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A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO ASSESS THE SAFETY, TOLERABILITY AND PRELIMINARY EFFICACY OF NLX-112 VERSUS PLACEBO IN LEVODOPA-INDUCED DYSKINESIA IN PARKINSON'S DISEASE

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3 LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation	Explanation
ADaM	Analysis Data Model
AE	Adverse event
ATC	Anatomical therapeutic chemical
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence interval
CGI-C	Clinical Global Impression of Change
CGI-S	Clinical Global Impression of Severity
CS	Clinically significant
CSP	Clinical study protocol
CSR	Clinical study report
C-SSRS	Columbia Suicide Severity Rating Scale
CT	Controlled terminology
CTC	Clinical Trial Consultants AB
CV	Coefficient of variation
DDP	Data display plan
ECG	Electrocardiogram
eCRF	Electronic case report form
ESS	The Epworth Sleepiness Scale
FAS	Full analysis set
FDA	United States Food and Drug Administration
HADS	The Hospital Anxiety Depression Scale
ICIQ-OAB	International Consultation on Incontinence Questionnaire Overactive Bladder Module
IG	Implementation guideline
IMP	Investigational medicinal product
KPPS	King's Parkinson's disease Pain Scale
L-DOPA	Levodopa, L-3,4-dihydroxyphenylalanine
LID	Levodopa-induced dyskinesia
LMM	Linear mixed model
LS	Least square
MAR	Missing at random
MedDRA	Medical dictionary for regulatory activities
NA	Not applicable/not available

Abbreviation	Explanation
NC	Not calculated
NCA	Non-compartmental analysis
NCS	Not clinically significant
PD	Parkinson's disease
PDQ39	The Parkinson's Disease Questionnaire
PK	Pharmacokinetic(s)
PKAS	PK analysis set
PT	Preferred term
Q	Quantile
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Standard deviation
SDTM	Study data tabulation model
SOC	System organ class
UDysRS	Unified Dyskinesia Rating Scale
UPDRS	Unified Parkinson's Disease Rating Scale
WHO	World Health Organization

4 INTRODUCTION

4.1 Study design

This is a double-blind, randomized, placebo-controlled Phase 2a study evaluating the safety, tolerability, and preliminary efficacy of up to 2 mg/day (1 mg BID) of NLX-112 versus placebo in patients with moderate to severe L-DOPA induced dyskinesia (LID) in Parkinson's disease (PD). NLX-112 will be up-titrated (patients will self-administer tablets) to either 2 mg/day or to the highest well-tolerated dose less than 2 mg/day over 4 weeks, maintained at the well-tolerated dose for an additional 2 weeks, and then down-titrated over 2 weeks.

For more details on the study design, please refer to the CSP.

4.2 Study objectives and endpoints

Objectives	**Endpoints**	**Assessments**	**Analyses**	**Data display plan (DDP)**
Primary objective	Primary endpoint	Assessments	Analyses	DDP
To evaluate the safety and tolerability of NLX-112, titrated up to a maximum of 2 mg/day, compared to placebo during 8 weeks of daily treatment in PD patients with LID.	Frequency, intensity and seriousness of AEs	AE reporting	Section 9.1.1	Section 10.2.2.1
	Clinically significant changes from baseline in: ECG, Vital signs, Safety laboratory parameters, and Physical examinations	ECG	Section 9.1.4	Section 0
		Vital signs	Section 9.1.3	Section 10.2.2.3
		Safety laboratory parameters	Section 9.1.6	Section 0
		Physical examinations	Section 9.1.2	Section 0
	Suicidal ideation/behavior as assessed by the Columbia Suicide Severity Rating Scale (C-SSRS).	C-SSRS	Section 9.1.5	Section 10.2.2.5
Secondary objective	Secondary endpoints	Assessments	Analyses	DDP
To assess the preliminary efficacy of NLX-112 treatment in reducing troublesome LID.	Change from baseline at the final efficacy clinic visit (Day 42) in the Unified Dyskinesia Rating Scale (UDysRS) total score [Timeframe: Baseline to Day 42]. Patients will be challenged with 150% of their standard L-DOPA dose (maximum L-DOPA dose 250 mg) 30 minutes prior to the first UDysRS assessment.	UDysRS	Section 9.2.1	Section 10.2.3.1
	Change from baseline in UDysRS total score at Day 28, after a 150% L-DOPA dose challenge.	UDysRS	Section 9.2.1	Section 10.2.3.1
	Change from baseline in total objective score (Parts III, IV) of the UDysRS at Day 28 and Day 42, after a 150% L-DOPA dose challenge.	UDysRS	Section 9.2.1	Section 10.2.3.1
	Change from baseline in ON Time Without Troublesome Dyskinesia (ON Without Dyskinesia plus ON With	ON Time Without Troublesome Dyskinesia	Section 9.2.3	Section 10.2.3.2

Objectives	Endpoints	Assessments	Analyses	Data display plan (DDP)
	Non-troublesome Dyskinesia) based on a PD Home Dyskinesia Diary.			
	Change from baseline in Unified Parkinson's Disease Rating Scale (UPDRS) scores (Part III, motor examination).	UPDRS	Section 9.2.4	Section 10.2.3.3
	Change from baseline in UPDRS combined scores (Parts I, II, III and IV).	UPDRS	Section 9.2.4	Section 10.2.3.3
	Clinical Global Impression of Change (CGI-C) in overall PD symptoms	CGI-C	Section 9.2.5	Section 10.2.3.4
	Change from baseline in dyskinesia scores measured by the Kinesia 360 (Great Lakes Neurotechnologies, Inc) wearable dyskinesia assessment system.	Kinesia 360	Section 9.2.6	Section 10.2.3.5
Exploratory objective	Exploratory endpoints	Assessments	Analyses	DDP
To assess the preliminary efficacy of NLX-112 treatment in improving selected non-motor symptoms of PD, including pain, bladder function, sleep function, mood and quality of living with PD.	Change from baseline in the King's Parkinson's Disease Pain Scale (KPPS) total score and in each of the seven pain domain sub-scores.	KPPS	Section 9.3.1	Section 10.2.4.1
	Change from baseline in the Parkinson's Disease Questionnaire (PDQ39) total score and domain scores.	PDQ39	Section 9.3.2	Section 10.2.4.2
	Change from baseline in the Hospital Anxiety Depression Scale (HADS)	HADS	Section 9.3.3	Section 10.2.4.3
	Change from baseline in the International Consultation on Incontinence Questionnaire (ICIQ) Overactive Bladder Module (ICIQ-OAB) total score.	ICIQ-OAB	Section 9.3.4	Section 10.2.4.4
	Change from baseline in the Epworth Sleepiness Scale (ESS).	ESS	Section 9.3.5	Section 10.2.4.5
To collect blood samples for potential NLX-112 plasma concentration analysis.	Plasma concentrations of NLX-112.	Plasma concentrations		

4.3 Randomization and number of subjects

On Day 1, patients were randomized to receive either NLX-112 or placebo with the ratio 2:1 for active treatment to placebo. This will give approximately 16 patients who received NLX-112 and 8 patients who received placebo in the study. In addition, approximately the same ratio was intended to be attained within each site. The study used competitive enrolment between 5 sites.

4.4 Subject replacement

Patients who were prematurely withdrawn from the study for any reason except the occurrence of AEs assessed as possibly or probably related to study treatment could be replaced during the course of the study.

4.5 Blinding

This is a double-blind study and the allocation of treatments will not be disclosed until clean file has been declared and the database has been locked.

5 STATISTICAL AND ANALYTICAL PLANS

5.1 Statistical hypotheses

Hypotheses tests will be performed at the 5% alpha level with the aim of proving superiority of NLX-112 compared to placebo on the change from baseline on a number of efficacy parameters. Any inference of superiority of NLX-112 compared to placebo will be based on these tests. Further testing within each treatment (NLX-112 or placebo respectively) at the 5% alpha level will be done with the aim of proving a beneficial shift from baseline, as a result of the IMP intervention.

Considering the small dimension of the study and the many tests performed, statistically significant findings should be viewed more as indicative results rather than confirmatory.

5.2 Sample size calculation

No formal sample size calculation has been performed. The sample size of 24 patients is considered sufficient to evaluate the primary objective and to allow for a preliminary efficacy evaluation.

5.3 Definition of analysis sets

The analysis sets defined for the study are outlined inTable 1.

Table 1 Analysis sets

Analysis set	Definition	Use of analysis set
Full analysis set (FAS)	The full analysis set (FAS) will comprise all randomized patients who were dosed.	Safety and efficacy evaluations. See section 10 below for more details.
Per protocol set (PPS)	The per protocol set (PPS) will consist of all patients included in the FAS population who do not have any major protocol violations assessed to compromise the analysis of study data. All protocol violations will be judged as major or minor prior to database lock. The patient must have an overall calculated compliance of 75% to be included in the PPS.	Efficacy evaluations. See section 10 below for more details.

5.4 Compliance

Percent compliance will be calculated as:

$$Compliance = 100 * \frac{number\ of\ delivered\ capsules - number\ of\ returned\ capsules}{expected\ number\ of\ used\ capsules}$$

Expected number of capsules is derived through the maximum dose tolerated and the steady state dose recorded in the eCRF, the dosing scheduled stipulated in the CSP, actual number of days in each dosing stage (the up-titration period and the stable dosing period) per patient and

comments of dosing stated in the eCRF and the monitoring reports. Data indicating individual treatment compliance will be listed and calculated compliance will be summarized descriptively.

5.5 Definition of baseline

Baseline will be defined as the last non-missing data point prior to the first administration of IMP.

5.6 Rounding principles

Generally, no rounding of data will be done prior to calculating statistics. However, if reported data contains more than 8 significant digits it will be rounded to 8 significant digits in the database.

In statistical output and descriptive summaries, the following principles will be followed:

- Data will be presented as reported in input data in listings.
- 2 significant digits will be used for percentages; p-values and similar statistical output will be presented using 4 decimal points.
- Descriptive summaries of all other numerical data (e.g. mean, SD, median etc.) will be presented with one extra decimal compared to reported input data.

5.7 Significance level

All hypothesis testing will be two-sided, using a 5% significance level (α=0.05).

5.8 Multiple comparisons/multiplicity

Statistical tests of efficacy outcomes will be for explorative purposes and no adjustment for multiple tests will be performed.

5.9 Handling of dropouts, missing data and outliers

Outliers will be included in summary tables and listings and will not be handled separately in any analyses. Generally, no imputation of data will be performed. However, in case of a substantial amount of missing data, judged to affect analyses conclusions related to secondary and exploratory endpoints, imputation methods might be considered or alternative analysis approaches, for example analysing mean scores instead of total scores.

In case of missing start and stop times of AEs that cannot be investigated further, missing data will be imputed according to a worst-case scenario. That is, start time will be imputed as the closest time point post first intake of IMP and end time as 23:59, resulting in the longest possible treatment emergent duration of the AE.

6 CHANGES FROM THE CLINICAL STUDY PROTOCOL

Changes to the planned analyses and the timing of these are summarised in Table 2.

Table 2 Changes in the planned statistical analyses

Change category	Timing of change	Description of change	Reason for change	Responsible for change
Change in the SAP compared to the CSP	Prior to DBL	The safety analysis set has been omitted.	Safety evaluations based on FAS is considered sufficient.	Joakim Englund
Change in the SAP compared to the CSP	Prior to DBL	The Chi2 test for the ON Time Without Troublesome Dyskinesia analysis has been replaced with a linear mixed model approach.	The CSP prescribes that a chi-square test be performed for ON Time Without Troublesome Dyskinesia data for the whole study period. As there are multiple measurements per patient and visit, it is not clear how this can be implemented. Hence a shift to a mixed model approach has been adopted.	Joakim Englund
Change in the SAP compared to the CSP	Prior to DBL	Wilcoxon signed rank tests have been replaced with linear mixed modeling with a non-parametric back-up plan should model assumptions fail.	In order to use all available data in the same model, potentially resulting in higher power in the analyses, a mixed model approach has been adopted instead.	Joakim Englund
Change in the SAP compared to the CSP	Prior to DBL	The Kinesia 360 wearable dyskinesia assessment system and PD home dyskinesia diary data for up to 4*24 hours prior to Visit 6 and 7 is included in the analyses.	The CSP prescribes data from only up to 2*24 hours to be used in Kinesia 360 wearable device and home diary analyses. However, using the cut-off point of 4*24 hours prior to Visit 6 and 7 respectively was deemed medically acceptable, whereas at the same time minimizing the amount of missing data in the corresponding analyses.	Joakim Englund

7 CLINICAL DATABASE PROCESSING

7.1 General information

The clinical database is processed and generated according to The Clinical Data Interchange Standards Consortium (CDISC). CDISC is a Standard Developing Organization which develops and publishes standards to normalise the structure of clinical study data and thereby simplify submissions to and reviews by authorities such as the Food and Drug Administration (FDA).

The CDISC standards for clinical studies are the Study Data Tabulation Model (SDTM) and the Analysis Data Model (ADaM). The study data will be structured into a database model reflecting the SDTM and be compliant to SDTM Implementation Guide (SDTM-IG) version 3.2. The data used for statistical analysis will be structured to reflect the Analysis Data Model (ADaM) and be compliant to ADaM Implementation Guide (ADaM-IG) version 1.1.

Data values are collected according to, or mapped into, Controlled Terminology (CT) codelists defined by CDISC, whenever possible. The codelists are updated biannually at CTC and the latest version available at study start will be used. As per default, CT codelists will be used in all tables, listings, and figures. Custom codelists for test or parameter names will be used if applicable upon Sponsor's request, to align with protocol texts, or to adhere to other standard naming conventions (e.g., PK parameter name "Tmax" will be used instead of the CDISC term "Time of CMAX"). These custom codelists will be mapped in the "Parameter Name" field in the ADaM structure, while the CT will be kept in the SDTM predecessor fields to provide traceability back to CDISC codelists.

7.1.1 CDISC Compliance

Full CDISC compliance will not be claimed for this study. The clinical database will be processed and generated according to CDISC standard to the greatest possible extent, but full compliance will not be claimed. No CDISC documentation (e.g., Define XML, Annotated eCRF, SDTM Reviewer's Guide and ADaM Reviewer's Guide) will be generated.

7.2 Database modeling of study design

The study design is mapped to a SDTM study design model containing the following structural components:

EPOCH: An interval of time in the planned conduct of a study. An epoch is associated with a purpose (e.g., screening, randomization, treatment, follow-up), and applies across all arms of the study. Study epochs follow a controlled terminology to represent the different study parts (e.g. SCREENING, TREATMENT, FOLLOW-UP)

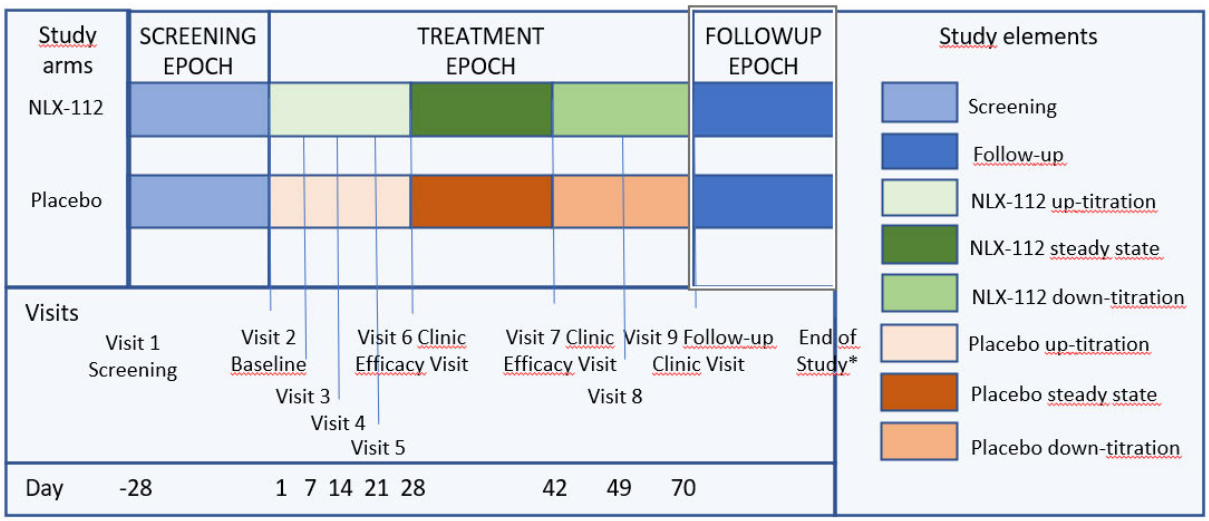
ELEMENT: Building blocks used to build up the entire study length for all subjects. Information on ELEMENTs is extracted from the study design and schedule of events in the protocol. ELEMENTs are defined to span the entire study without gaps. One EPOCH may contain one or several ELEMENTs. All ELEMENTs must have transition rules in accordance with the protocol to determine start and end.

ARM: Subjects are allocated to study arms depending on the study design, either by randomization or other allocation processes defined in the study protocol. ARMs are defined as the total number of planned ways a subject can go through the study (unique combination of study ELEMENTs). All ARMs must contain a unique sequence of ELEMENTs.

VISIT: Study visits are defined as planned timepoints during the study where study data is collected. A visit can be performed in clinic, by off-site contact with study personnel (phone call, video conference or similar), or by subject initiated recordings of data. The visit schedule is extracted from protocol and eCRF design.

A schematic representation of the SDTM study design is presented in Figure 1.

Figure 1 Schematic representation of the SDTM study design



* End of study is modeled as a unique visit, but is performed together with the last participation in the study

8 STATISTICAL DELIVERABLES

The following items will be delivered:

- Statistical analyses, summary tables, listings and figures as described in Section 10.
- Clinical study database delivered as a SAS-export file.

9 STATISTICAL METHODOLOGY

Generally, all collected data will be listed. Listings will be sorted by treatment followed by patient.

Due to small sample size, there will be no summaries using site as a grouping variable. However, site will be specified in listings.

Details on statistical analyses and descriptive summaries are specified below. A complete definition of output produced is given in Section 10 below.

All statistical analysis and descriptive summaries will be performed using SAS version 9.4 or later (SAS institute, Cary, NC).

9.1 Analysis of the primary endpoints

9.1.1 Adverse events

An overview of all AEs, including SAEs, intensity, relationship to IMP, and deaths will be presented by treatment. Incidence of AEs will be summarized by SOC and PT by treatment. Separate tables will be provided, if relevant, for serious AEs (SAEs) or events leading to withdrawal from study. Separate tables will be provided with summaries per titration period as well (up-titration, stable dosing and down-titration).

9.1.2 Physical examination

Clinically significant and non-clinically significant abnormal findings will be specified and presented by patient and summarized by treatment.

9.1.3 Vital signs

Vital signs (systolic/diastolic blood pressure, orthostatic blood pressure, pulse, respiratory rate and body temperature) will be summarized by treatment. Data will be presented with absolute and percent change from baseline.

9.1.4 12-lead ECG

All ECGs will be categorized as ”normal”, ”abnormal, not clinically significant”, or ”abnormal, clinically significant” (as judged by the Investigator) and summarized by treatment using frequency tables.

9.1.5 Columbia Suicide Severity Rating Scale (C-SSRS)

C-SSRS data will be listed by treatment, patient and visit and summarized by treatment.

9.1.6 Safety laboratory analyses

Safety laboratory data will be summarized by treatment with absolute and percent change from baseline at each visit.

9.2 Analysis of secondary endpoints

9.2.1 Statistical inferential analysis of efficacy endpoints

Absolute change from baseline in efficacy endpoints (secondary and exploratory endpoints) will generally be analysed using a linear mixed model with treatment, visit and the interaction

treatment*visit as fixed categorical effects and subject within treatment as a random effect. The baseline value of the dependent variable will be included in the model as a continuous covariate, to account for possible differences in change from baseline outcomes due the starting baseline level. Visit will be modelled as a repeated effect. Kenward-Roger's approximation for degrees of freedom will be used.

Providing a significant type III F-test for the interaction effect treatment*visit, differences between least square estimates of NLX-112 and placebo for the same visit (i.e. from the interaction term treatment*visit, where visit is the same for both NLX-112 and placebo) will be estimated and the corresponding p-value will be presented in tables. In addition, differences between least square estimates of each post-baseline visit and baseline for NLX -112 and placebo respectively (i.e. from the interaction term treatment*visit, where treatment is the same for the post-baseline and the baseline visit) will be estimated and the corresponding p-value will be presented in tables.

The model proposed above will be used for FAS and is valid, as long as the underlying data is missing at random (MAR). As a sensitivity analysis, the model will also be run for PPS, serving as a validity check for the main FAS analysis. The sensitivity analysis will be a complete case analysis, i.e., only patients with no missing data for the dependent variable will be used.

Model diagnostics, for example Shapiro-Wilk's test for a normally distributed residual term and Leven's test for the homoscedasticity assumption of the residual term as well as Q-Q plots and plotting residuals vs. predicted values, will be performed. If model assumptions are deemed to be violated, an attempt will be made to transform the dependent variable in order to fulfil model diagnostics.

A box-cox model will be used to find the most appropriate transformation of data. Lambda values between -3 and 3 will be tested using increments of 0.25. The dependent variable will be transformed accordingly, and the linear mixed model rerun on transformed data. Subsequently, the same model diagnostics as described above will be performed. If model assumptions are deemed to be violated, the linear mixed model approach will not be further pursued for the corresponding dependent variable.

If transforming data according to the above method fails, the analysis will be done using non-parametric methods. A Wilcoxon rank sum test will be used to assess statistically significant differences between active treatment and placebo for relative change from baseline in efficacy endpoints for all post-baseline visits respectively. Furthermore, a Wilcoxon signed rank test will be performed for each post-baseline visit and baseline for NLX -112 and placebo respectively to assess statistically significant differences between each post-baseline visit and baseline for each treatment separately.

9.2.2 Unified Dyskinesia Rating Scale (UdysRS) total score

The UDysRS is a rating instrument designed to assess the core features of dyskinesia in Parkinson's Disease. The UDysRS consists of 4 parts:

• Part I, historical disability with regard to the patient's perceptions of the impact on activities of ADL of on-dyskinesia.

• Part II, historical disability with regard to the patient's perceptions of the impact on ADL of off-dystonia.

• Part III, objective impairment, which assesses severity of dyskinesia, affected body parts, and type of impairment (choreic vs. dystonic).

• Part IV, objective disability, based on an evaluation of Part III activities.

Each item in the UDysRS is scored from 0 to 4, with a possible maximum total score of 104.

The UDySRS assessment will be performed at baseline (Day 1, Visit 2), Day 28 and Day 42 (Visits 6 and 7), see Table 8.1-1, starting approximately 30 minutes after the L-DOPA challenge on these days. The UDysRS (Parts III and IV) will be repeated 3 times after each L-DOPA challenge, 30 minutes apart, and will hence be performed approximately 30, 60 and 90 minutes after each challenge.

The data for all 3 assessments performed at each visit will be entered in the eCRF and the Investigator will highlight which of the assessments, corresponding to the assessment where the patient had most severe dyskinesia, that will be used in the descriptive summaries of data and statistical analyses. However, an additional analysis of only Part III and IV data will be performed using the average of the 3 assessment sessions, instead of the assessment marked as most severe.

UdysRS total score at each visit will be summarized using descriptive statistics. The patients' highest recorded score per UDysRS questionnaire item will be used to calculate total UDysRS score. However, an additional analysis of only Part III data will be performed using the sum of each questionnaire item instead of the highest score. UdysRS total score will be analysed using inferential statistics as described under 9.2.1 above.

The analysis UDysRS total score will be done using data from all Parts as well as using data from Part III and IV only (UDysRS total objective score).

In total, the different analyses outlined above result in the following tables being produced (see section 10.2.3.1 below for more details):

Table 3 UDyRS analyses to be performed

Table ID	UDysRS Parts	Repeated assessments (30, 60 and 90 minutes respectively)	Questionnaire item data handling method
UD 1	I, II, III and IV	Session marked as most severe by the investigator	Highest score
UD 2	III and IV	Session marked as most severe by the investigator	Highest score
UD 3	III and IV	Average of all sessions	Highest score
UD 4	III	Session marked as most severe by the investigator	Sum of each questionnaire scores
UD 5	III	Average of all sessions	Sum of each questionnaire scores

9.2.3 ON Time Without Troublesome Dyskinesia

Change from baseline in ON Time Without Troublesome Dyskinesia (ON Without Dyskinesia plus ON With Non-troublesome Dyskinesia) based on a PD Home Dyskinesia Diary will be summarized using descriptive statistics for all assessment time points. In this analysis, the number of records of ON Without Dyskinesia plus ON With Non-troublesome Dyskinesia divided by the number of non-missing awake records (sleeping records are excluded) for all measurements prior to Visit 2 and for all measurements from 4*24 hours prior to and up until Visit 6 and 7 respectively will be used as input data for each patient respectively. If there is not

at least 8 hours recorded data available for each patient and visit window, the corresponding timepoint is set to missing for the patient. ON Time Without Troublesome Dyskinesia will be analysed using inferential statistics as described under 9.2.1 above.

9.2.4 Unified Parkinson's Disease Rating Scale (UPDRS)

Change from baseline in UPDRS combined scores (Parts I, II, III and IV) to Visit 6 (Day 28) and Visit 7 (Day 42) respectively will be summarized using descriptive statistics. UPDRS combined scores will be analysed using inferential statistics as described under 9.2.1 above. The same analysis will be done for UPDRS Part III only.

9.2.5 Clinical Global Impression of Change (CGI-C) in overall PD symptoms

Change from baseline in CGI-C in overall PD symptoms to Visit 6 (Day 28) and Visit 7 (Day 42) respectively will be summarized using descriptive statistics. In this analysis, rating 0, indicating "no assessment" will be excluded. CGI-C will be analysed using inferential statistics as described under 9.2.1 above.

9.2.6 Dyskinesia measured by a wearable dyskinesia assessment device

Change from baseline in dyskinesia measured by the Kinesia 360 (Great Lakes Neurotechnologies, Inc) wearable dyskinesia assessment system to Visit 6 (Day 28) and Visit 7 (Day 42) respectively will be summarized using descriptive statistics. In this analysis, the mean of all measurements prior to Visit 2 and the mean of all measurements from 4*24 hours prior to and up until Visit 6 and 7 respectively for each patient will be used as input data. However, recorded episodes of less than 30 minutes have not been used in the analysis. Furthermore, if there is not at least 8 hours of valid data according to the rules stipulated above for a specific patient and visit, the corresponding timepoint is set to missing for Kinesia 360 data and hence, not used in the analysis. The Kinesia 360 variable "Dyskinesia detect" will be analyzed this way and reported in the CSR. Dyskinesia detect will be analysed using inferential statistics as described under 9.2.1 above.

9.3 Analysis of tertiary/exploratory endpoints

9.3.1 King's Parkinson's Disease Pain Scale (KPPS) total score

Change from baseline in the KPPS individual pain domain scores and total score to Visit 6 (Day 28) and Visit 7 (Day 42) respectively will be summarized using descriptive statistics. KPPS individual pain domain scores and total score will be analysed using inferential statistics as described under 9.2.1 above.

9.3.2 Parkinson's Disease Questionnaire (PDQ39) total score

The PDQ39 questionnaire assesses how often people affected by PD experience difficulties across 8 dimensions of daily living. The standard PDQ39 assesses quality of life over the previous month. In this study the initial time period assessed at the Baseline Visit will be the previous month, with subsequent assessments for the intervening period since the last clinic visit (about 3 weeks).

The 8 quality of life dimensions covered in the questionnaire are:

- Mobility (10 items #1-10)
- ADL (6 items #11-16)

- Emotional Well Being (6 items #17-22)
- Stigma (4 items #23-26)
- Social Support (3 items #27-29)
- Cognition (4 items #30-33)
- Communications (3 items #34-36)
- Bodily Discomfort (3 items #37-39)

Individual items are rated by the patient on a categorical scale which will be re-coded to a scale of 0 to 4.

Change from baseline in the PDQ39 quality of life dimensions scores and total score to Visit 6 (Day 28) and Visit 7 (Day 42) respectively will be summarized using descriptive statistics. In this analysis each quality-of-life dimensions will be weighted to a scale of 0 to 100 using the formula

Calculated dimension score = total registered score point for the dimension * 100 / maximum possible score points for the dimension

, to allow each dimension to have an equal impact on the total score. PDQ39 quality of life dimensions scores and total score will be analysed using inferential statistics as described under 9.2.1 above.

9.3.3 Hospital Anxiety Depression Scale (HADS)

Change from baseline in the HADS to Visit 6 (Day 28) and Visit 7 (Day 42) respectively will be summarized using descriptive statistics. Summaries will be made for the total anxiety score and total depression score respectively. HADS will be analysed using inferential statistics as described under 9.2.1 above.

9.3.4 International Consultation on Incontinence Questionnaire Overactive Bladder Module (ICIQ-OAB) total score

Change from baseline in the ICIQ-OAB total score to Visit 6 (Day 28) and Visit 7 (Day 42) respectively will be summarized using descriptive statistics. In this analysis, individual ICIQ-OAB answers will be re-coded to a scale of 0-4. ICIQ-OAB total score will be analysed using inferential statistics as described under 9.2.1 above.

9.3.5 Epworth Sleepiness Scale (ESS)

Change from baseline in the ESS total score to Visit 6 (Day 28) and Visit 7 (Day 42) respectively will be summarized using descriptive statistics. ESS total score will be analysed using inferential statistics as described under 9.2.1 above.

9.4 Description of study population

Other study population/demographics data will be presented in listings and summarized descriptively as described in section 10 below.

10 DATA DISPLAY PLAN

Tables and figures will only be generated if sufficient data, with sufficient variability exist to justify specific output being produced.

10.1 Table of contents DDP

List of tables

10.2 Study tables

10.2.1 Demographic data

Table DM 1 Baseline characteristics, demographics and estimated compliance (Full analysis set)

Assessment (unit)		NLX-112 (N=XX)	Placebo (N=XX)	Total (N=XX)
Age (years)	n	x	x	x
	Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx x)
	Median (Min, Max)	xx.x (xx, xx)	xx.x (xx, xx)	xx.x (xx, xx)
Height (cm)	n	x	x	x
	Mean (SD)	xxx.x (xx.x)	xxx x (xx.x)	xxx.x (xx.x)
	Median (Min, Max)	xxx.x (xxx, xxx)	xxx x (xxx, xxx)	xxx.x (xxx, xxx)
Weight (kg)	n	x	x	x
	Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
	Median (Min, Max)	xx.xx (xx.x, xx.x)	xx.xx (xx.x, xx.x)	xx.xx (xx.x, xx.x)
Body Mass Index (kg/m2)	n	x	x	X
	Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
	Median (Min, Max)	xx.xx (xx.x, xx.x)	xx.xx (xx.x, xx.x)	xx.xx (xx.x, xx.x)
Sex	Female	xx (xx%)	xx (xx%)	xx (xx%)
	Male	xx (xx%)	xx (xx%)	xx (xx%)
Ethnicity	Hispanic or latino	xx (xx%)	xx (xx%)	xx (xx%)
	Not hispanic or latino	xx (xx%)	xx (xx%)	xx (xx%)
	Not reported	xx (xx%)	xx (xx%)	xx (xx%)
	Unknown	xx (xx%)	xx (xx%)	xx (xx%)
Race	American Indian or Alaska Native	xx (xx%)	xx (xx%)	xx (xx%)
	Asian	xx (xx%)	xx (xx%)	xx (xx%)
	Black or African American	xx (xx%)	xx (xx%)	xx (xx%)

Assessment (unit)		NLX-112 (N=XX)	Placebo (N=XX)	Total (N=XX)
	Native Hawaiian or Other Pacific Islander	xx (xx%)	xx (xx%)	xx (xx%)
	White	xx (xx%)	xx (xx%)	xx (xx%)
Compliance (%)	n	x	x	x
	Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx x)
	Median (Min, Max)	xx.x (xx, xx)	xx.x (xx, xx)	xx.x (xx, xx)

Data based on the Full analysis set. N: number of subjects in treatment group. Mean values and percentages are based on n. n: Number of observations. SD: Standard deviation. SAS program: [PROGRAM NAME].sas. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. Data extracted at: YYYY-MM-DDTHH:MM:SS

Table DS 1 Subject disposition (All subjects)

	Total (N=XXX)
Screened subjects	xxx
Withdrawn prior to dose	xxx
Reason for withdrawal prior to dose	
--- Reason 1	xxx
--- Reason 2	xxx
--- …	xxx
Subjects included in study	xxx
Allocated to arm	
--- NLX-112	xxx
--- Placebo	xxx
Withdrawn subjects	
--- [REASON 1]	xxx
--- [REASON 2]	xxx
--- …	xxx
Completed subjects	xxx
Included in Full analysis set	xxx

	Total (N=XXX)
Included in Per protocol set	xxx
Subjects at each visit	
--- Visit 1	xxx
--- Visit 2	xxx
--- Visit 3	xxx
--- Visit 4	xxx
--- Visit 5	xxx
--- Visit 6	xxx
--- Visit 7	xxx
--- Visit 8	xxx
--- Visit 9	xxx

Data based on All subjects. SAS program: [PROGRAM NAME].sas. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. Data extracted at: YYYY-MM-DDTHH:MM:SS

Table MH 1 Medical/psychiatric history events by system organ class and preferred term (Full analysis set)

	NLX-112 (N=XX)		Placebo (N=XX)		Total (N=XX)	
System organ class Preferred term	n (%)	m	n (%)	m	n (%)	m
Total	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[SOC 1]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[SOC 1 PT 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 1 PT 2]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 1 PT …]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 2]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[SOC 2 PT 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 2 PT 2]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 2 PT …]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC …]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[SOC … PT 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC … PT 2]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC … PT …]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx

Data based on the Full analysis set. n, number of subjects. m, number of events. Percentages are based on the number of subjects in the treatment period. The following events are coded with multiple terms and are represented as separate events in tables and listings: '[MH TERM 1], [MH TERM 2]'. See listings for detailed information. SAS program: [PROGRAM NAME].sas. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. Data extracted at: YYYY-MM-DDTHH:MM:SS

Table CM 1 Prior medications by ATC levels 1, 3 and 5 (Full analysis set)

	NLX-112 (N=XX)		Placebo (N=XX)		Total (N=XX)	
ATC Name Level 1 ATC Name Level 3 ATC Name Level 5	n (%)	m	n (%)	m	n (%)	m
Total	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[L1 1]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[L1 1 L3 1 L5 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[L1 1 L3 2 L5 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[L1 1 L3 …L5 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[L1 2]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[L1 2 L3 1 L5 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[L1 2 L3 2 L5 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[L1 2 L3 …L5 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[L1 …]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[L1 … L3 1 L5 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[L1 … L3 2 L5 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[L1 … L3 …L5 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx

Data based on the Full analysis set. n, number of subjects. m, number of events. Percentages are based on the number of subjects in the treatment period. The following records are coded with multiple terms and are represented as separate events in tables and listings: '[CM TERM 1], [CM TERM 2]'. See listings for detailed information. SAS program: [PROGRAM NAME].sas. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. Data extracted at: YYYY-MM-DDTHH:MM:SS

Table CM 2 Concomitant medications by ATC levels 1, 3 and 5 (Full analysis set)

	NLX-112 (N=XX)		Placebo (N=XX)		Total (N=XX)	
ATC Name Level 1 ATC Name Level 3 ATC Name Level 5	n (%)	m	n (%)	m	n (%)	m
Total	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[L1 1]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[L1 1 L3 1 L5 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[L1 1 L3 2 L5 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[L1 1 L3 …L5 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[L1 2]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[L1 2 L3 1 L5 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[L1 2 L3 2 L5 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[L1 2 L3 …L5 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[L1 …]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[L1 … L3 1 L5 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[L1 … L3 2 L5 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[L1 … L3 …L5 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx

Data based on the Full analysis set. n, number of subjects. m, number of events. Percentages are based on the number of subjects in the treatment period. The following records are coded with multiple terms and are represented as separate events in tables and listings: '[CM TERM 1], [CM TERM 2]'. See listings for detailed information. SAS program: [PROGRAM NAME].sas. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. Data extracted at: YYYY-MM-DDTHH:MM:SS

10.2.2 Primary endpoint(s)

10.2.2.1 Adverse events

Table AE 1 Overview of adverse events (Full analysis set)

	NLX-112 (N=XX)		Placebo (N=XX)		Total (N=XX)	
	n (%)	m	n (%)	m	n (%)	m
Any AE	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Any SAE	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Any AE leading to withdrawal from study	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Any AE leading to death	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Action taken with study drug	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Dose Not Changed	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Dose Rate Reduced	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Dose Reduced	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Drug Interrupted	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Drug Withdrawn	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Not Applicable	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Causality	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Unlikely	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Possible	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Probable	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Severity	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Mild	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Moderate	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Severe	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Life-Threatening	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Death	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx

Data based on the Full analysis set. N: number of subjects in treatment group. Percentages are based on N. n, number of subjects. m, number of events. The following AEs are coded with multiple MedDRA terms and are represented as separate AEs in tables and listings: '[AE TERM 1]', '[AE TERM 2]', '[AE TERM 3]. See listings for detailed information. SAS program: [PROGRAM NAME].sas. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. Data extracted at: YYYY-MM-DDTHH:MM:SS

Table AE 2 Adverse events by system organ class and preferred term (Full analysis set)

System organ class Preferred term	NLX-112 (N=XX) n (%)	m	Placebo (N=XX) n (%)	m	Total (N=XX) n (%)	m
Total	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[SOC 1]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[SOC 1 PT 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 1 PT 2]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 1 PT …]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 2]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[SOC 2 PT 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 2 PT 2]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 2 PT …]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC …]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[SOC … PT 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC … PT 2]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC … PT …]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx

Data based on the Full analysis set. n, number of subjects. m, number of events. Percentages are based on the number of subjects in the treatment period. The following events are coded with multiple terms and are represented as separate events in tables and listings: '[AE TERM 1], [AE TERM 2]'. See listings for detailed information. SAS program: [PROGRAM NAME].sas. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. Data extracted at: YYYY-MM-DDTHH:MM:SS

If considered appropriate, produce the table above for SAEs only.

Table AE 3 Overview of adverse events per titration period (Full analysis set)

Use the same template as for Table AE 1, but include columns (NLX-112 and Placebo respectively) for the up-titration period (up to Visit 6), the stable dosing period (Visit 6 to Visit 7), the down-titration period (from Visit 7) and the Total column -> 7 results columns in all.

Table AE 4 Adverse events by system organ class and preferred term per titration period (Full analysis set)

Use the same template as for Table AE 2, but include columns (NLX-112 and Placebo respectively) for the up-titration period (up to Visit 6), the stable dosing period (Visit 6 to Visit 7), the down-titration period (from Visit 7) and the Total column -> 7 results columns in all.

10.2.2.2 Physical examination

Table PE 1 Physical examinations (Full analysis set)

Assessment	Assessment timepoint		NLX-112 (N=XX)	Placebo (N=XX)	Total (N=XX)
[PARAMETER 1]	[Assessment timepoint 1]	[RESULT 1]	x (xx%)	x (xx%)	x (xx%)
		[RESULT 2]	x (xx%)	x (xx%)	x (xx%)
		[RESULT 3]	x (xx%)	x (xx%)	x (xx%)
	[Assessment timepoint 2]	[RESULT 1]	x (xx%)	x (xx%)	x (xx%)
		[RESULT 2]	x (xx%)	x (xx%)	x (xx%)
		[RESULT 3]	x (xx%)	x (xx%)	x (xx%)

Data based on the Full analysis set. SAS program: [PROGRAM NAME].sas. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. Data extracted at: YYYY-MM-DDTHH:MM:SS

10.2.2.3 Vital signs

Table VS 1 Vital signs measurements (Full analysis set)

Assessment (unit)	Result category	Assessment timepoint		NLX-112 (N=XX)	Placebo (N=XX)	Total (N=XX)
[PARAMETER 1] (unit)	Measured value	[Assessment timepoint 1]	n	xx	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		[Assessment timepoint 2]	n	xx	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	Absolute change from baseline	[Assessment timepoint 2]	n	xx	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	Relative change from baseline (%)	[Assessment timepoint 2]	n	xx	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)

Data based on the Full analysis set. n: Number of observations. SD: Standard deviation. NC: Not calculated - number of evaluable observations less than 3. NA: Not available - no evaluable observations. SAS program: [PROGRAM NAME].sas. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. Data extracted at: YYYY-MM-DDTHH:MM:SS

10.2.2.4 12-lead ECG

Table EG 1 ECG measurements (Full analysis set)

Assessment (unit)	Result category	Assessment timepoint		NLX-112 (N=XX)	Placebo (N=XX)	Total (N=XX)
[PARAMETER 1] (unit)	Measured value	[Assessment timepoint 1]	n	xx	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		[Assessment timepoint 2]	n	xx	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	Absolute change from baseline	[Assessment timepoint 2]	n	xx	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	Relative change from baseline (%)	[Assessment timepoint 2]	n	xx	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)

Data based on the Full analysis set. n: Number of observations. SD: Standard deviation. NC: Not calculated - number of evaluable observations less than 3. NA: Not available - no evaluable observations. SAS program: [PROGRAM NAME].sas. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. Data extracted at: YYYY-MM-DDTHH:MM:SS

Table EG 2 ECG interpretations (Full analysis set)

Assessment	Assessment timepoint		NLX-112 (N=XX)	Placebo (N=XX)	Total (N=XX)
[PARAMETER 1]	[Assessment timepoint 1]	[RESULT 1]	x (xx%)	x (xx%)	x (xx%)
		[RESULT 2]	x (xx%)	x (xx%)	x (xx%)
		[RESULT 3]	x (xx%)	x (xx%)	x (xx%)
	[Assessment timepoint 2]	[RESULT 1]	x (xx%)	x (xx%)	x (xx%)
		[RESULT 2]	x (xx%)	x (xx%)	x (xx%)
		[RESULT 3]	x (xx%)	x (xx%)	x (xx%)

Data based on the Full analysis set. SAS program: [PROGRAM NAME].sas. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. Data extracted at: YYYY-MM-DDTHH:MM:SS

10.2.2.5 Columbia Suicide Severity Rating Scale (C-SSRS)

Table CS 1 Columbia Suicide Severity Rating Scale (C-SSRS) changes over time (Full analysis set)

Use the same template as outlined in Section 0 above.

10.2.2.6 Safety laboratory analyses

Table LB 1 Safety laboratory measurements - clinical chemistry (Full analysis set)

Assessment (unit)	Result category	Assessment timepoint		NLX-112 (N=XX)	Placebo (N=XX)	Total (N=XX)
[PARAMETER 1] (unit)	Measured value	[Assessment timepoint 1]	n	xx	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		[Assessment timepoint 2]	n	xx	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	Absolute change from baseline	[Assessment timepoint 2]	n	xx	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	Relative change from baseline (%)	[Assessment timepoint 2]	n	xx	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)

Data based on the Full analysis set. n: Number of observations. SD: Standard deviation. NC: Not calculated - number of evaluable observations less than 3. NA: Not available - no evaluable observations. SAS program: [PROGRAM NAME].sas. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. Data extracted at: YYYY-MM-DDTHH:MM:SS

Table LB 2 Safety laboratory measurements - haematology (Full analysis set)

Use the same format as for Table LB 1.

Table LB 3 Safety laboratory measurements - coagulation (Full analysis set)

Use the same format as for Table LB 1.

Table LB 4 Safety laboratory interpretations - urinalysis (Full analysis set)

Use the same format as for Table LB 1.

10.2.3 Secondary endpoint(s)

10.2.3.1 Unified Dyskinesia Rating Scale (UDysRS) total score

Table UD 1 UDysRS total score for all Parts (Full analysis set)

Result category	Assessment timepoint		NLX-112 (N=XX)	Placebo (N=XX)	Total (N=XX)
Measured value	[Assessment timepoint 1]	n	xx	xx	xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	[Assessment timepoint 2]	n	xx	xx	xx
		…	…	…	…
Absolute change from baseline	[Assessment timepoint 2]	n	xx	xx	xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		LMM[a] p-value	x.xxxx[b]	x.xxxx[c]	x.xxxx[d]
	[Assessment timepoint 3]	n	x.xxxx	x.xxxx	x.xxxx
		…	…	…	…
Relative change from baseline (%)	[Assessment timepoint 2]	n	xx	xx	xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	[Assessment timepoint 3]	n	x.xxxx	x.xxxx	x.xxxx
		…	…	…	…

[a)] Linear mixed model (LMM) with treatment, visit and the interaction treatment*visit as fixed categorical effects and subject within treatment as a random effect. The baseline value of the dependent variable has been included in the model as a continuous covariate. Kenward-Roger's approximation for degrees of freedom will be used.
[b)] p-value for the difference between NLX-112 at the assessment timepoint and at baseline.
[c)] p-value for the difference between placebo at the assessment timepoint and at baseline.
[d)] p-value for the difference between NLX-112 and placebo absolute change from baseline at the assessment timepoint.
Data based on the Full analysis set. The session marked as most severe for Part III and IV have been used. For Part III, the highest score for each individual questionnaire item has been used. All UDysRS item scores for Part I, II, III and IV have been summarized pre patient and assessment timepoint and used as input data to the table. N: Number of observations. SD: Standard deviation. NC: Not calculated – number of evaluable observations less than 3. NA: Not available – no evaluable observations. SAS program: [PROGRAM NAME].sas. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. Data extracted at: YYYY-MM-DDTHH:MM:SS

Produce the table above for PPS as well, providing there is any de facto difference between the analysis sets. If the LMM is performed using transformed data, insert a footnote about this as well. If the LMM approach is dropped in favour of non-parametric tests, update the table and footnotes accordingly.

Table UD 2 UdysRS total score for Part III and IV – Most severe assessment session and highest questionnaire item score (Full analysis set)

Use the same format as for Table UD 1. Produce the table above for PPS as well, providing there is any de facto difference between the analysis sets. If the LMM is performed using transformed data, insert a footnote about this as well. If the LMM approach is dropped in favour of non-parametric tests, update the table and footnotes accordingly.

Table UD 3 UdysRS total score for Part III and IV – Average of assessment sessions and highest questionnaire item score (Full analysis set)

Use the same format as for Table UD 1, but update the explanatory footnote to reflect the content of the table. Produce the table above for PPS as well, providing there is any de facto difference between the analysis sets. If the LMM is performed using transformed data, insert a footnote about this as well. If the LMM approach is dropped in favour of non-parametric tests, update the table and footnotes accordingly.

Table UD 4 UdysRS total score for Part III– Most severe assessment session and sum of questionnaire item scores (Full analysis set)

Use the same format as for Table UD 1, but update the explanatory footnote to reflect the content of the table. Produce the table above for PPS as well, providing there is any de facto difference between the analysis sets. If the LMM is performed using transformed data, insert a footnote about this as well. If the LMM approach is dropped in favour of non-parametric tests, update the table and footnotes accordingly.

Table UD 5 UdysRS total score for Part III– Average of assessment sessions and sum of questionnaire item scores (Full analysis set)

Use the same format as for Table UD 1, but update the explanatory footnote to reflect the content of the table. Produce the table above for PPS as well, providing there is any de facto difference between the analysis sets. If the LMM is performed using transformed data, insert a footnote about this as well. If the LMM approach is dropped in favour of non-parametric tests, update the table and footnotes accordingly.

10.2.3.2 ON Time Without Troublesome Dyskinesia

Table ON 1 ON Time Without Troublesome Dyskinesia (Full analysis set)

Use the same format as for Table UD 1. Add a footnote stating that the sum of records of ON Without Dyskinesia plus ON With Non-troublesome Dyskinesia for the 2*24 hours measurements prior to each visit has been used as input data for each patient respectively. Produce the table above for PPS as well, providing there is any de facto difference between the analysis sets. If the LMM is performed using transformed data, insert a footnote about this as well. If the LMM approach is dropped in favour of non-parametric tests, update the table and footnotes accordingly.

10.2.3.3 Unified Parkinson's Disease Rating Scale (UPDRS)

Table UP 1 UPDRS total scores for all Parts (Full analysis set)

Use the same format as for Table UD 1. Include all visits with UPDRS data in the table. Produce the table above for PPS as well, providing there is any de facto difference between the analysis sets. If the LMM is performed using transformed data, insert a footnote about this as well. If the LMM approach is dropped in favour of non-parametric tests, update the table and footnotes accordingly.

Table UP 2 UPDRS total scores for Part III (Full analysis set)

Use the same format as for Table UD 1. Include all visits with UPDRS data in the table. Produce the table above for PPS as well, providing there is any de facto difference between the analysis sets. If the LMM is performed using transformed data, insert a footnote about this as well. If the LMM approach is dropped in favour of non-parametric tests, update the table and footnotes accordingly.

10.2.3.4 Clinical Global Impression of Change (CGI-C) in overall PD symptoms

Table CG 1 CGI-S and CGI-C in overall PD symptoms (Full analysis set)

Assessment	Assessment timepoint		NLX-112 (N=XX)	Placebo (N=XX)	Total (N=XX)
CGI-S	[Assessment timepoint 1]	n	xx	xx	xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
CGI-C	[Assessment timepoint 2]	n	xx	xx	xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
CGI-C		LMM[a] p-value	x.xxxx[b]	x.xxxx[c]	x.xxxx[d]
	[Assessment timepoint 3]	n	xx	xx	xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		LMM[a] p-value	x.xxxx[b]	x.xxxx[c]	x.xxxx[d]

Data based on the Full analysis set. SAS program: [PROGRAM NAME].sas. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. Data extracted at: YYYY-MM-DDTHH:MM:SS

Specify CGI-S or CGI-C in the assessment column. Do not include rating 0, indicating "no assessment" in the summary/analysis. There is no result category column, since change from baseline is included in the definition of CGI-C. Produce the table above for PPS as well, providing there is any de facto difference between the analysis sets. If the LMM is performed using transformed data, insert a footnote about this as well. If the LMM approach is dropped in favour of non-parametric tests, update the table and footnotes accordingly.

10.2.3.5 Dyskinesia scores measured by a wearable dyskinesia assessment device

Table DA 1 Kinesia 360 wearable dyskinesia assessment system (Full analysis set)

Use the same format as for Table UD 1. Add a footnote describing that the mean values per patient and visit have been used as input data to the table. Produce the table above for PPS as well, providing there is any de facto difference between the analysis sets. If the LMM is performed using transformed data, insert a footnote about this as well. If the LMM approach is dropped in favour of non-parametric tests, update the table and footnotes accordingly.

10.2.4 Exploratory endpoint(s)

10.2.4.1 King's Parkinson's Disease Pain Scale (KPPS) total score

Table KP 1 KPPS individual pain domains scores and total score (Full analysis set)

Assessment (unit)	Result category	Assessment timepoint		NLX-112 (N=XX)	Placebo (N=XX)	Total (N=XX)
[PARAMETER 1] (unit)	Measured value	[Assessment timepoint 1]	n	xx	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		[Assessment timepoint 2]	n	xx	xx	xx
			…	…	…	…
	Absolute change from baseline	[Assessment timepoint 2]	n	xx	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
			LMM[a] p-value	x.xxxx[b]	x.xxxx[c]	x.xxxx[d]
	Relative change from baseline (%)	[Assessment timepoint 2]	n	xx	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)

Data based on the Full analysis set. n: Number of observations. SD: Standard deviation. NC: Not calculated - number of evaluable observations less than 3. NA: Not available - no evaluable observations. SAS program: [PROGRAM NAME].sas. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. Data extracted at: YYYY-MM-DDTHH:MM:SS

Produce the table above for PPS as well, providing there is any de facto difference between the analysis sets. If the LMM is performed using transformed data, insert a footnote about this as well. If the LMM approach is dropped in favour of non-parametric tests, update the table and footnotes accordingly.

10.2.4.2 Parkinson's Disease Questionnaire (PDQ39) total score

Table PD 1 PDQ39 calculated dimensions scores and total score (Full analysis set)

Use the same format as for Table KP 1. Produce the table above for PPS as well, providing there is any de facto difference between the analysis sets. If the LMM is performed using transformed data, insert a footnote about this as well. If the LMM approach is dropped in favour of non-parametric tests, update the table and footnotes accordingly.

10.2.4.3 Hospital Anxiety Depression Scale (HADS)

Table HA 1 HADS anxiety and depression scores (Full analysis set)

Use the same format as for Table KP 1. Produce the table above for PPS as well, providing there is any de facto difference between the analysis sets. If the LMM is performed using transformed data, insert a footnote about this as well. If the LMM approach is dropped in favour of non-parametric tests, update the table and footnotes accordingly.

10.2.4.4 International Consultation on Incontinence Questionnaire Overactive Bladder Module (ICIQ-OAB) total score

Table IC 1 ICIQ-OAB total score (Full analysis set)

Use the same format as for Table UD 1. Produce the table above for PPS as well, providing there is any de facto difference between the analysis sets. If the LMM is performed using transformed data, insert a footnote about this as well. If the LMM approach is dropped in favour of non-parametric tests, update the table and footnotes accordingly.

10.2.4.5 Epworth Sleepiness Scale (ESS)

Table ES 1 ESS total score (Full analysis set)

Use the same format as for Table UD 1. Produce the table above for PPS as well, providing there is any de facto difference between the analysis sets. If the LMM is performed using transformed data, insert a footnote about this as well. If the LMM approach is dropped in favour of non-parametric tests, update the table and footnotes accordingly.

10.3 Study listings

16.2.1 Discontinued patients

- Listing 16.2.1- 1 Discontinued patients (All patients)

Include reason for discontinuation and site in the listing.

- Listing 16.2.1- 2 Non-eligible patients (All patients)
- Listing 16.2.1- 3 Disposition (All patients)
- Listing 16.2.1- 4 Patient visits (All patients)
- Listing 16.2.1- 5 Patient elements (All patients)

16.2.2 Protocol deviations

- Listing 16.2.2- 1 Protocol deviations (All patients)

Include site in the listing.

16.2.3 Population definitions

- Listing 16.2.3- 1 Patients excluded from Per protocol set (All patients)
- Listing 16.2.3- 2 Population definitions (All patients)

16.2.4 Demographic data

- Listing 16.2.4- 1 Demography (Full analysis set)
- Listing 16.2.4- 2 Medical and psychiatric History (Full analysis set)
- Listing 16.2.4- 3 Prior and concomitant medications (Full analysis set)
- Listing 16.2.4- 4 Hoehn and Yahr scale (Full analysis set)
- Listing 16.2.4- 5 MMSE (Full analysis set)

16.2.5 Compliance and/or Drug Concentration Data

- Listing 16.2.5- 1 Compliance – Evaluation (Full analysis set)
- Listing 16.2.5- 2 Compliance – NLX-112 plasma concentrations (Full analysis set)

Listing 16.2.5- 3 IMP administration (Full analysis set)

16.2.6 Individual Efficacy Response Data

- Listing 16.2.6- 1 UDysRS (Full analysis set)
- Listing 16.2.6- 2 UPDRS, parts I-IV (Full analysis set)
- Listing 16.2.6- 3 CGI-S, CGI-C (Full analysis set)
- Listing 16.2.6- 4 KPPS (Full analysis set)
- Listing 16.2.6- 5 PDQ39 (Full analysis set)
- Listing 16.2.6- 6 HADS (Full analysis set)
- Listing 16.2.6- 7 ICIQ-OAB (Full analysis set)
- Listing 16.2.6- 8 ESS (Full analysis set)
- Listing 16.2.6- 9 Kinesia 360 wearable device data (Full analysis set)
- Listing 16.2.6- 10 PD Home Dyskinesia Diary (Full analysis set)

16.2.7 Adverse event listings (each patient)

- Listing 16.2.7- 1 Adverse events (Full analysis set)

Include site in the listing.

- Listing 16.2.7- 2 Serious adverse events (Full analysis set)

Include site in the listing.

16.2.8 Listings of individual laboratory measurements by patient

- Listing 16.2.8- 1 Safety laboratory measurements (Full analysis set)

Abnormal values and assessment of clinical significance must be included.

- Listing 16.2.8- 2 Other laboratory measurements (Full analysis set)

16.2.9 Listings of vital signs, ECG, physical examination and C-SSRS data by patient

- Listing 16.2.9- 1 Vital signs (Full analysis set)
- Listing 16.2.9- 2 ECG (Full analysis set)
- Listing 16.2.9- 3 Physical examinations (Full analysis set)
- Listing 16.2.9- 4 C-SSRS (Full analysis set)