Cellular, Tissue, and Gene Therapies Advisory Committee (CTGTAC) Meeting

October 12, 2017

***Errata* - FDA Briefing Document**

1. Page 14, Section 4.2.1, in the second sentence of the second paragraph, change: "The injection interval between the two eyes of each subject varied from **7 days to 21 days (14 ± 7 days).**"

   to

   "The injection interval between the two eyes of each subject varied from **6 days to 18 days (12 ± 6 days).**"

2. Page 19, Section 4.2.6, in the second sentence of the first paragraph, change: "Subjects who entered into the trial, who could not complete the course at the highest level of luminance > 400 lux, did not successfully complete the course at subsequent visits, regardless of treatment course."

   to

   "Subjects who entered into the trial, who could not complete the course at the highest level of luminance **of** 400 lux, did not successfully complete the course at subsequent visits, regardless of treatment course."

3. Page 24, Section 5.3, in the second sentence of the first paragraph, change: "The injection interval between the two eyes of each subject varied from **7 days to 21 days (14 ± 7 days)**"

   to

   "The injection interval between the two eyes of each subject varied from **6 days to 18 days (12 ± 6 days).**"

4. Page 28, Section 5.5, in the first sentence of the fifth paragraph, change: "Among the 11 subjects who had a 2-level or more score change in MLMT using both-treated eyes, a VA improvement of LogMAR 0.3 occurred in seven (7) subjects in the first-treated eye and **three (3)** subjects in the second-treated eye."

   to

   "Among the 11 subjects who had a 2-level or more score change in MLMT using both-treated eyes, a VA improvement of LogMAR 0.3 occurred in seven (7) subjects in the first-treated eye and **four (4)** subjects in the second-treated eye."

5. Page 32, Section 6.2.1, Table 1, change: "**11 (14%)**" in row 5: column 3

Ocular AEs	Subjects (n=41)	Treated Eyes (n=81)
Any ocular AE	30 (73%)	51 (63%)
Conjunctival hyperemia	9 (22%)	9 (11%)
Intraocular pressure (IOP) increased	8 (20%)	10 (12%)
Cataract development*	7 (17%)	**11 (14%)**
Retinal tear	4 (10%)	4 (5%)
Eye pain	4 (10%)	4 (5%)
Corneal dellen	3 (7%)	3 (4%)
Eye Inflammation	3 (7%)	5 (6%)
Subretinal deposits	3 (7%)	3 (4%)
Endophthalmitis	1 (2%)	1 (1%)
Eye irritation	3 (7%)	3 (4%)
Macular hole	3 (7%)	3 (4%)
Maculopathy (including macular pucker)	2 (5%)	3 (4%)
Foveal thinning and loss of foveal function	1 (2%)	2 (2%)
Retinal hemorrhage	1 (2%)	1 (1%)
Fovea dehiscence	1 (2%)	1 (1%)

*Cataract development includes both extracted and unextracted cataracts

to **"12 (15%)"**

Ocular AEs	Subjects (n=41)	Treated Eyes (n=81)
Any ocular AE	30 (73%)	51 (63%)
Conjunctival hyperemia	9 (22%)	9 (11%)
Intraocular pressure (IOP) increased	8 (20%)	10 (12%)
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Eye irritation	3 (7%)	3 (4%)
Macular hole	3 (7%)	3 (4%)
Maculopathy (including macular pucker)	2 (5%)	3 (4%)
Foveal thinning and loss of foveal function	1 (2%)	2 (2%)
Retinal hemorrhage	1 (2%)	1 (1%)
Fovea dehiscence	1 (2%)	1 (1%)

6. Page 32 Section 6.2.1, in the first sentence of the second paragraph, change: "Cataract: Among the 81 eyes that received voretigene neparvovec, **eleven (11) eyes (14%)** of seven (7) subjects had documented progression of existing cataract or formation of new cataract."

to

"Cataract: Among the 81 eyes that received voretigene neparvovec, **twelve (12) eyes (15%)** of seven (7) subjects had documented progression of existing cataract or formation of new cataract."

7. Page 33, Section 6.2.2, Table 2, change "cataract extracted at **Day 189**" in row 2: column 4 and "Foveal thinning in both eyes at Days 30 & 90 (**left: 157 to 70; right: 256 to 102**)**"** in row 3: column 4.

Table 13 Serious Adverse Events (SAEs)

Subject	Age, gender	Study	Events	Outcome
1	21 year old, male	102*	• Endophthalmitis at Week 4; vitreous culture positive for Staphylococcus epidermidis, treated with anti-infective drugs and periocular steroids • Elevated IOP between Days 90 - 180 due to periocular steroids • Optic nerve cupping right eye on Day 172; trabeculectomy done • Cataract following trabeculectomy; cataract extracted at **Day 189**	Irreversible optic atrophy due to sustained increased IOP
2	19-year old, female	302**	• Bleb elevated the fovea in both eyes • Decreased central vision at Day 30 • Foveal thinning in both eyes at Days 30 & 90 **(left: 157 to 70; right: 256 to 102)** • Visual acuity continues to drop from Day 30 to Day 90 • Improved retinal sensitivity • No recovery of central vision at Year 1	Permanent loss of central vision in the right eye from 20/150 at baseline down to 20/320

to

"cataract extracted at **Day 543",** and **"**Foveal thinning in both eyes at Days 30 & 90 **(left: 157 to 71; right: 154 to 100)"**

Table 13 Serious Adverse Events (SAEs)

Subject	Age, gender	Study	Events	Outcome
1	21 year old, male	102*	• Endophthalmitis at Week 4; vitreous culture positive for Staphylococcus epidermidis, treated with anti-infective drugs and periocular steroids • Elevated IOP between Days 90 - 180 due to periocular steroids • Optic nerve cupping right eye on Day 172; trabeculectomy done • Cataract following trabeculectomy; cataract extracted at **Day 543**	Irreversible optic atrophy due to sustained increased IOP
2	19-year old, female	302**	• Bleb elevated the fovea in both eyes • Decreased central vision at Day 30 • Foveal thinning in both eyes at Days 30 & 90 **(left: 157 to 71; right: 154 to 100)** • Visual acuity continues to drop from Day 30 to Day 90 • Improved retinal sensitivity • No recovery of central vision at Year 1	Permanent loss of central vision in the right eye from 20/150 at baseline down to 20/320