EG-Mirotin: *First-in-Class* recombinant polypeptide novel subcutaneous drug containing RGD-motif targeted to suppress edema and vascular leakage for Non-proliferative Diabetic Retinopathy (NPDR)

EyeGene Inc.

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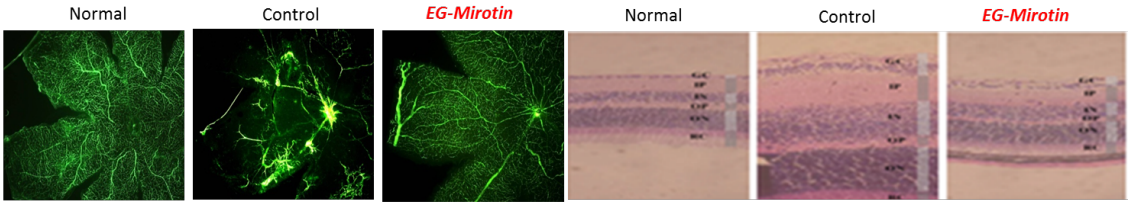
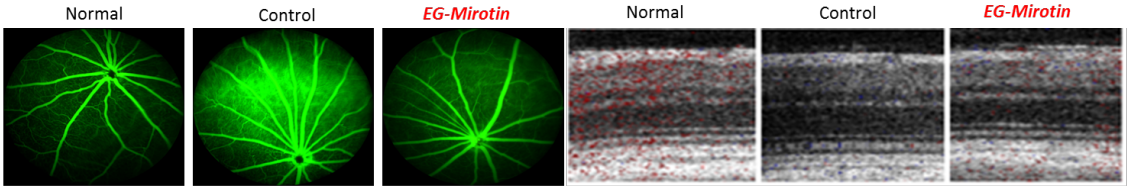
Industry Sector	Biotechnology
Therapeutic Area	Other therapeutic
Stage of Development	Phase II

1. Summary

- ***EG-Mirotin*** is a RGD-motif containing human recombinant polypeptide (compound name: EGT022 / 58 amino acids / MW: 6.1-kDa).
- ***First in Class*** novel **subcutaneous** drug targeted to suppress edema and vascular leakage in abnormal retinal microvasculature through that normalization and stabilization of damaged retinal microvasculature.
- Pre-clinical toxicity studies were successfully completed both in-house and in Europe (Switzerland) with no signs of toxicity and/or genotoxicity. Additional studies confirmed there were no undesirable angiogenesis and effects on tumor growth. Pre-clinical efficacy studies were conducted in both the Oxygen-Induced Retinopathy model and Streptozotocin-induced diabetic rat model. Retinal flat mount and angiography results have demonstrated formation of stabilized and mature retinal vasculature, and Optical Coherence Tomography (OCT) measurements have shown a statistically significant reduction in macular edema.



Retinal Flat Mount and OCT images from Oxygen Induced Retinopathy model (Source: EyeGene, Korea)

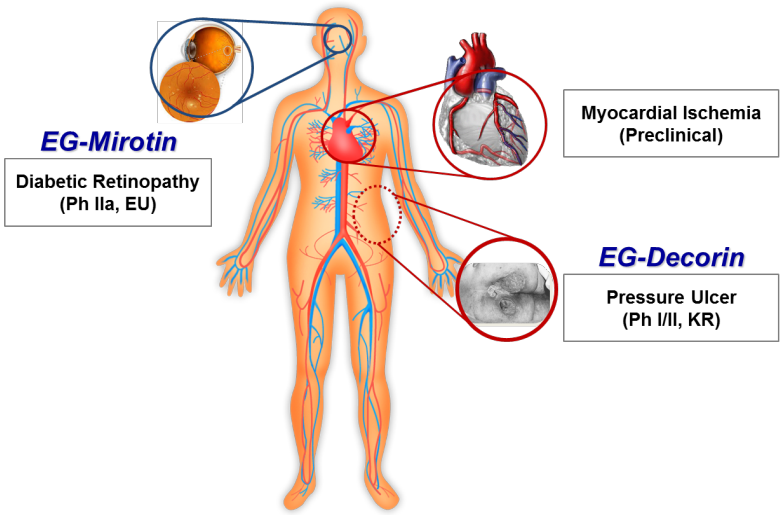


Fundus fluorescein angiography and OCT images from Streptozotocin-induced diabetic rat model (Source: Comparative BioSciences, USA)

- Phase I safety studies conducted in Europe (Netherlands) was successful. Treatment with EG-Mirotin in single and multiple doses was well tolerated in all subjects (both healthy and diabetic patients).
- Phase IIa proof-of-concept studies are currently being conducted in Europe (France).

2. Applications

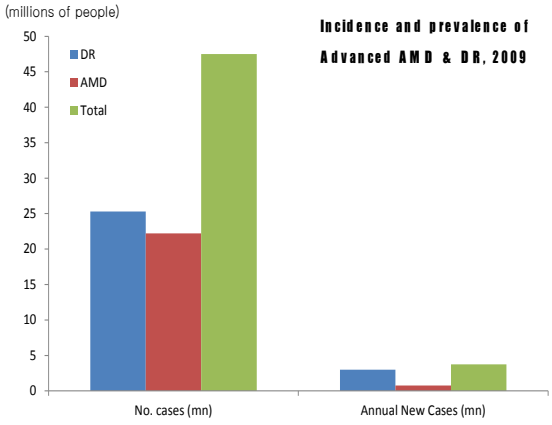
- EGT022 and its potential applications



3. Market Feasibility

Incidence and prevalence of Diabetic Retinopathy (Global)

- Recent studies have shown that there were approximately 220 million people with diabetes globally (either diagnosed or undiagnosed) in 2009; Latest WHO statistics have this figure at 347 million as of 2012
- Current prevalence of DR – both NPDR and PDR – is over 100 million worldwide
- 74.7mn estimated with early stage DR symptoms or NPDR



(Source: Visiongain 2010)

4. Type of Business Relationship Sought (include licensing availability)

- Available for out-licensing
- Seeking co-development, Strategic partnerships

5. Technical Advantages

- Laser Photocoagulation has been widely used to treat eye diseases, but only covers Proliferative Diabetic Retinopathy and Age-related Macular Degeneration. Drugs such as anti-VEGF and steroids are available, but vary in efficacy/side effects, and are usually for late-stage Diabetic Retinopathy.
- *First in Class* novel subcutaneous therapeutic for Non-proliferative Diabetic Retinopathy that is competitive in terms of both *route of administration* and *cost* versus current alternate treatments.

6. Technical Highlighted Summary

- Novel sub-cutaneous therapeutic for Diabetic Retinopathy (Non-proliferative Diabetic Retinopathy / NPDR)
- Targeted to suppress edema and vascular leakage in abnormal capillaries in NPDR patients

EG-Mirotin vs. marketed drugs

Company Name	EyeGene	Roche	Regeneron
Product Name	EG-Mirotin	Lucentis	Eylea
Compound	EGT022 (recombinant polypeptide)	Ranibizumab (monoclonal antibody)	Aflibercept (recombinant fusion protein)
Mechanism	Normalization and stabilization of retinal vasculature	Anti-VEGF preventing retinal neovascularization	VEGF-trap preventing retinal neovascularization
Indication	NPDR, DR, DME	wAMD, DME, RVO	wAMD, DME, RVO
Manufacturing	*Pichia pastoris*	*E. coli*	CHO K1
Route of Administration	Subcutaneous Injection (non-invasive)	Intravitreal Injection (invasive)	Intravitreal Injection (invasive)
Dosage	1mg or 2mg	wAMD : 0.5mg DME : 0.3mg	wAMD : 2.0mg DME : 2.0mg
Dosing Regimen	5 daily subcutaneous injections	Once a month (every 28 days)	Once a month (every 4 weeks)
Side Effects	general disorders and administration site conditions, NO systemic side effect reported in Phase 1 safety studies	conjunctival hemorrhage, eye pain, vitreous floaters, increased intraocular pressure, and intraocular inflammation	conjunctival hemorrhage, eye pain, cataract, vitreous detachment, floaters, and ocular hypertension

Treatment Cost	Approximately 50% of marketed products	$2,000 per injection	$1,850 per injection

7. Mechanism (MOA)

EG-Mirotin, a human recombinant protein, stabilizes and normalizes abnormal and partially damaged blood vessels. The mechanistic action of EG-Mirotin not only treats the fundamental symptoms of early stage diabetic retinopathy, it is also able to prevent the progression to the latter severe proliferative stages of diabetic retinopathy.

- Active Pharmaceutical Ingredient: EGT022
- Derived from human metalloprotease ADAM15
- Structure
  - Human-origin RGD motif-containing recombinant protein; size of 6.1kDa consisting of 58 amino acids
  - Stable protein for long period storage
  - Production by yeast expression system - easy mass production

8. Patent Information and Status

EyeGene has more than 45 issued and 24 pending patents globally including US, EU, Japan and China. EyeGene secured comprehensive intellectual property for a new mechanism of EGT022.

9. Patent Number(s)

Title	Country	Patent Application No.	Original Assignee	Filing Date	Inventors
PHARMACEUTICAL COMPOSITION FOR TREATING VASCULAR-RELATED DISEASES COMPRISING PEPTIDE	PCT	PCT/KR2007/000330	EyeGene Inc. et al.	2007.01.19	Yang-Je Cho et al.
	Korea	10-2008-7020099		2008.08.14	
		10-2011-7010863		2011.05.13	
	US	14/044,692		2008.07.14	
	EU	10163446.7		2010.05.20	
	Japan	2008-551191 (Original application)		2008.07.16	
		2012-118360 (Divisional application)		2012.05.24	
	China	201110235661.9		2011.08.10	

10. Key Words

Diabetes, Diabetic Retinopathy, DR, Non-Proliferative Diabetic Retinopathy, NPDR, Diabetic Macular Edema, DME, EG-Mirotin, EGT022, Recombinant Protein, Recombinant Polypeptide, Blindness, Diabetic Complication, Retinal Neovascularization, Retinal ischemia, Retinopathy of Prematurity, RGD motif

11. Company Description

EyeGene Inc. is clinical stage proteomics & bio-pharmaceutical venture based in South Korea dedicated to developing therapeutics, diagnostics, and technologies in eye-related diseases & vaccines.

Since incorporation in 2000, we have focused on the development of new therapeutics and diagnostics for eye-related diseases such as Diabetic Retinopathy (DR) and Retinopathy of Prematurity (ROP). In this respect, we currently have a First in Class novel candidate for Non-Proliferative Diabetic Retinopathy in European Phase 2a clinical trials. In addition, we have a pool of vaccines under development with our novel proprietary immune adjuvant, of which our HPV vaccine is currently in clinical trials