

(File Attachment comment)

From: Morris, Nevitt  
To: jennifer.wellman@sparktx.com  
Cc: Morris, Nevitt; jim.wang@sparktx.com  
Subject: BLA 125610 Information Request 7/27/17  
Date: Thursday, July 27, 2017 9:42:13 AM  
Attachments: image001.png

Hi Jennifer and Jim:

Please provide responses to the following Information Request, dated 7/27/17, by the end of next week, August 4, 2017. If more time is needed, please let us know.

Information Request:

1.

In your clinical report for the primary efficacy endpoint (Study 301), you state that the mean (SD) bilateral MLMT change score at Year 1 was 1.8 (1.1) for the Intervention group and 0.2 (1.0) for the Control group, resulting in a mean group difference of 1.6. The mean group difference of 1.6 measures the absolute difference between the mean value in two different groups. This measure only provides an idea of how much difference there is between the averages of the MLMT scores of the experimental group and control groups. The "mean difference" (taking the difference between each pair of scores for each subject, and then taking the mean of all those differences) for the intervention group and the control should be calculated. We believe that the mean of the changes for each group (intervention vs. controlled), and not difference of the averages of the scores, will provide more meaningful information regarding the efficacy of study subjects on the MLMT. Please provide an analysis of the MLMT scores for the intervention and control groups that presents the mean score differences at the 95% confidence intervals. Additionally, please perform this analysis for the right eye, left eye and both eyes.

2.

Please stratify results of the final MLMT scores for each subject by age groupings and by disease diagnoses (grouped) showing those who improved with treatment, remained the same with treatment, or worsened with treatment. This may be helpful in identifying which subjects with inherited retinal diseases benefit most from the

treatment and can be used to establish appropriate labeling for patient population identification.

3.

Please perform a correlation analysis of the final MLMT Scores in comparison to the Full-field light sensitivity threshold (FST) and Visual Acuity outcomes stratified by age groupings to establish whether or not there is an association between the psychophysical outcome measures and the functional vision performance achieved by the study subjects. We recommend a regression analysis and suggest a presentation as in the following table:

Correlation

Analysis

of

Final

MLMT

Scores

to

Psychophysical

Testing

By

Regression

Analyses

(Unsigned signature field (Click to sign)) Signature field is unsigned

Final FST Visual

MLMT Acuity

Score

= 10

years

of  
age age  
>10  
years  
of  
age

4.

Your study results report a large proportion of subjects as improved over baseline

relative to the scoring method you devised to demonstrate efficacy of voretigene

neparvovec;AAV2-hRPE65v2. We believe that it is important to understand the

profiles of study subjects who worsened and/or stayed the same after treatment.

Please provide a subanalysis of the subjects who did not improve their MLMT scores

(both accuracy and speed) and those whose scores were worse after treatment as

compared to before treatment. This analysis should include

stratifications by age,

disease, and baseline MLMT scores in tabular form as well as narrative discussion of

these analyses.

5.

Please provide a tabular analysis for each of the three efficacy studies you conducted

by showing the proportion of subjects whose MLMT lux scores improved by stratifying

the lux scores at baseline by the lux scores achieved after treatment across the

assessment time intervals in your approved protocol. This should be done according

to the age strata that you used in your enrollment. We suggest a table such as the

following:

Baseline 1 lux 4 lux 10 lux 50 lux 125 lux 250 lux 400 lux

1 lux N (%) N (%)

4 lux N (%) N (%)

10 lux N (%) N (%)

50 lux N (%) N (%)

125 lux N (%) N (%)

250 lux N (%) N (%)

400 lux N (%) N (%)

Thanks and please acknowledge receipt of this email request once received.

Nevitt

Nevitt  
Morris

Nevitt  
Morris,  
RN,  
BSN,  
BS  
Consumer  
Safety  
Officer  
Office  
of  
Tissues  
and  
Advanced  
Therapies  
Center  
for  
Biologics  
Evaluation  
and  
Research  
(CBER)

U.S.  
Food  
and  
Drug  
Administration  
Building  
71,  
Room  
4207  
10903  
New  
Hampshire  
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