

**Supplemental Table 3: All study eye adverse events up to 200 days post-dose, with outcomes, and early-onset adverse events, by treatment group**

Preferred term	All adverse events		Unresolved		Onset within 7 days after dosing	
	Control n of 330 (%) <sup>a</sup>	Ocriplasmin n of 737 (%) <sup>b</sup>	Control n of 330 (%) <sup>a</sup>	Ocriplasmin n of 737 (%) <sup>b</sup>	Control n of 330 (%) <sup>a</sup>	Ocriplasmin n of 737 (%) <sup>b</sup>
Vitreous floaters	21 (6.4)	145 (19.7)	12 (3.6)	108 (14.7)	5 (1.5)	115 (15.6)
Conjunctival haemorrhage	33 (10.0)	106 (14.4)	33 (10.0)	106 (14.4)	22 (6.7)	96 (13.0)
Photopsia	9 (2.7)	100 (13.6)	7 (2.1)	95 (12.9)	5 (1.5)	88 (11.9)
Eye pain	18 (5.5)	95 (12.9)	17 (5.2)	91 (12.3)	7 (2.1)	72 (9.8)
Vision blurred	8 (2.4)	64 (8.7)	6 (1.8)	47 (6.4)	2 (0.6)	48 (6.5)
Visual impairment	6 (1.8)	54 (7.3)	3 (0.9)	45 (6.1)		41 (5.6)
Macular hole progression	18 (18.4)	50 (25.0)	14 (14.3)	38 (19.0)		17 (8.5)
Visual acuity reduced	23 (7.0)	46 (6.2)	10 (3.0)	35 (4.7)		28 (3.8)
Colour vision tests abnormal	9 (2.7)	40 (5.4)	7 (2.1)	34 (4.6)	1 (0.3)	22 (3.0)
Anterior chamber cell	9 (2.7)	38 (5.2)	8 (2.4)	36 (4.9)	1 (0.3)	24 (3.3)
Photophobia		37 (5.0)		37 (5.0)		34 (4.6)
Intraocular pressure increased	21 (6.4)	35 (4.7)	19 (5.8)	30 (4.1)	3 (0.9)	12 (1.6)
Conjunctival hyperaemia	5 (1.5)	26 (3.5)	5 (1.5)	25 (3.4)	4 (1.2)	20 (2.7)
Retinal oedema	3 (0.9)	25 (3.4)		17 (2.3)		17 (2.3)
Metamorphopsia	4 (1.2)	24 (3.3)	2 (0.6)	17 (2.3)		15 (2.0)
Ophthalmological examination abnormal	11 (3.3)	23 (3.1)	6 (1.8)	19 (2.6)	2 (0.6)	7 (0.9)
Ocular discomfort	4 (1.2)	22 (3.0)	4 (1.2)	21 (2.8)	4 (1.2)	15 (2.0)
Retinal haemorrhage	6 (1.8)	21 (2.8)	4 (1.2)	14 (1.9)		4 (0.5)
Cataract	12 (3.6)	20 (2.7)	6 (1.8)	6 (0.8)	1 (0.3)	1 (0.1)
Cataract nuclear	6 (1.8)	19 (2.6)	3 (0.9)	9 (1.2)		1 (0.1)
Iritis		19 (2.6)		16 (2.2)		12 (1.6)
Macular oedema	3 (0.9)	19 (2.6)	1 (0.3)	9 (1.2)		3 (0.4)
Chromatopsia	2 (0.6)	18 (2.4)	2 (0.6)	16 (2.2)	1 (0.3)	12 (1.6)
Foreign body sensation in eyes	8 (2.4)	17 (2.3)	8 (2.4)	16 (2.2)	7 (2.1)	11 (1.5)
Punctate keratitis	3 (0.9)	17 (2.3)	2 (0.6)	16 (2.2)	2 (0.6)	12 (1.6)
Lacrimation increased	4 (1.2)	16 (2.2)	3 (0.9)	15 (2.0)	2 (0.6)	9 (1.2)
New macular hole	10 (4.3)	16 (3.0)	7 (3.0)	8 (1.5)		2 (0.4)
Dry eye	5 (1.5)	14 (1.9)	2 (0.6)	4 (0.5)	1 (0.3)	4 (0.5)
Retinal detachment	4 (1.2)	14 (1.9)	3 (0.9)	10 (1.4)		10 (1.4)
Subretinal fluid	1 (0.3)	14 (1.9)	1 (0.3)	12 (1.6)	1 (0.3)	6 (0.8)
Blepharitis	2 (0.6)	13 (1.8)		8 (1.1)		2 (0.3)
Corneal disorder	3 (0.9)	13 (1.8)	3 (0.9)	11 (1.5)		10 (1.4)
Eyelid oedema	2 (0.6)	13 (1.8)	2 (0.6)	13 (1.8)		7 (0.9)
Maculopathy	4 (1.2)	13 (1.8)		5 (0.7)		
Vitreous detachment	2 (0.6)	13 (1.8)	1 (0.3)	3 (0.4)		7 (0.9)
Retinal tear	10 (3.0)	12 (1.6)	9 (2.7)	10 (1.4)	1 (0.3)	2 (0.3)
Conjunctival oedema	6 (1.8)	11 (1.5)	6 (1.8)	11 (1.5)	4 (1.2)	9 (1.2)
Eye irritation	7 (2.1)	11 (1.5)	6 (1.8)	10 (1.4)	7 (2.1)	8 (1.1)
Eye pruritus	3 (0.9)	11 (1.5)	3 (0.9)	10 (1.4)	1 (0.3)	4 (0.5)
Macular fibrosis	1 (0.3)	11 (1.5)		1 (0.1)		1 (0.1)
Retinal pigment epitheliopathy	1 (0.3)	10 (1.4)	1 (0.3)	1 (0.1)		1 (0.1)
Visual field defect	3 (0.9)	10 (1.4)	2 (0.6)	9 (1.2)		6 (0.8)
Anterior chamber flare	2 (0.6)	9 (1.2)	2 (0.6)	9 (1.2)	1 (0.3)	8 (1.1)
Retinal degeneration	2 (0.6)	9 (1.2)		1 (0.1)		
Anterior chamber inflammation	1 (0.3)	8 (1.1)	1 (0.3)	8 (1.1)		5 (0.7)
Cataract subcapsular	1 (0.3)	8 (1.1)	1 (0.3)	4 (0.5)		1 (0.1)

Preferred term	All adverse events		Unresolved		Onset within 7 days after dosing	
	Control n of 330 (%) <sup>a</sup>	Ocriplasmin n of 737 (%) <sup>b</sup>	Control n of 330 (%) <sup>a</sup>	Ocriplasmin n of 737 (%) <sup>b</sup>	Control n of 330 (%) <sup>a</sup>	Ocriplasmin n of 737 (%) <sup>b</sup>
Vitreous floaters	21 (6.4)	145 (19.7)	12 (3.6)	108 (14.7)	5 (1.5)	115 (15.6)
Conjunctival bleb	2 (0.6)	8 (1.1)	2 (0.6)	8 (1.1)	2 (0.6)	8 (1.1)
Conjunctivitis	1 (0.3)	8 (1.1)	1 (0.3)	7 (0.9)		4 (0.5)
Corneal oedema	1 (0.3)	8 (1.1)	1 (0.3)	8 (1.1)		4 (0.5)
Macular degeneration	2 (0.6)	8 (1.1)				
Ocular hyperaemia	1 (0.3)	8 (1.1)	1 (0.3)	6 (0.8)	1 (0.3)	6 (0.8)
Macular cyst	4 (1.2)	7 (0.9)	2 (0.6)	4 (0.5)	1 (0.3)	1 (0.1)
Posterior capsule opacification	5 (1.5)	7 (0.9)	2 (0.6)	2 (0.3)		
Vitreous adhesions	6 (1.8)	7 (0.9)	3 (0.9)	5 (0.7)	1 (0.3)	1 (0.1)
Vitreous haemorrhage	2 (0.6)	7 (0.9)	2 (0.6)	5 (0.7)	1 (0.3)	1 (0.1)
Colour blindness acquired		6 (0.8)		4 (0.5)		5 (0.7)
Colour blindness		5 (0.7)		5 (0.7)		5 (0.7)
Conjunctivitis allergic	1 (0.3)	5 (0.7)	1 (0.3)	3 (0.4)		1 (0.1)
Corneal abrasion		5 (0.7)		5 (0.7)		4 (0.5)
Detachment of retinal pigment epithelium	1 (0.3)	5 (0.7)		3 (0.4)		
Diplopia	2 (0.6)	5 (0.7)	1 (0.3)	2 (0.3)		
Keratitis	2 (0.6)	5 (0.7)	2 (0.6)	5 (0.7)	2 (0.6)	5 (0.7)
Miosis		5 (0.7)		4 (0.5)		5 (0.7)
Pupillary reflex impaired	1 (0.3)	5 (0.7)	1 (0.3)	5 (0.7)		4 (0.5)
Scotoma		5 (0.7)		1 (0.1)		2 (0.3)
Vitritis		5 (0.7)		5 (0.7)		4 (0.5)
Conjunctival irritation		4 (0.5)		4 (0.5)		3 (0.4)
Eye inflammation		4 (0.5)		4 (0.5)		2 (0.3)
Macular reflex abnormal	1 (0.3)	4 (0.5)	1 (0.3)	1 (0.1)		2 (0.3)
Ocular hypertension		4 (0.5)		4 (0.5)		1 (0.1)
Visual acuity tests abnormal	2 (0.6)	4 (0.5)		2 (0.3)		
Xanthopsia		4 (0.5)		3 (0.4)		3 (0.4)
Cataract cortical	6 (1.8)	3 (0.4)	2 (0.6)			
Corneal erosion	3 (0.9)	3 (0.4)	3 (0.9)	3 (0.4)	1 (0.3)	2 (0.3)
Corneal striae		3 (0.4)		2 (0.3)		2 (0.3)
Eye discharge	1 (0.3)	3 (0.4)		3 (0.4)	1 (0.3)	
Hyphaema	1 (0.3)	3 (0.4)	1 (0.3)	3 (0.4)		1 (0.1)
Iridocyclitis		3 (0.4)		3 (0.4)		1 (0.1)
Lenticular opacities	1 (0.3)	3 (0.4)		1 (0.1)		
Night blindness		3 (0.4)		2 (0.3)		2 (0.3)
Pupils unequal		3 (0.4)		2 (0.3)		2 (0.3)
Retinal deposits		3 (0.4)		1 (0.1)		
Retinal vascular disorder		3 (0.4)		1 (0.1)		1 (0.1)
Vitreous disorder		3 (0.4)		1 (0.1)		1 (0.1)
Vitreous opacities	3 (0.9)	3 (0.4)		2 (0.3)	1 (0.3)	1 (0.1)
Accommodation disorder		2 (0.3)		2 (0.3)		2 (0.3)
Anterior chamber pigmentation		2 (0.3)		1 (0.1)		
Asthenopia		2 (0.3)				
Blindness transient		2 (0.3)		2 (0.3)		2 (0.3)
Corneal epithelium defect		2 (0.3)		1 (0.1)		
Corneal opacity		2 (0.3)		1 (0.1)		1 (0.1)
Cystoid macular oedema	2 (0.6)	2 (0.3)	2 (0.6)	1 (0.1)		
Diabetic retinopathy		2 (0.3)				
Eye allergy		2 (0.3)				

Preferred term	All adverse events		Unresolved		Onset within 7 days after dosing	
	Control n of 330 (%) <sup>a</sup>	Ocriplasmin n of 737 (%) <sup>b</sup>	Control n of 330 (%) <sup>a</sup>	Ocriplasmin n of 737 (%) <sup>b</sup>	Control n of 330 (%) <sup>a</sup>	Ocriplasmin n of 737 (%) <sup>b</sup>
Vitreous floaters	21 (6.4)	145 (19.7)	12 (3.6)	108 (14.7)	5 (1.5)	115 (15.6)
Iris adhesions	1 (0.3)	2 (0.3)		1 (0.1)		1 (0.1)
Macular pseudohole	2 (0.6)	2 (0.3)		1 (0.1)		
Periorbital haematoma	1 (0.3)	2 (0.3)	1 (0.3)	2 (0.3)	1 (0.3)	
Photosensitivity reaction		2 (0.3)		2 (0.3)		2 (0.3)
Posterior capsule rupture		2 (0.3)		2 (0.3)		
Retinal disorder	1 (0.3)	2 (0.3)	1 (0.3)	1 (0.1)		
Retinal neovascularisation		2 (0.3)		1 (0.1)		
Retinogram abnormal		2 (0.3)		2 (0.3)		1 (0.1)
Sicca syndrome		2 (0.3)		1 (0.1)		1 (0.1)
Visual acuity reduced transiently		2 (0.3)		2 (0.3)		2 (0.3)
Abnormal sensation in eye	1 (0.3)	1 (0.1)	1 (0.3)	1 (0.1)	1 (0.3)	1 (0.1)
Adenoviral conjunctivitis		1 (0.1)		1 (0.1)		
Angle closure glaucoma		1 (0.1)		1 (0.1)		
Anisometropia		1 (0.1)				
Blepharospasm		1 (0.1)		1 (0.1)		1 (0.1)
Borderline glaucoma		1 (0.1)				
Chalazion	1 (0.3)	1 (0.1)	1 (0.3)			
Choroidal detachment	1 (0.3)	1 (0.1)	1 (0.3)	1 (0.1)		
Choroidal dystrophy		1 (0.1)				
Choroidal neovascularisation		1 (0.1)				
Ciliary hyperaemia		1 (0.1)		1 (0.1)		1 (0.1)
Ciliary muscle spasm		1 (0.1)		1 (0.1)		1 (0.1)
Corneal deposits	2 (0.6)	1 (0.1)	2 (0.6)	1 (0.1)		
Corneal dystrophy	1 (0.3)	1 (0.1)				1 (0.1)
Corneal exfoliation		1 (0.1)		1 (0.1)		1 (0.1)
Diabetic retinal oedema		1 (0.1)				
Episcleritis		1 (0.1)		1 (0.1)		1 (0.1)
Eye disorder		1 (0.1)				
Eye infection		1 (0.1)		1 (0.1)		1 (0.1)
Eyelid pain		1 (0.1)				
Eyelid ptosis	2 (0.6)	1 (0.1)	1 (0.3)			
Flat anterior chamber of eye	1 (0.3)	1 (0.1)	1 (0.3)	1 (0.1)		1 (0.1)
Foreign body in eye	1 (0.3)	1 (0.1)	1 (0.3)	1 (0.1)	1 (0.3)	1 (0.1)
Glaucoma	1 (0.3)	1 (0.1)				
Glaucomatous optic disc atrophy		1 (0.1)				1 (0.1)
Halo vision		1 (0.1)				
Hordeolum		1 (0.1)		1 (0.1)		
Injection site pain		1 (0.1)		1 (0.1)		1 (0.1)
Keratitis herpetic		1 (0.1)				
Keratoconjunctivitis sicca		1 (0.1)				
Lacrimal disorder		1 (0.1)				
Lacrimation decreased	1 (0.3)	1 (0.1)		1 (0.1)	1 (0.3)	1 (0.1)
Lens dislocation		1 (0.1)				
Lenticular pigmentation		1 (0.1)		1 (0.1)		
Loss of visual contrast sensitivity		1 (0.1)				1 (0.1)
Migraine		1 (0.1)		1 (0.1)		
Narrow anterior chamber angle		1 (0.1)		1 (0.1)		
Ocular vascular disorder		1 (0.1)				

Preferred term	All adverse events		Unresolved		Onset within 7 days after dosing	
	Control n of 330 (%) <sup>a</sup>	Ocriplasmin n of 737 (%) <sup>b</sup>	Control n of 330 (%) <sup>a</sup>	Ocriplasmin n of 737 (%) <sup>b</sup>	Control n of 330 (%) <sup>a</sup>	Ocriplasmin n of 737 (%) <sup>b</sup>
Vitreous floaters	21 (6.4)	145 (19.7)	12 (3.6)	108 (14.7)	5 (1.5)	115 (15.6)
Open angle glaucoma		1 (0.1)		1 (0.1)		
Optic nerve cup/disc ratio increased		1 (0.1)				
Pain		1 (0.1)		1 (0.1)		
Periorbital contusion		1 (0.1)		1 (0.1)		1 (0.1)
Pterygium		1 (0.1)		1 (0.1)		
Retinal aneurysm		1 (0.1)				
Retinal artery embolism		1 (0.1)				
Retinal artery occlusion		1 (0.1)		1 (0.1)		1 (0.1)
Retinal artery stenosis		1 (0.1)				
Retinal injury	2 (0.6)	1 (0.1)	2 (0.6)			
Retinal ischaemia		1 (0.1)		1 (0.1)		1 (0.1)
Retinal neoplasm		1 (0.1)				
Retinal pigment epithelial tear		1 (0.1)				
Retinal toxicity		1 (0.1)				1 (0.1)
Retinal vasculitis		1 (0.1)		1 (0.1)		
Retinopathy of prematurity		1 (0.1)				
Retinopathy proliferative		1 (0.1)		1 (0.1)		1 (0.1)
Retinoschisis		1 (0.1)		1 (0.1)		1 (0.1)
Scintillating scotoma		1 (0.1)		1 (0.1)		1 (0.1)
Synchysis scintillans	1 (0.3)	1 (0.1)	1 (0.3)	1 (0.1)		
Trichiasis		1 (0.1)				
Uveitis		1 (0.1)		1 (0.1)		
Visual brightness		1 (0.1)				1 (0.1)
Visual field tests abnormal		1 (0.1)				
Vitreous cells		1 (0.1)				
Vitreous degeneration		1 (0.1)				1 (0.1)
Anterior chamber fibrin	1 (0.3)		1 (0.3)			
Conjunctivitis viral	1 (0.3)		1 (0.3)			
Corneal scar	1 (0.3)					
Cutis laxa	1 (0.3)					
Ecchymosis	1 (0.3)		1 (0.3)			
Endophthalmitis	1 (0.3)		1 (0.3)			
Eyelids pruritus	1 (0.3)		1 (0.3)			
Haemorrhage subcutaneous	1 (0.3)		1 (0.3)		1 (0.3)	
Hippus	1 (0.3)		1 (0.3)			
Optic nerve sheath haemorrhage	1 (0.3)		1 (0.3)			
Papilloedema	1 (0.3)		1 (0.3)			

<sup>a</sup>Control group denominator is 98 for macular hole progression and 232 for new macular hole.

<sup>b</sup>Ocriplasmin denominator is 200 for macular hole progression and 537 for new macular hole.