PHARNEXT

INTEGRATED CLINICAL AND STATISTICAL REPORT

International, multi-center, randomized, double-blind, placebo-controlled phase III study assessing in parallel groups the efficacy and safety of 2 doses of PXT3003 in patients with Charcot-Marie-Tooth Disease type 1A treated 15 months

PRODUCT NAME: PXT3003

INDICATION: Charcot-Marie-Tooth Disease Type 1A (CMT1A)

STUDY PROTOCOL NUMBER: CLN-PXT3003-02

IND/EUDRACT NUMBER: 122505/2015-002378-19

PHASE: 3

Date First Subject Screened	11 December 2015
Date Last Subject Completed	22 March 2018
Sponsor	Pharnext *Until end of 2018*: 11 Rue des Peupliers 92130 Issy Les Moulineaux France *From 2019 on*: Immeuble Vivaldi 11 Rue René Jacques 92130 Issy Les Moulineaux France
Sponsor's Responsible	Daniel Cohen, MD, PhD Chief Executive Officer Pharnext
Sponsor Contact Person	Agnès Daoust, PhD Clinical Project Leader Pharnext
Version and Date of this Report	Version 2.0, 8 July 2019

This study was performed in compliance with Good Clinical Practices and applicable regulatory requirements, including the archiving of essential documents.

1. APPROVAL SIGNATURES

STUDY TITLE: International, multi-center, randomized, double-blind, placebo-controlled phase III study assessing in parallel groups the efficacy and safety of 2 doses of PXT3003 in patients with Charcot-Marie-Tooth Disease type 1A treated 15 months

STUDY NUMBER: CLN-PXT3003-02

I, the undersigned, have read this report and confirm that to the best of my knowledge, it accurately describes the conduct and results of the study.

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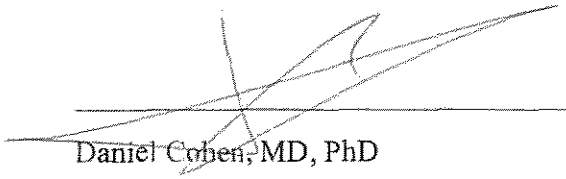	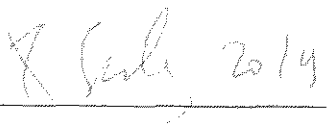
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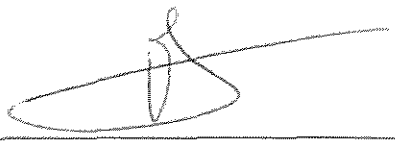	
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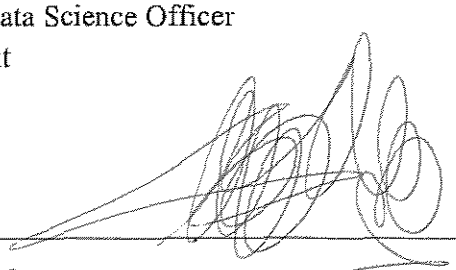	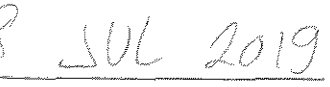
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2. SYNOPSIS

Name of Sponsor: Pharnext	**(For National Authority Use only)**
Name of Finished Product: PXT3003	
Name of Active Ingredient: D-sorbitol, naltrexone hydrochloride (HCl), and (*RS*)-baclofen	
TITLE OF STUDY:	International, multi-center, randomized, double-blind, placebo-controlled phase III study assessing in parallel groups the efficacy and safety of 2 doses of PXT3003 in patients with Charcot-Marie-Tooth Disease type 1A treated 15 months Study Name: PLEO-CMT Protocol Number: CLN-PXT3003-02 EudraCT Number: 2015-002378-19 IND number: 122505 NCT number: NCT02579759
COUNTRY COORDINATORS:	Multi-center Shahram Attarian, Marianne De Visser, Teresa Sevilla, Mark Roberts, Philip Van Damme, Peter Young, Florian Thomas, Jack Puymirat.
STUDY CENTERS:	30 centers in 8 countries in Europe (France, Germany, Spain, Belgium, Netherlands, the United Kingdom (UK)), the United States of America (USA), and Canada
PUBLICATION (REFERENCE):	None
STUDY PERIOD:	Date First Subject Screened 11 December 2015 Date Last Subject Completed: 22 March 2018
PHASE OF DEVELOPMENT	Phase III
OBJECTIVES: Primary:	The primary objective of this double-blind study was to assess the efficacy of two doses of fixed dose combination of (*RS*)-baclofen, naltrexone hydrochloride, and D-sorbitol (PXT3003) compared to placebo on the disability measured by the Overall Neuropathy Limitation Scale (ONLS) clinical score in Charcot-Marie-Tooth disease type 1A (CMT1A) subjects treated for 15 months.
Secondary:	The secondary objectives were to assess the following: • The efficacy of two doses of PXT3003 compared to placebo on other outcomes including the impairment clinical score (Charcot-Marie-Tooth Neuropathy Score version 2 [CMTNS-v2]), functional tests (Walking test, Quantified Muscular Testing [QMT], Nine-Hole-Peg test [9-HPT]), electrophysiological parameters, and measures of quality of life. • The safety and tolerability of two doses of PXT3003 compared to placebo. • Pharmacokinetic (PK) parameters of PXT3003 components (baclofen, naltrexone, and 6β-naltrexol) in the two tested dosages of PXT3003. • The change over time of potential blood biomarkers.

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- Molecular changes in skin biopsy, when this procedure was possible (ancillary sub-study).
- To explore new potential imaging biomarkers by leg Magnetic Resonance Imaging (MRI), when this procedure was possible (ancillary sub-study and centralized reading).

Skin biopsy and magnetic resonance imaging data were not consolidated in the study clinical database.

METHODOLOGY:

This was an international, multi-center, double-blind, randomized, placebo-controlled, phase III prospective study, comparing 2 doses of PXT3003 to Placebo in parallel-groups in outpatients with CMT1A disease. The study was planned to be conducted in at least 20 centers in Europe and United States of America (USA).

The study was planned to be performed in a total of at least 300 subjects presenting with a diagnosis of CMT1A, genetically proven, of mild-to-moderate severity (assessed by CMTNS-v2 score >2 and ≤18), and with muscle weakness in at least foot dorsiflexion, and nerve conduction velocity (NCV) ≥15 m/s. The subjects were randomized in investigational sites in various European countries, the US, and Canada.

SAMPLE SIZE CALCULATION

A minimum clinically relevant difference in ONLS (Cohen's d = 0.3) should be detected versus Placebo with a power of 90% at a two-sided 2.5% significance level when the sample size reaches at least 89 patients per group. Assuming a drop-out rate of ~10%, the aim was to recruit 100 patients per group for a total of 300 patients.

RANDOMISATION

Patients were to be randomized (1:1:1) into 3 parallel groups: PXT3003 Dose 1, PXT3003 Dose 2, and Placebo.

NUMBER OF SUBJECTS:

Planned : ≥ 300 Screened : 437 Enrolled : 323

	PXT3003 Dose 2	PXT3003 Dose 1	Placebo
Full Analysis Set	113	109	101
Modified Full Analysis Set	55	93	87
Completers Selection	49	85	80
Per Protocol Selection	38	68	60
Safety Selection	113	109	101

DIAGNOSIS & MAIN CRITERIA FOR INCLUSION & EXCLUSION:

Male and female subjects 16 to 65 years of age with a proven genetic diagnosis of CMT1A of mild-to-moderate severity assessed by CMTNS-v2, with a score >2 and ≤18. Subjects had to have clinically confirmed muscle weakness in at least foot dorsiflexion and motor nerve conduction of the ulnar nerve of at least 15 m/s.

Subjects with any other associated cause of peripheral neuropathy such as diabetes or with another significant neurological disease or a concomitant major systemic disease were not allowed to participate.

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TEST PRODUCT

The tested active drug PXT3003 is a fixed dose combination of (*RS*)-baclofen, naltrexone HCl, and D-sorbitol.

DOSE

Two active doses of PXT3003 were tested:
Dose 1: 3 mg baclofen, 0.35 mg naltrexone, and 105 mg sorbitol
Dose 2: 6 mg baclofen, 0.70 mg naltrexone, and 210 mg sorbitol

Composition of PXT3003 Clinical Formulations

Active Substance	Dose 1	Dose 2
D-sorbitol	21 mg/mL	42 mg/mL
Naltrexone HCl	0.07 mg/mL	0.14 mg/mL
(*RS*)-baclofen	0.6 mg/mL	1.2 mg/mL

List of excipients (PXT3003 and Placebo): acetate buffer, sodium methyl paraben, sodium propyl paraben, and 2-methylbutyl acetate (banana oil); pH = 5.5

MODE OF ADMINISTRATION

orally (per os [po]) twice per day (bis in die [BID])

BATCH NUMBERS

Campaign number	PXT3003 group	Manufacturing Batch number Quay Pharma	Labeling, packaging Batch number Theradis Pharma	Kit numbers
1	Dose 1	PHR/15/0209	P15045	K10001 to K10390
	Dose 2	PHR/15/0210		
1 Relabeled Expiry date extended	Dose 1	PHR/15/0209	P16010	K10163 to K10390
	Dose 2	PHR/15/0210		
2	Dose 1	PHR/15/0223	P16002	K10391 to K11422
	Dose 2	PHR/15/0224		
3	Dose 1	PHR/16/0244	P16039	K12431 to K13462
	Dose 2	PHR/16/0249		
4	Dose 1	PHR/16/0239	P16035	K11423 to K12430
	Dose 2	PHR/16/0240		
5	Dose 1	PHR/16/0243	P17002 and P17008	K13463 to K14470
	Dose 2	PHR/16/0245		
6	Dose 1	PHR/16/0292	P17014	K14471 to K14914
	Dose 2	PHR/16/0293		
8	Dose 1	PHR/17/0341	P17034	K14915 to K15454
	Dose 2	PHR/17/0342		

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CONTROL PRODUCT: Matching placebo

MODE OF ADMINISTRATION: orally (per os [po]) twice per day (bis in die [BID])

BATCH NUMBERS:

Campaign number		**Manufacturing Batch number Quay Pharma**	**Labeling, packaging Batch number Theradis Pharma**	**Kit numbers**
1	Placebo	PHR/15/0208	P15045	K10001 to K10390
1	Placebo	PHR/15/0208	P16010	K10163 to K10390
2	Placebo	PHR/15/0222	P16002	K10391 to K11422
3	Placebo	PHR/16/0238	P16039	K12431 to K13462
4	Placebo	PHR/16/0234	P16035	K11423 to K12430
5	Placebo	PHR/16/0242	P17002 and P17008	K13463 to K14470
6	Placebo	PHR/16/0291	P17014	K14471 to K14914
8	Placebo	PHR/16/0291	P17034	K14915 to K15454

DURATION OF TREATMENT: Subjects were to be randomized after a Screening Period of up to 30 days, during which the selection criteria were verified, and baseline assessments, such as electrophysiological testing, laboratory tests, and electrocardiogram (ECG), were performed. After randomization, the subjects were included in the study and received the double-blind study drug for up to 15 months.

ENDPOINTS:

Efficacy:

Primary Efficacy Endpoint

The primary efficacy endpoint was the main effect of the studied treatment on the improvement of disability measured by the ONLS total score, summarized at 12 and 15 months, defined by the mean change of the ONLS from Baseline to the 2 post baseline measures at 12 and 15 months.

Secondary Efficacy Endpoints

The secondary endpoints were restricted to the following:

- Time to walk 10 meters (10 Meter Walking Test).
- Sensory Score derived from the Charcot-Marie-Tooth Neuropathy Score version 2 (CMTNS-v2) and calculated as the sum of items 1+4+5 (Sensory symptoms, Pinprick sensibility, and Vibration).

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	• CMT Examination Score (CMTES) defined as Charcot-Marie-Tooth Neuropathy Score version 2 (CMTNS-v2) limited to impairment items and excluding electrophysiological items (sum-score of items 1 to 7). • Best result of the Nine-Hole Peg Test (9-HPT), performed on the non-dominant hand. <u>Exploratory Endpoints</u> • Arm and leg sub-items of ONLS. • Number of steps performed (10 Meter Walking Test). • Response at the end of treatment based on the following definitions: o Therapy response 1, defined as subjects improving on ONLS at the end of treatment (at least 1 point). o Therapy response 2, defined as subjects not deteriorating on ONLS at the end of treatment. • CMTNS-v2: o Total score. o Corrected total score. o Individual items: Sensory symptoms, Motor symptoms legs, Motor symptoms arms, Pinprick sensibility, Vibration, Strength (legs), Strength (arms), CMAP amplitude, Radial SNAP amplitude. • Quantified Muscular Testing (QMT) by Hand grip and Foot dorsiflexion dynamometry (mean of both sides) • Electrophysiological parameters assessing sensory and motor responses of ulnar and radial nerves (non-dominant side) including: o Compound Muscle Action Potential (CMAP) Amplitude. o Motor Nerve Conduction Velocity (NCV). o Distal Motor Latency (DML). o Radial Sensory Nerve Action Potential (SNAP) Amplitude. • Quality of life measured by: o EuroQol health related Quality of Life questionnaire (EQ-5D-5L) consisting of assessments of Mobility, Self-Care, Usual Activities, Pain/Discomfort, and Anxiety/Depression, and a Visual Analog Scale (VAS). o Self-assessment of impairment in daily activities. At baseline the patient defines the worst and second worst impairment and assesses these by means of a VAS. At subsequent visits impairment of the same 2 activities are assessed by means of a VAS.
Safety:	Safety and tolerability of PXT3003 were compared to placebo on the following parameters: • Incidence of treatment-emergent adverse events (TEAEs); they were evaluated by type/nature, severity/intensity, seriousness, and relationship to study drug.

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	• Incidence of related TEAEs (including possibly and probably related TEAEs) with a moderate or severe intensity. • Incidence of TEAEs leading to withdrawal of study drug. • Incidence of serious adverse events (SAEs). • Changes in physical examination, vital signs (blood pressure and heart rate), 12-lead ECG, and laboratory data (hematology and blood chemistry).
Other Exploratory Endpoints:	The following other exploratory endpoints were analyzed: • PXT3003 components plasma concentration • Blood biomarkers
STATISTICAL METHODS:	**Original Protocol** The statistical analysis plan as defined in the original protocol calculated power for only the primary endpoint on the FAS to detect a change in ONLS score of 0.3 points. Such a difference should be detected versus placebo with a power of 90% at a two-sided 2.5% significance level when the sample size reached at least 89 patients per group. Assuming a dropout rate of 10%, the sample size was calculated to be 300 patients (100 per group). The study was not powered to detect any statistically significant changes on secondary and exploratory endpoints. The main analysis was to be performed on the FAS, using ANCOVA, and missing data imputed using a linear model estimated on the placebo group. This analysis was to be repeated on other quantitative efficacy endpoints. **Intercurrent Event** An intercurrent event involving the appearance of crystals in some vials of the highest Dose. This event resulted in the discontinuation of two patient subsets: a random subset of patients from Germany across all three groups due to a decision from BfArM and subsequently a random subset of the Dose 2 arm due to the sponsor's decision. This resulted in an unexpectedly high rate of dropouts (33.7%) prior to the Month 12 visit. It was immediately apparent that the dropouts due to this event were purely accidental and unrelated with treatment outcome. Under appropriate statistical techniques, these missing data are known not to bias the results with the only disadvantage of reducing statistical power. Nevertheless, the statistical power remained at 75% even with the unexpected level of missing data. Moreover, at the time of the intercurrent event, two-thirds of the study had already been completed and the blinded assessment of the safety profile was favorable. Thus, the sponsor decided to continue the trial as planned and the preliminary Statistical Analysis Plan (SAP) was adapted prior to database lock.

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Changes to the Statistical Analysis Plan (SAP)

The intercurrent event imposed a necessary adaptation to the SAP. The original plan was to impute all missing data following the placebo trend. However, this was based on a conservative 10% dropout rate assumed from the previous Phase 2 study and was no longer a reasonable option given the 33.7% dropout rate.

An independent, blinded Adjudication Committee (ADC) was convened to qualify each dropout as Outcome-Related (OR) or Outcome-Unrelated (OU) prior to the database lock. Any dropouts judged as OU could be therefore a priori excluded or imputed with no bias in accordance with ICH guidelines. This assumption could then be validated posteriori with several pre-defined sensitivity analyses including the analysis as planned in the protocol.

Efficacy:

Main Analysis
The main analysis was defined to remain as close as possible to the protocol and was defined as follows:

- Analysis population: a modified Full Analysis Set (mFAS) excluding dropouts prior to Month 12 judged as OU by the ADC while retaining OR dropouts (estimated less than 10% in the protocol).
- Statistical model: ANCOVA remained the statistical model as described in the protocol.
- Imputation of missing values: multiple imputation of OR missing data and, as per protocol, according to placebo distribution.

Primary Analysis
The primary analysis was the main analysis performed on the primary efficacy endpoint: the improvement of disability measured by the ONLS score, summarized at 12 and 15 months, defined by the mean change of the ONLS from Baseline to the 2 post-baseline measures at 12 and 15 months.

Sensitivity Analyses
Several sensitivity analyses were conducted to test the main assumptions supporting the primary analysis. The following analyses were specified to evaluate alternative patient selections, imputation strategies, and statistical models.

Primary Sensitivity Analysis
The primary sensitivity analysis was defined to investigate a potential bias arising from the deselection of outcome-unrelated dropouts from the FAS (i.e. use of the mFAS as the primary analysis population). This analysis was performed on the FAS, using ANCOVA, and multiple imputation assigning a value to OR missing data according to placebo distribution and a value to OU missing data according to their core arm distribution (a hybrid imputation strategy considered as the main strategy). It was expected to provide the same unbiased estimate of the treatment effect as the primary analysis.

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	Additional Main Sensitivity Analyses A sensitivity analysis was performed to confirm that retaining OR missing data imputed according to placebo is a conservative approach. This analysis was performed on the Completers and PP Selections, using ANCOVA, and no imputation (NI). The results of these analyses were expected to be superior compared to the primary analysis. A sensitivity analysis was performed to consider values exact timepoints throughout treatment (compared to ANCOVA which only considers the mean of 12 and 15 months). This analysis was performed on the mFAS and FAS, using a longitudinal model (LG), and no imputation (NI). As only few timepoints were available, the sponsor opted for a linear LG model. Therefore, consistency with ANCOVA could be attenuated if the time-effect relationship was not linear. This analysis has the advantage of fewer dropouts at the 6 months visit and therefore results were expected to be more significant with the FAS compared to the mFAS. The results were also expected to be consistent with the primary analysis. The same analysis scheme was used for the secondary efficacy endpoints. All efficacy endpoints not used in the primary or secondary analysis were analyzed in the exploratory analyses. For the analysis of the relationship of dose and PK, the effect of the PXT3003 was studied based on the exact dose and measured drug plasma concentration doses instead of considering the 2 doses as independent. This investigation consisted of approximating the dose-effect relations by linear relationships. This analysis was performed using the endpoints of the primary and secondary analyses.
Safety:	Safety and tolerability were assessed based on AEs, clinical laboratory data, ECG parameters, physical examinations, and vital signs.
Plasma Concentration:	Descriptive statistics (N, arithmetic mean, standard deviation, minimum, median, maximum) of each analyte concentration (trough and peak) values of baclofen, naltrexone, and 6β-naltrexol) were presented by visit and treatment group and time point. The table was repeated by gender.
Other exploratory endpoints:	Potential blood biomarkers identified in the previous phase II trial were to be confirmed in this trial. These included tryptophan, alanine, serotonin, T4 and free cholesterol. Skin biopsy and MRI data were to be listed only.
RESULTS: Efficacy:	**Primary Endpoint: ONLS** The treatment effect of Dose 2 was statistically significant, with estimate of the difference in final value between Dose 2 and Placebo groups of -0.37 (97.5% CI: [-0.68; -0.06], p=0.008). The treatment effect was consistent across several of the sensitivity analyses, notably on the primary sensitivity analysis performed on the FAS (Dose 2 effect of -0.39, 97.5% CI: [-0.71 ; -0.07], p=0.007). When analyzed using the longitudinal (LG) model on the

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FAS, the estimate of the difference between Dose 2 and Placebo was -0.30 per year (97.5% CI: [-0.56 ; -0.04], p=0.009). Data on Completers Selection and PP Selection were, as expected, superior with an effect of -0.40 (97.5% CI: [-0.72 ; -0.08], p=0.005) and -0.55 (97.5% CI: [-0.92 ; -0.18], p<0.001), respectively.

The estimate difference in final value between Dose 1 and Placebo groups was -0.13 (97.5% CI: [-0.39; 0.14], p=0.287). Although not statistically significant, there was a significant drug dose effect relationship with an effect estimate of -0.17 per dose unit increase (95% CI: [-0.31 ; -0.04], p=0.013). This result was consistent across several sensitivity analyses. Notably, when analyzed using the longitudinal (LG) model on the FAS, the estimate of the difference between Dose 1 and Placebo was -0.22 (97.5% CI: [-0.44 ; -0.01], p=0.020).

To show the benefit at the individual patient level, two responders' analyses were performed on the Completers Selection. The assessments calculated the chance for a patient to improve from his/her baseline value by at least one point (Therapy Response 1) or to remain stable/not deteriorate (Therapy Response 2). The odds ratio of Dose 2 versus Placebo was 2.09 (p=0.097) for Therapy Response 1 and 3.39 (p=0.026) for Therapy Response 2.

Secondary and Exploratory Endpoints:
Results on the Primary Endpoint were strongly supported by a consistent trend of efficacy for most of the secondary and exploratory endpoints with constant superiority of Dose 2.

10 Meter Walking Test
The 10MWT was one of the four secondary endpoints. The treatment effect of Dose 2 was statistically significant, with estimate of the difference in final value between Dose 2 and Placebo groups of -0.47 seconds (97.5% CI: [-0.91; -0.03], p=0.016). Improvement of the 10MWT was already detectable and significant at 6 months (-0.42, 97.5% CI: [-0.78 ; -0.06], p=0.008).

The estimate difference in final value between Dose 1 and Placebo groups was -0.28 (97.5% CI: [-0.65; 0.08], p=0.084). Although not statistically significant, a clear dose effect relationship was found with an estimate of -0.22 per dose unit increase (95% CI: [-0.41 ; -0.04], p=0.015).

CMTNS-v2 Sensory Symptoms
This exploratory endpoint demonstrated the highest standard mean difference compared to Placebo with an improvement of -0.29 (97.5% CI: [-0.58 ; -0.00], p=0.023) for Dose 2.

Self-Assessed Endpoints
Several self-assessed endpoints, namely quality of life endpoints, tended to improve for both doses tested compared to Placebo. However, Dose 1 tended to perform better than Dose 2, especially for two endpoints utilizing

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visual analog scales (VAS) (EuroQol-5D VAS and Self-Assessed Impairment 1) and the EuroQol-5D Self Care subitem.

Safety:

Treatment Exposure
Median treatment duration of Dose 1 group and Placebo group was consistent with the foreseen period of 15 months. For Dose 2 group it is less (approximately 11 months) due to the intercurrent event.

Adverse Events
The adverse events profiles of all three groups were similar and the safety profile of PXT3003 was favorable.

	PXT3003 Dose 2 (N=113)	**PXT3003 Dose 1 (N=109)**	**Placebo (N=101)**
TEAEs	87 (77.0%)	89 (81.7%)	83 (82.2%)
Treatment-related TEAEs	38 (33.6%)	39 (35.8%)	34 (33.7%)
Moderate or severe	5 (4.4%)	8 (7.3%)	10 (9.9%)
TEAE leading to drug withdrawal	6 (5.3%)	6 (5.5%)	6 (5.9%)
Treatment-related TEAEs	2 (1.8%)	3 (2.8%)	2 (2.0%)
Serious TEAEs	3 (2.7%)	10 (9.2%)	5 (5.0%)
Treatment-related serious TEAEs	0 (0.0%)	0 (0.0%)	0 (0.0%)
Serious TEAEs leading to drug withdrawal	0 (0.0%)	1 (0.9%)	0 (0.0%)
Deaths	0 (0.0%)	0 (0.0%)	0 (0.0%)

Clinical Laboratory Evaluation
There were no notable changes during the study in the means of laboratory parameters and no notable differences between the treatment groups in during the study. Most laboratory data fell within the normal range. No laboratory abnormalities were reported as serious adverse events.

Plasma Concentrations:

The mean plasma exposure of each of the active components increased proportionally with the administered dose of PXT3003. The mean values of the three components in the combination at 6, 12, and 15 months are variable, but nevertheless comparable. The mean values of the components in the combination are in line with values already published for each drug administered individually.

Blood Biomarkers:

Mean values of tryptophan, alanine, and T4 decreased at subsequent visits. There were no notable differences between the three groups.

CONCLUSION:

This pivotal Phase 3 clinical trial was designed to assess the effect of two dose levels of PXT3003 versus placebo in patients from 16 to 65 years with mild to moderate CMT1A after up to 15 months of drug exposure. Despite the intercurrent event which unpredictably generated an unusually high rate of missing data, PXT3003 Dose 2 clearly demonstrated statistically and clinically significant improvement of the primary efficacy endpoint ONLS versus Placebo. This difference was consistent across multiple patient selections, alternative statistical techniques and various missing data

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imputation approaches. The treatment effect was additionally supported by a robust trend of efficacy for most secondary and exploratory endpoints. Notably among them, the 10 Meter Walking Test, significantly improved, a result which was also supported by multiple sensitivity analyses. Interestingly, the exploratory endpoint CMTNS Sensory Symptoms raised the highest standard mean difference. Drug and drug exposure effect relationships were consistently observed across most endpoints, especially for ONLS and 10MWT.

The efficacy results are clinically meaningful for three major reasons:

1. ONLS and 10MWT improved over time and are associated with quality of life.
2. PXT3003 demonstrated recovery towards normal state beyond stabilization of the disease progression. This recovery can be detected as early as 6 months of treatment.
3. Motor and sensory improvements seem to predominate on the lower limbs which are the most affected in this neuropathy.
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PXT3003 demonstrated an excellent safety profile, in line with former safety evaluations and the relatively low dosage of the individual components. The benefit/risk of PXT3003 at Dose 2 can therefore be considered as being particularly favorable and beneficial for a patient at a mild to moderate stage suffering from this neurodegenerative disease with a high, unmet medical need.

DATE OF THE REPORT:	8 July 2019