (Visit 9), and [redacted] at the end of the Maintenance Period (Visit 10).

Subject [redacted] reported a low level of daytime sleepiness during the study. The total ESS score was [redacted] at the Baseline Visit (Visit 2), [redacted] at the beginning of the Maintenance Period (Visit 9), and [redacted] at the end of the Maintenance Period (Visit 10) (Listing 8).

No nocturnal akinesia or dystonia was reported by Subject [redacted] during the study (all scores were 0.0) (Listing 18); [redacted] were reported at the Baseline Visit (Visit 2) only (score=0.5).

Subject [redacted] reported minimal problems associated with Parkinson's disease during the study. The PDQ-39 responses were similar at the Screening Visit (Visit 1), Baseline Visit (Visit 2), and at the start and end of the Maintenance Period (Visit 9 and Visit 10, respectively) (Listing 21). Most of the PDQ-39 responses at these visits were "never."

Subject [redacted] showed high cognitive functioning during the study. The ACE-R score was [redacted] at the Baseline Visit (Visit 2) and [redacted] at the end of the Maintenance Period (Visit 10) (Listing 1). Increases in memory score ([redacted] and fluency score ([redacted]) accounted for this difference.

Safety results: Raw data on AEs, vital signs (systolic BP, diastolic BP, and pulse rate), physical and neurological examinations, modified Minnesota Impulsive Disorders Interview (mMIDI), and the Columbia Suicide Severity Rating Scale are presented in listings. All safety

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Name of finished product: Neupro®	**Volume:** Not applicable	
Name of active ingredient: Rotigotine	**Page:** Not applicable	

data except AEs are presented for Subject [redacted] only.

Subject [redacted] was randomized to placebo and the first patch was applied at the Baseline Visit (Visit 2) (Listing 35 and Listing 29). At the start of the Maintenance Period (Visit 9), the subject was applying 2 placebo patches, which were identical in appearance to two rotigotine 8mg/24h patches (16mg/24h) (Listing 6). Drug accountability for Subject [redacted] is provided in Listing 7.

Two subjects reported a total of 6 AEs during the study (Listing 2). Subject [redacted] had a pretreatment AE of mild musculoskeletal pain. The pain was treated with [redacted] and resolved; however, the subject withdrew consent and was considered a screen failure (Listing 14 and Listing 31). Subject [redacted] reported 5 TEAEs during the study (PTs) − constipation, rhinitis, vertigo, lethargy, and tension headache (Listing 2). All events were mild in intensity, considered not related to study medication by the investigator, and no dose changes in study medication were required. None of the events met the criteria of serious. Both the tension headache and the rhinitis were treated with [redacted] (Listing 14). All events resolved except for constipation. The subject completed the study (Listing 31).

Since Subject [redacted] was postmenopausal, no urine pregnancy tests were performed during the study (Listing 3 and Listing 12).

Brief physical examinations were performed at the Screening Visit (Visit 1) and at the end of the Maintenance Period (Visit 10) (Listing 23). No physical abnormalities were identified upon examination of Subject [redacted] at the Screening Visit (Visit 1) (Listing 24).

No neurological abnormalities were identified upon examination of Subject [redacted] at the Screening Visit (Visit 1) or at the end of the Maintenance Period (Visit 10) (Listing 19).

Subject [redacted] entered the study with [redacted] (Listing 13). Subject's systolic BP was high during the study, ranging from [redacted] mmHg to [redacted] mmHg. Diastolic BP ranged from [redacted] mmHg to [redacted] mmHg. Pulse rate was within the normal range ([redacted] beats per minute) (Listing 33).

The mMIDI did not identify any impulsive control disorders for Subject [redacted] at the Screening Visit (Visit 1) or at the end of the Maintenance Period (Visit 10) (Listing 16).

The Columbia Suicide Severity Rating Scale data for Subject [redacted] are presented in Listing 4.

Conclusions: Due to poor subject enrollment in SP0919, the study was terminated by the sponsor. None of the planned efficacy or safety analyses were performed.

Report date: 02 Oct 2013

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Reference:

American Academy of Sleep Medicine. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications. Darien: AASM; 2007.