2. SYNOPSIS

<table>
<tr><td>Name of Sponsor/Company:
Impax Pharmaceuticals, Inc.</td><td rowspan="3">Individual Study Table Referring to Part of the Dossier
Volume:
Page:</td><td rowspan="3">(For National Authority Use Only)</td></tr>
<tr><td>Name of Finished Product:
IPX066</td></tr>
<tr><td>Name of Active Ingredient:
carbidopa-levodopa</td></tr>
<tr><td colspan="3">Title of Study: An Open-Label Extension Study of the Safety and Clinical Utility of IPX066 in Subjects with Parkinson’s Disease</td></tr>
<tr><td colspan="3">Principal Investigator: Paul Nausieda, MD, Wisconsin Institute for Neurologic and Sleep Disorders, S.C.945 North 12th Street, Suite 4602, Milwaukee, WI 53233
Investigators: 80</td></tr>
<tr><td colspan="3">Study center(s): 80 sites in North America and Europe</td></tr>
<tr><td colspan="3">Publications (reference): Not applicable</td></tr>
<tr><td colspan="2">Study period (years):
Date first subject enrolled: March 25, 2010
Date last subject completed: October 19, 2011</td><td>Phase of development: 3</td></tr>
<tr><td colspan="3">Objectives:
To evaluate the long-term safety and clinical utility of IPX066 in subjects with Parkinson’s disease (PD)</td></tr>
<tr><td colspan="3">Methodology: This was a multicenter open-label extension study of IPX066, with a planned enrollment of approximately 500 subjects who had successfully completed phase 2 Study IPX066 B08 11 or 1 of the 2 phase 3 Studies IPX066 B08-05 or IPX066 B09-02. The termination visit of the antecedent study generally served as the first visit (baseline). However, in the instance in which a subject had completed the antecedent study 4 weeks or more before enrollment in the extension study, the subject was required to return to the study site for completion of all first visit procedures and assessments. Subjects returned to the study site for Visits 2, 3, and 4 assessments, scheduled at Month 1, Month 5, and Month 9, or early termination. Dose adjustment was allowed as needed.</td></tr>
<tr><td colspan="3">Number of subjects (planned and analyzed): 500 planned; 617 enrolled and analyzed</td></tr>
<tr><td colspan="3">Diagnosis and main criteria for inclusion: Parkinson’s disease and successful completion of study IPX066-B08-05, IPX066-B08-11, or IPX066-B09-02.</td></tr>
<tr><td colspan="3">Test product, dose and mode of administration, batch number:
The investigational product was IPX066, an extended-release (ER) multiparticulate, capsule formulation of CD and LD in a 1:4 ratio. Subjects received individualized dosing regimens of IPX066 (95, 145, 195, or 245 mg capsules up to 5 times per day) for up to 9 months. The daily IPX066 dosage was individually adjusted to achieve maximum benefit throughout the study.

IPX066 was provided in four dosage strengths from the corresponding lots:
IPX066, 23.75–95 mg CD–LD —Lots RB09042-120, RB10010-120, RB10014-120
IPX066, 36.25–145 mg CD–LD—Lots RB09041-120, RB10004-120, RB10011-120, RB10015-120, RB10024-120
IPX066, 48.75–195 mg CD–LD—Lots RB09040-120, RB10005-120, RB10012-120, RB10025-120
IPX066, 61.25–245 mg CD–LD—Lots RB09027-120, RB09039-120, RB10006-120, RB10013-120, RB10026-120</td></tr>
<tr><td colspan="3">Duration of treatment: Up to 9 months</td></tr>
</table>

Reference therapy, dose and mode of administration, batch number: None

Criteria for evaluation:

Clinical Utility and Quality of Life Instruments

Month 1, Month 5, and Month 9, or Early Termination Visits: Unified Parkinson's Disease Rating Scale (UPDRS), Patient Global Impression (PGI), and Parkinson's Disease Questionnaire-39 (PDQ-39)

Month 5 and Month 9, or Early Termination Visits: Health Related Quality of Life States (EQ-5D) and Health Survey Questionnaire (SF-36 v2 Acute)

Safety

Month 1, Month 5, and Month 9, or Early Termination Visits: adverse events (AEs), vital signs, and concomitant medications

Month 1and Month 9, or Early Termination Visits: clinical safety laboratory tests and electrocardiograms (ECGs)

Statistical methods: As this was an open-label extension trial with no comparator, all available data were summarized, and no formal statistical analyses were performed. Data sets for all subjects were analyzed for the overall population as well as the early PD and advanced PD subpopulations.

The Unified Parkinson's Disease Rating Scale (UPDRS), Total UPDRS, each of its components (Parts I through IV), and Part II + Part III were summarized across six time points (Baseline Previous Trial, Final Previous Trial, Baseline, Month 1, Month 5, and Month 9) to assess the sustainability of the clinical effect of IPX066 over the 9-month study. To provide a reference point for changes in UPDRS scores during the extension trial, UPDRS questionnaire values from the Final Previous Trial visit were used. A Baseline measure in the extension trial was only collected if there were 4 weeks or more between the Final Previous Trial visit and the first visit of the extension trial. Subjects' general satisfaction with treatment (PGI) of IPX066 was summarized over Months 1, 5, and 9 to assess whether satisfaction with IPX066 treatment was sustained. The Parkinson's Disease Questionnaire (PDQ-39) and its subscores were assessed at the same time points as the UPDRS.

The safety analysis for this report included data from all subjects who received at least 1dose of IPX066 during this open-label extension study and all safety data reported. AEs, vital signs, and ECGs were summarized across IPX066 exposure, from antecedent studies through the open-label extension study. Descriptive statistics and shift tables were provided for each continuous laboratory parameter.

SUMMARY – CONCLUSIONS

CLINICAL UTILITY AND QUALITY OF LIFE RESULTS:

There was no overall worsening of the mean UPDRS Part II + Part III scores at Month 9 compared to antecedent study final scores, and overall scores improved compared to the antecedent study. Subjects with early PD previously on placebo, on average, improved, with scores approaching those of subjects receiving IPX066 in the previous trial (mean UPDRS score of 24.9 vs. 24.0). For subjects with advanced PD, those randomized to IPX066 in the antecedent trial maintained their improvement on average, while those randomized to IR CD-LD in the antecedent trial, improved on IPX066 to a similar level as those randomized to IPX066.

PGI results indicated that 83.6% of subjects were at least Somewhat Satisfied and 49.6% were at least Very Satisfied with IPX066 treatment on a 7-point scale. No consistent pattern was seen in PDQ-39 results. Based on responses to the EQ-5D and SF-3 quality of life questionnaires, there was little or no evidence of worsening of PD symptoms between Baseline and Month 9.

The median total daily dose of IPX066 was 720 mg (corresponding to approximately 500 mg IR LD) for subjects with early PD, which is similar to the median dose studied in the placebo-controlled Study B08-05. The median total daily dose was 1450 mg (corresponding to approximately 1000 mg IR LD)

for subjects with advanced PD, which is similar to the dose used in Study B09-02. The dosing frequency established during the antecedent studies was maintained throughout the long-term study for most subjects. Specifically, 80%, 82%, and 83% of subjects who took IPX066 3 or fewer, 4, or 5 times daily in the antecedent studies still took IPX066 3 or fewer, 4, or 5 times daily after exposure to IPX066 for up to an additional 9 months.

The following conclusions are based on the clinical utility results observed in Study IPX066-B09-03:

- The reduction in PD symptoms associated with IPX066 treatment in the original trials was sustained with longer exposure to IPX066.
- The dosing established during the antecedent studies generally was maintained throughout the long-term study.

SAFETY RESULTS:

Of the 617 subjects entering the extension study, 353 (57.2%) subjects reported AEs; other than fall (reported by 32 [5.2%] subjects), no single AE was reported by 5% or more subjects. In general, a lower percentage of subjects reported AEs during this trial compared to the percentages who reported AEs in the antecedent trials of shorter duration, and the nature of the AEs reported in this open-label extension was similar to that reported previously. Each new AE in the extension trial not previously reported by any of the subjects in the antecedent trial was reported in ≤1% of subjects.

Four subjects (0.6%) died during this trial. The causes of death were different for each subject and included hemorrhagic stroke, hemorrhagic pancreatitis, prostate cancer, and unknown cause. None of these deaths were considered by the Investigator as related to IPX066.

Forty-three subjects (7.0%) reported events which met the criteria for SAEs. Most SAEs were reported by a single subject. Events reported by more than one subject included femoral neck fracture (3 subjects), fall (2 subjects), atrial fibrillation (2 subjects), gastritis (2 subjects), hyponatremia (2 subjects), spinal column stenosis (2 subjects), and spinal osteoarthritis (2 subjects).

Sixteen (2.6%) subjects reported AEs as the reason for withdrawal from the study. Two subjects each reported nausea, hallucinations, and dizziness as reasons for withdrawal. No other AE was reported more than once as a reason for termination.

With the exception of atrial fibrillation, right bundle branch block, fall, dyskinesia, hallucination, cerebrovascular insufficiency, and basal cell carcinoma, AEs of interest (neurologic, sleep, psychiatric, gastrointestinal, cardiovascular, and neoplastic) were reported less frequently with increased exposure to IPX066 in this extension study.

No clinically significant changes in laboratory, vital signs, or ECG values were observed over time in the overall population.

The following conclusions are based on the safety results observed in Study IPX066-B09-03:

- No unusual AEs or cluster of AEs appeared in subjects in this 9-month extension trial.
- Four subjects died during the open-label extension; none of these deaths were considered by the Investigator as related to IPX066.
- Forty-three subjects reported events that met the criteria for SAEs; most SAEs were single reports and no pattern could be discerned.
- No clinically relevant patterns of change were noted in blood and urine laboratory assessments, ECGs, or vital signs, although individual abnormalities were seen in subjects

with comorbid medical conditions.

- The safety findings in this study were consistent with the known effects of commercially available CD-LD products in the PD population.

CONCLUSION:
The reduction in PD symptoms associated with IPX066 treatment in the original trials was sustained with longer exposure to IPX066. In addition, IPX066 demonstrated a favorable safety profile over an extended duration of dosing in mostly older subjects with PD, most of whom had multiple medical comorbidities.

Date of the report: April 9, 2012