2. STUDY SYNOPSIS

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Title of Study: An Open-Label, Multicenter, Extension Study to Evaluate the Long-Term Safety and Efficacy of Dexpramipexole (BIIB050) in Subjects With Amyotrophic Lateral Sclerosis

Principal Investigator/Coordinating Investigator:

[redacted] USA

Dr. [redacted] signature indicating [redacted] approval of this clinical study report is provided in Appendix 16.1.5.

Study Period:	**Phase of Development:**
Date of first treatment: 06 June 2012 Date of early study termination: 04 January 2013 End of study date: 15 February 2013	3

Study Objectives:

Primary study objective:

- To evaluate the long-term safety profile of dexpramipexole in subjects with amyotrophic lateral sclerosis (ALS).

Secondary study objective:

- To evaluate the long-term efficacy of dexpramipexole in this study population using clinical endpoints measuring function and survival.

Study Design:

This was an open-label, multicenter, extension study of the long-term safety and efficacy of dexpramipexole administered 150 mg twice daily to subjects with ALS. Subjects who completed either the Phase 2 Study KNS-760704-CL211 (CL211) or the Phase 3 Study 223AS302 (302) [also referred to as lead-in studies] were eligible to participate in the extension study.

The study consisted of a Baseline Visit, a treatment period of up to 36 months, and a Safety Follow-Up Visit. If possible, the last visit of the lead-in study was combined with the Baseline Visit of the extension study. Otherwise, subjects were required to enroll within 14 days of their last visit in Study CL211 or Study 302, as described in Section 4.3.1 of the study protocol (see Appendix 16.1.1).

All study assessments were performed during in-clinic visits or remotely by telephone or home visits. The study design allowed subjects who were participating in End-of-Life Accommodations

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(e.g., housebound or under hospice care) to provide data required for enrollment or continued participation in the study by telephone interview and home visits, as described in Section 4.3.7 of the study protocol (see Appendix 16.1.1).

Subjects enrolled in the study had the option of participating in a biomarker substudy. Blood samples collected from these subjects were to be used to analyze suspected ALS-related biomarkers and markers that have been proposed to be related to ALS classification and progression (e.g., neurofilament levels, proteomic assessment, messenger ribonucleic acid [RNA] assessment, and microRNA assessment).

All data were recorded in the Case Report Form (CRF). A sample CRF is provided in Appendix 16.1.2.

Number of Subjects (Planned and Analyzed):

Up to 850 subjects from Study CL211 and Study 302 who met the inclusion and exclusion criteria were eligible to enroll, and 616 subjects entered the study. Approximately 2 months after enrollment was complete, the study was terminated based on results from the recently completed Phase 3 Study 302. Study 302 failed to meet its primary endpoint, joint rank analysis of function and survival, and no efficacy was observed for the individual components of function or survival. Study 302 also failed to show efficacy in its key secondary endpoints.

Select data from all 616 subjects collected through the end of the extension study (15 February 2013) were analyzed, as described below in the Statistical Methods section, under changes in planned analyses.

Study Population:

Main inclusion criteria:

- Subject had the ability to understand the purpose and risks of the study and provide signed and dated informed consent (or have the consent confirmed by a witness if unable to write) and authorization to use protected health information in accordance with national and local subject privacy regulations.
- Subject was enrolled in either Study CL211 or Study 302.
- Subject completed his/her last visit in Study CL211 or Study 302.
- Subjects of childbearing potential had to practice effective contraception during the study and be willing and able to continue contraception for 1 month (females) or 3 months (males) after their last dose of study treatment.

Main exclusion criteria:

- Subject withdrew prematurely from Study CL211 or Study 302.
- Subject permanently discontinued study treatment in Study CL211 or Study 302 for any reason other than enrollment into this study.

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- Subject from Study CL211 or Study 302 had a significant change in medical history (including laboratory tests or a clinically significant condition) that, in the opinion of the Investigator, would impair the subject's medical fitness for participation and preclude treatment.

A complete list of exclusion criteria is provided in Section 8 of the protocol (see Appendix 16.1.1)

Study Treatment, Dose, Mode of Administration, Batch Number(s):

All subjects enrolled in the study received open-label dexpramipexole 150 mg administered orally twice daily. The study treatment was taken with water, or if it became necessary during the study, the tablet could be crushed and suspended in water or mixed in unsweetened applesauce for oral administration or administration through standard gastrostomy tubes.

At the Baseline Visit, the first dose of study treatment was administered in the clinic by authorized site personnel. Subjects who were participating in End-of-Life Accommodations at the time of enrollment received study treatment at home during the Baseline Visit under a nurse's observation. Subjects were instructed to take the second dose of study treatment 12 hours after the first dose at this visit. Following the Baseline Visit, subjects were instructed to take 1 dose at approximately the same time of day each morning and again 12 hours later for the duration of the study. If a dose of study treatment was missed, subjects were to take the missed dose immediately. However, no more than 1 missed dose (1 tablet) was to be taken at any time (i.e., no more than 2 tablets of study treatment were to be taken in any 12-hour period).

Dose Interruption or Reduction

No dose interruptions or modifications were allowed during the study with the following exceptions, as discussed in Section 10.3 of the protocol (see Appendix 16.1.1):

- Neutropenia - treatment with dexpramipexole was temporarily withheld for subjects who developed Common Toxicity Criteria Grade 3 or 4 neutropenia (absolute neutrophil count [ANC] $\leq 1.0 \times 10^3/\mu l$). Subjects were given the option to resume study treatment at the 150 mg twice daily dose once the neutropenia resolved, unless dosing was suspended for more than 4 consecutive weeks or 2 cumulative months over a 6-month period. A permanent reduction in the dose of dexpramipexole to 150 mg once daily was required for subjects who experienced a second case of neutropenia (ANC $\leq 1.0 \times 10^3/\mu L$) after resuming dexpramipexole 150 mg twice daily dosing.
- QTc prolongation - a dose interruption was required for subjects with a mean QT interval corrected for heart rate using Fridericia's correction formula (QTcF) >500 msec (based on duplicate readings). Any risk factors for QTc prolongation (e.g., electrolyte abnormalities, congestive heart failure, and long QT syndrome) in these subjects was also corrected or controlled. Subjects were given the opportunity to reinitiate treatment at the 150 mg twice daily

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dose when mean QTcF returned to <500 msec.

- Disallowed therapies – study treatment was temporarily withheld for subjects requiring concomitant use of any dopamine agonist (including pramipexole) or any other agent with dopaminergic activity, or oral or intravenous drugs that are known to inhibit renal tubular secretion of organic acids via the organic cationic transport system during the study. After completion of the concomitant treatment, subjects were allowed to resume dexpramipexole 150 mg twice daily dosing following a 3-day washout period, as long as study treatment was not suspended for more than 4 consecutive weeks or 2 cumulative months over a 6-month period.

Dexpramipexole capsule-shaped compressed film-coated tablets were supplied at a dose strength of 150 mg. This is the dose strength of the drug product in its salt form, dexpramipexole dihydrochloride. Each 150 mg tablet of dexpramipexole dihydrochloride is equivalent to 112 mg of the active moiety, dexpramipexole. Lot numbers for dexpramipexole distributed to study sites prior to termination of the study were [redacted]

Comparator Therapy/Therapies, Dose, Mode of Administration, Batch Number(s):

This was an open-label study. No comparator was used in the study.

Duration of Treatment and Follow-Up:

The duration of treatment with dexpramipexole in this study was to be for up to 36 months. The study consisted of a Baseline Visit, a treatment period of up to 36 months, and a Safety Follow-Up Visit.

Treatment Period:

All subjects received open-label treatment with dexpramipexole 150 mg twice daily. Following the Baseline Visit, subjects were to report to the clinic for visit-specific procedures at Months 1, 2, 4, and 6, and every 4 months starting at Month 10 and ending at Month 36/End of Study. Study assessments were to be conducted remotely by telephone or home visits at Months 3 and 5, and every 4 months starting at Month 8 through Month 32.

Safety Follow-up Visit:

Subjects who completed dosing per the protocol were to return to the study site for a Safety Follow-Up Visit 30 days (±7) days after their last dose of study treatment.

Follow-Up After Early Study Treatment Discontinuation

Subjects who prematurely discontinued study treatment but continued to participate in the study were to have all assessments listed in the End of Study Visit performed within 7 days after their last dose of study treatment. Thereafter, subjects were to be followed for assessment of living status and other safety and efficacy assessments, as described in Section 7.2.5 of the protocol (see Appendix 16.1.1). Assessments were to be performed every 2 months through Month 36/End of Study, unless the subject withdrew from the study or was lost to follow-up.

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Criteria for Evaluation:

Following is a description of all safety, efficacy, and other assessments that were originally planned for this extension study. The timing of these assessments can be found in the schedule of events, Section 4.2 of the protocol (see Appendix 16.1.1).

Safety: adverse event (AE) and serious adverse event (SAE) monitoring and recording, clinical laboratory evaluations (hematology, blood chemistry, and urinalysis), vital signs (systolic and diastolic blood pressure, respiratory rate, heart rate, and temperature), body weight, 12-lead electrocardiogram (ECG) measurements, physical examinations, concomitant therapy and procedure recording, and for women of childbearing potential, serum and urine beta human chorionic gonadotropin qualitative.

Note: For remote visits, samples for clinical laboratory evaluations were collected at the subject's home for central laboratory processing.

Study Treatment Concentration Measurements: If a subject experienced an SAE, a blood sample for dexpramipexole plasma concentration was to be collected within 24 hours after the SAE, if possible. Every effort was made to document the date and time of the most recent dose of study treatment taken prior to the collection of the blood sample.

At the Month 4 clinic visit only, paired ECG monitoring and pharmacokinetic blood sample collection were to be done relative to dosing with dexpramipexole. ECG monitoring was to occur 2 to 3 hours after dosing and a blood sample was to be collected within 15 minutes after the ECG to determine the plasma concentration of dexpramipexole.

Clinical Efficacy Assessments: Amyotrophic Lateral Sclerosis Functional Rating Scale (revised) [ALSFRS-R]; sniff nasal inspiratory pressure (SNIP); time to death; time to death or death equivalent (tracheostomy or permanent assisted ventilation, defined as use of noninvasive ventilation [NIV] for ≥22 hours per day for ≥10 days); time to recommended gastrostomy tube placement; and time to recommended wheelchair utilization or death, up to 36 months.

Health Economics and Subject- and Caregiver-Reported Outcomes: ALS-related health quality, as measured by change in the total score on the Amyotrophic Lateral Sclerosis Assessment Questionnaire (5-item form) [ALSAQ-5], European Quality of Life-5 Dimensions (EQ-5D), Caregiver Burden Inventory (CBI), and Health Resources Utilization Questionnaire.

Subjects Receiving End-of-Life Accommodations

For subjects receiving End-of-Life Accommodations who were unable to travel to the study site for study visits, the minimum data required for enrollment and continued participation in the study (i.e., to remain on study treatment) included clinical laboratory evaluations, AE and concomitant medication reporting, and ALSFRS-R scores. Data were collected at the protocol-scheduled visits until the subject completed or withdrew from the study, or until the subject died, whichever occurred first.

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If a subject receiving End-of-Life Accommodations prematurely discontinued study treatment but continued to participate in the study, data collected included living status, ALSFRS-R scores, and AEs, as described above (see Duration of Treatment and Follow-up) or in Section 7.2.5 of the protocol (see Appendix 16.1.1).

Statistical Methods:

Planned Analyses

All data were to be analyzed based on prior treatment received in Study CL211 or Study 302 and summarized for the following 3 treatment groups: subjects from Study CL211, subjects who received dexpramipexole 150 mg twice daily in Study 302, and subjects who received placebo in Study 302.

Demography and Baseline Disease Characteristics

Demographic and Baseline data were to be summarized using descriptive statistics for continuous variables and frequency and percentage for discrete variables.

Safety

Safety analyses were to be based on the safety population, defined as all subjects who received at least 1 dose of study treatment during the extension study.

Primary Endpoints

The primary endpoints that were to be evaluated in the extension study included the following:

*Adverse Event*s

The incidence of treatment-emergent AEs was to be summarized by system organ class (SOC) and preferred term (PT) overall, and by maximum intensity and highest relationship to study treatment. A treatment-emergent AE was defined as any AE that had onset on or after the first dose of dexpramipexole, or any pre-existing condition that worsened after the first dose of study treatment. The incidence of SAEs and AEs leading to premature discontinuation were to be summarized by SOC and PT, and any reported deaths listed by treatment group. AEs were to be coded using the Medical Dictionary for Regulatory Activities (MedDRA).

Clinical Laboratory Evaluations

Laboratory data were to be summarized using shift tables. For quantitative laboratory data, descriptive statistics for raw values, as well as change from Baseline for each parameter, were to be presented by treatment group. The number and percentage of subjects with potentially clinically significant laboratory results were to be tabulated for each parameter, as appropriate.

Vital Signs and Body Weight

Vital sign and body weight measurements as well as change from Baseline values were to be

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summarized by treatment group using descriptive statistics. Vital signs and body weights collected after the first dose of treatment were to be examined to determine the incidence of clinically relevant abnormalities according to the criteria presented in Section 16.4.3.3, Table 6 of the study protocol (see Appendix 16.1.1).

Electrocardiograms

ECG measures as well as change from Baseline were to be summarized by treatment group using descriptive statistics. ECG findings that were determined to be potentially clinically significant were to be summarized.

The correlation between the timed QTc interval using QTcF and the plasma concentration of dexpramipexole collected at Month 4 was to be explored graphically. A similar analysis was to be provided to explore the correlation between the timed QTcF change from Baseline and the plasma concentration of dexpramipexole collected at Month 4.

Physical Examination

The physical examination findings were to be presented in data listings.

Efficacy

Efficacy analyses were to be based on the efficacy population, defined as all subjects who received at least 1 dose of study treatment during the extension study and had at least 1 postbaseline assessment for the efficacy parameter analyzed, or who died during the study period.

Secondary Endpoints

The secondary endpoints that were to be evaluated included the following:

Change in ALSFRS-R Total Scores and SNIP Testing

A mixed-effects slope model was to be used to analyze the ALSFRS-R score and the SNIP data. The model includes treatment, time, and treatment-by-time interaction as fixed effects, and has a random intercept and a random slope for time with an unstructured covariance.

Descriptive statistics for the ALSFRS-R total scores and SNIP data, and change from Baseline for both assessments were to be summarized by treatment group and visit.

Time to Death

Time to death was defined as the duration between the date of death and the date the first dose of dexpramipexole was taken. If the subject was still alive, the time to death was to be censored and would be the time the subject was last known to be alive.

Time to death was to be analyzed using a Cox Proportional Hazards model and Kaplan-Meier curve to evaluate group differences (subjects who received 150 mg dexpramipexole twice daily in Study 302

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versus subjects who received placebo in Study 302).

Time to Death or Death Equivalent

Time to death or death equivalent was defined as the duration between the minimum of the following dates: the date of tracheostomy, or the date of the 10th consecutive day that NIV was used for ≥22 hours per day, or the date of death, and the date the first dose of study treatment was taken.

Time to death or death equivalent up to 36 months was to be analyzed using the methods described for time to death.

Tertiary Endpoints

The tertiary endpoints that were to be evaluated included the following:

Change in ALSAQ-5 Total Score

The change from Baseline in ALSAQ-5 total score and the ALSAQ-5 total score were to be analyzed using a mixed-effects slope model as described for ALSFRS-R score and the SNIP data.

Descriptive statistics for the ALSAQ-5 scores and change from Baseline in the ALSAQ-5 scores were to be summarized by treatment group and visit.

Change in CBI Score

Descriptive statistics for the CBI score and change from Baseline values up to 36 months were to be summarized by treatment group and visit.

Change in EQ-5D Scores

The change from Baseline in EQ-5D visual analogue scale (VAS) score and the EQ-5D VAS score were to be analyzed using a mixed-effects slope model as described for ALSFRS-R score and the SNIP data.

Descriptive statistics for the VAS scores, and change from Baseline in the VAS scores were to be summarized by treatment group and visit. In addition, the number and percent of subjects with self-reported response to each level of the 5 questions were to be summarized by treatment group and visit.

Change in Health Resource Use

The change from Baseline in health resource use parameters up to 36 months was to be analyzed.

Descriptive statistics for each endpoint and change from Baseline values up to 36 months were to be summarized by treatment group and visit.

Time to Recommended Wheelchair Utilization or Death

Time to recommended wheelchair utilization or death up to 36 months was to be analyzed using the methods described for time to death.

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Time to Recommended Gastrostomy Tube Placement or Death

Time to recommended gastrostomy tube placement or death up to 36 months was to be analyzed using the methods described for time to death.

Sample Size Calculations

No formal sample size calculation was performed for this extension study. The number of eligible subjects was determined by the number of subjects who participated in the lead-in studies, CL211 and 302.

Changes in the Planned Analyses

As noted above, this extension study was terminated early by the Sponsor after enrollment was complete with 616 subjects, based on results from the Phase 3 Study 302 that failed to meet the primary and key secondary endpoints. Since the majority of subjects had participated for less than 3 months when the study was stopped, no efficacy data were analyzed. There was also no analysis of blood samples collected to determine dexpramipexole concentration or ALS-related biomarkers.

Results:

Data presented in the summary tables that are discussed in this section are summarized by treatment group, including prior treatment received in Study 302 (dexpramipexole or placebo) and Study CL211 (dexpramipexole), and for all subjects. Since the study was terminated early, only data for the all subjects group is described in this report.

All summary tables and a listing of deaths can be found in Section 3.1 (Study Subjects) and Section 3.2 (Safety Data).

Disposition of Subjects

A total of 616 subjects were enrolled in the extension study at 80 investigational sites in 11 countries worldwide. Six hundred of these subjects entered the study after completion of Study 302; 298 subjects had received dexpramipexole 150 mg twice daily and 302 subjects had received placebo in the lead-in study for up to 18 months or until the last subject completed 12 months of treatment, whichever came first. The remaining 16 subjects were enrolled from Study CL211 and previously received dexpramipexole 150 mg twice daily in that lead-in study for up to 180 weeks.

The first subject in the extension study was treated on 06 June 2012, and the study was terminated by the Sponsor on 04 January 2013. All subjects were instructed to discontinue dosing and complete an Early Termination and Safety Follow-up Visit within 30-37 days of their last dose.

All 616 subjects enrolled received at least 1 dose of dexpramipexole during the extension study (Table 1). Among subjects who either discontinued study treatment prematurely or who withdrew from the study prematurely for reasons other than early termination of the study by the Sponsor, the most

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frequent reason was death (53 [9%] and 71 [12%], respectively). Eight of the 616 subjects enrolled did not have a reason for withdrawal from the study.

It should be noted that there were 77 deaths (13%) in total reported in this extension study, 4 of which occurred after the subject's end of study date, 71 that lead to premature withdrawal from the study, and 2 that were not recorded as the reason for discontinuation from the study on the (CRF) [Table 1].

Demography and Baseline Characteristics

Demography

Baseline demographic characteristics are summarized in Table 2 by prior treatment received in Study 302 and Study CL211, and for all subjects.

Median age for subjects enrolled was 57 years (range: 20 to 83 years). Most subjects were male (67%) and White (95%). The percentage of subjects enrolled in the United States and Europe was similar, approximately 45%. Of 154 subjects with body weight recorded at Baseline, the median weight was 73.0 kg (range: 43.0 to 140.6 kg) and median body mass index was 23.6 kg/m^2 (range: 16.1 to 52.9 kg/m^2).

ALS History

ALS history is summarized in Table 3 by prior treatment received in Study 302 and Study CL211, and for all subjects.

Ninety-four percent of subjects reported having no familial history of ALS. The site of onset for most subjects (81%) was other than bulbar. Median time since symptom onset was 29.7 months (range: 14.1 to 115.7 months), and the median time since ALS diagnosis was 21.0 months (range: 13.0 to 97.7 months). Approximately three-quarters of the subjects reported concomitant use of riluzole.

Most subjects were in 1 of 3 El Escorial diagnostic categories that included definite (31%), probable (36%), and probable laboratory supported (23%). The median ALSFRS-R total score at Baseline was 28.0 (range: 1.0 to 47.0).

Time on Study Treatment

Time on treatment is summarized in Table 4 by prior treatment received in Study 302 and Study CL211, and for all subjects.

The protocol specified that all subjects were to receive dexpramipexole 150 mg twice daily for up to 36 months. Because the study was terminated early, the median time on study treatment was much shorter, 2.8 months (range: 0 to 7 months). Thirty-two percent of subjects received dexpramipexole for ≥3 months but <6 months, and 2% were treated for ≥6 months but <9 months.

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Safety

Safety analyses were performed on the safety population, defined as all subjects who received at least 1 dose of study treatment. Of the 616 subjects who were enrolled in the extension study, all were included in the safety population.

Adverse Events

In this study, AEs were coded using MedDRA, version 15.0 (01 March 2012). All AEs were analyzed based on the principle of treatment emergence. A treatment-emergent AE is defined as having an onset date that was on or after the start of study treatment, or that worsened after the start of study treatment. Any subject having the same AE more than once was counted only once in the incidence of that event.

Summary of Adverse Events

An overall summary of AEs is presented in Table 5 by prior treatment received in Study 302 and Study CL211, and for all subjects.

Most subjects (74%) reported at least 1 AE during treatment. Twenty-one percent of subjects had a severe AE, and 16% had an AE that was considered by the Investigator to be related to treatment with dexpramipexole. Seventy-three subjects (12%) died during participation in the study due to an AE. All of the deaths were considered not related to study treatment with the exception of 1 AE of ALS, which was categorized as related (see the section related to Deaths below and Table 8). SAEs were reported by 25% of subjects. AEs leading to premature discontinuation of dexpramipexole or premature withdrawal from the study were reported by 5% and 8% of subjects, respectively.

It should be noted that the number of subjects who prematurely discontinued dexpramipexole due to an AE in the overall summary of AEs (30 subjects [5%]; Table 5)is greater than the number of subjects listed in the accounting of subjects (20 subjects [3%]; Table 1). The additional 10 subjects included in Table 5 but not summarized in Table 1 as subjects who prematurely discontinued study treatment due to an AE were subjects who experienced an AE with an outcome of death and whose reason for study treatment discontinuation was noted as death rather than as an AE in Table 1. This also accounts for the observed difference in AEs leading to premature withdrawal from the study in the 2 tables (48 subjects [8%] versus 11 subjects [2%]).

Analysis of Adverse Events

The incidence of AEs is summarized in Table 6 by SOC and PT, by prior treatment received in Study 302 and Study CL211, and for all subjects.

The overall incidence of AEs was 74%. The most frequent (≥10%) AE SOC categories were the following: infections and infestations (25%); gastrointestinal disorders (25%); respiratory, thoracic, and mediastinal disorders (20%); nervous system disorders (14%); general disorders and administration site conditions (14%); injury, poisoning, and procedural complications (14%); and musculoskeletal and

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connective tissue disorders (10%).

The most common AEs (incidence ≥5%) were fall (11%), respiratory failure (8%), constipation (8%), urinary tract infection (5%), nausea (5%), and oedema peripheral (5%). Most other AEs were reported by <1% of subjects.

Deaths, Serious Adverse Events, and Other Significant Events

Deaths

The incidence of SAEs that occurred during a subject's participation in the study with an outcome of death is summarized in Table 7 by SOC and PT, by prior treatment received in Study 302 and Study CL211, and for all subjects. A listing of all deaths reported in the extension study by prior treatment and PT can be found in Table 8.

Overall, 73 subjects (12%) had an SAE that resulted in death. With the exception of respiratory failure (43 of 616 subjects [7%]) and ALS (14 of 616 subjects [2%]), the incidence of all other individual SAEs with an outcome of death was <1%. None of the SAEs leading to death was considered by the Investigator to be related to treatment with dexpramipexole with the exception of Subject [redacted] who died on Day 65 [redacted] due to an SAE of ALS, which was recorded on the CRF as related to study treatment (Table 8). This subject had previously received placebo in the lead-in Study 302.

As discussed above, 4 additional deaths occurred after the subject's end of study date (Table 8). None of these deaths was considered related to study treatment.

Other Serious Adverse Events

The incidence of SAEs is summarized in Table 9 by SOC and PT, by prior treatment received in Study 302 and Study CL211, and for all subjects.

The overall incidence of SAEs was 25%. With the exception of respiratory failure (8%), ALS and dysphagia (3% each), and pneumonia (2%), the incidence of individual SAEs was <1%.

Discontinuation of Study Treatment Due to Adverse Events

The incidence of AEs that led to premature discontinuation of study treatment is summarized in Table 10 by SOC and PT, by prior treatment received in Study 302 and Study CL211, and for all subjects.

The overall incidence of AEs leading to discontinuation of study treatment was 5%. With the exception of respiratory failure (1%), the incidence of individual AEs that led to discontinuation of dexpramipexole was <1%.

Withdrawal From Study Due to Adverse Events

The incidence of AEs that led to premature withdrawal from the study is summarized in Table 11 by SOC and PT, by prior treatment received in Study 302 and Study CL211, and for all subjects.

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Name of Finished Product: Dexpramipexole (BIIB050, KNS 760704)	**Name of Active Ingredient:** Dexpramipexole (BIIB050, KNS 760704)	**Study Indication:** Amyotrophic Lateral Sclerosis
The overall incidence of AEs leading to withdrawal from the study was 8%. With the exception of respiratory failure (4%) and ALS (1%), the incidence of individual AEs that led to withdrawal from the study was <1%.		
Conclusion: The extension Study 304 was terminated early by the Sponsor due to results from the Phase 3 Study 302 that failed to meet its primary and key secondary endpoints. Based on a median exposure to study treatment of <3 months in the extension study and the safety analyses that were performed for the study, no new safety signals were observed in ALS subjects following continued exposure to dexpramipexole 150 mg twice daily or in subjects who were newly treated with the 150 mg twice daily dose of dexpramipexole, having received placebo in the lead-in Study 302.		
Publication(s) Based on the Study: None		
Date of Report: 26 March 2013		