

# **SHAPERON Inc.**

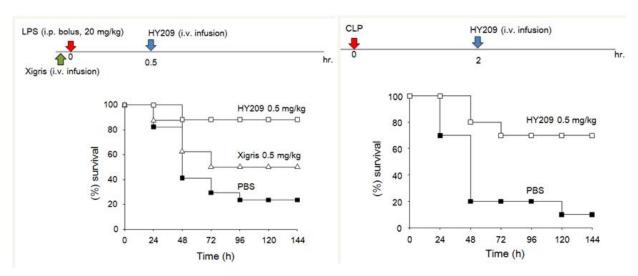


#### 1) Key Technology Highlights

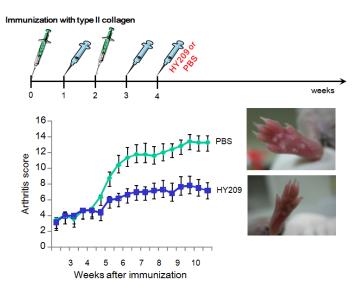
Anti-inflammation (GPCR131 agonist): Based on the novel theory we suggested in 2004 on Nature Reviews Immunology, we identified a novel compound (HY209) that can ameliorate inflammatory diseases such as sepsis, collagen-induced arthritis and atopic dermatitis. It activates GPCR131 pathway inducing Myeloid-derived suppressor cells and regulatory B cells that can suppress inflammatory responses. Because HY209 increases myeloid-derived suppressor cells and regulatory B cells in vivo, the indication might be expanded to various inflammatory diseases like Alzheimer's disease.

#### 2) Technology Overview

**Anti-inflammatory compound (GPCR131 agonist).** Since 2005, we have received \$1.5 million from Korea's Ministry of Education Science and Technology to develop a novel anti-inflammatory drug. We



identified HY209 with novel mode of actions. This compound is an agonist targeting G-protein coupled receptor 131. It contains sodium taurodeoxycholic acid (HY209) as an active ingredient for intravenous infusion. It inhibits NF-kB activation, proinflammatory cytokine production, NO production and



costimulatory molecule expression on inflammatory cells. The survival rate of septic mice increased when 0.25 mg/kg of this compound was infused intravenously once. HY209 shows a survival rate over 80% in experimental mouse sepsis models including LPS-injection model and Cecal-Ligation and Puncture model. The survival rate by HY209 is over 2 times better than Xigris<sup>TM</sup> (Eli Lilly), the only existing drug licensed for sepsis worldwide. Xigris<sup>TM</sup> is an activated protein C and has been approved by the FDA for patients with severe



sepsis. However, it was reported that Xigris<sup>TM</sup> shows increased

Control

DNCB

DNCB+HY209

28 day survival in 6% of patients and has side effects such as an severe risk of bleeding. HY209 increases myeloid derived suppressor cells and regulatory B cells after treatment in vivo. It suggests that HY209 might be applicable to various inflammatory diseases, such as atopic dermatitis, Alzheimer's disease, arteriosclerosis, rheumatoid arthritis and degenerative arthritis, based on our model suggested earlier in Nature Reviews Immunology (2004, 4(6), 469) and also based on our findings in mouse collagen-induced arthritis model and atopic dermatitis mouse model. When we evaluated the toxicity of HY209 after a single intravenous infusion, no significant systemic toxicity was observed under 300 mg/kg in rodents (effective dose = 0.5 mg/kg). Local thrombophlebitis at the injection site was observed in 60% of females when given 300 mg/kg. When given once every day for 28 days, no significant systemic toxicity was observed under 150 mg/kg, but local thrombophlebitis was observed in 50% of male and 60% of female mice over 20mg/kg. The significant toxicity in beagle dogs was observed over 300 x of effective dose given once and over 100x of effective dose when given daily for 28 days. We are seeking partners for clinical studies of HY209.

#### 3) The market

Section	2009yr	2010yr	2011yr(E)	
Overseas Market	Sales of Xigris(Eli Lil	\$ 4 billion*		
Domestic Market			\$ 20 M	

<sup>\* &</sup>lt;a href="http://www.researchandmarkets.com/reports/249867/global\_forecast\_market\_size">http://www.researchandmarkets.com/reports/249867/global\_forecast\_market\_size</a> for sepsis

#### 4) Competitive companies

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Company	Country	Developed title	Phase	A field of enterprise	Strengths & weaknesses	Compared with applied company(Superiority)
Eisai	Japan	Eritoran	Phase 3	Sepsis; Endotoxic shock	Immunomodulator; TLR-4 antagonist;LPS modulator	Impossible to control complement and coagulation.
AM- Pharma	Netherland	Alkaline phosphatase	Phase 2	Sepsis; Renal failure	Anti-inflammatory; LPS binding agent; Renal system agent	Not clear mode of action
Wyeth(Pfizer)	USA	ERB-257	Phase 1	Sepsis	Estrogen receptor beta agonist	Impossible to control complement and coagulation activation.
ChongKun Dang Pharm.	Korea	CKD-712	Phase 1	Sepsis; Cancer	NF-kappa B modulator; JAK- 2/STAT-1 modulator; HO- 1 modulator	Impossible to control complement and coagulation activation
Fibrex Medical	Germany	FX-06 analog	Preclinical	Sepsis	Leukocyte migration inhibitor Anti-inflammatory	Impossible to control complement and coagulation activation.



Atox Bio		AB-103	Preclinical	Septic shock; Endotoxic shock	LPS antagonist	Unknown mode of action
Wyeth(Pfizer)	USA	RAGE antibody	Preclinical	Sepsis	Advanced glycosylation product receptor agonist	Impossible to control TLR4 pathway, complement and coagulation activation.
Arpida	Swiss	CB-610	Preclinical	Sepsis	DPP I inhibitor	Impossible to control TLR4 pathway, complement and coagulation activation.
Seoul Pharma -Postech	Korea	-	Preclinical	Sepsis	Immunomodulator; Anti-inflammatory	Unknown mode of action
Huons - Sungkyunkwan University	Korea	-	Preclinical	Sepsis; Septic shock	_	Impossible to control TLR4 pathway, complement and coagulation activation.

### 5) Dotonto

No.	Title	Pat. #	Issue Date	Status
1	USE OF BIOLOGICAL SURFACTANT AS ANTI-INFLAMMATORY AGENT AND TISSUE PRESERVATIVE SOLUTION	Korea: 10-0785656	2007.12.07.	Registered
4	Recombinant Fusion protein for dendritic cell based cancer immunotherapy	Korea: 10-2009-0120104	2009.12.04	Pending
5	Anti-MUC1 single domain antibody	Korea: 10-2010-0013470	2010.02.12	Pending
6	USE OF BIOLOGICAL SURFACTANT AS ANTI-INFLAMMATORY AGENT AND TISSUE PRESERVATIVE SOLUTION	PCT/KR2008/002698	2008.05.14	Pending
7	USE OF BIOLOGICAL SURFACTANT AS ANTI-INFLAMMATORY AGENT AND TISSUE PRESERVATIVE SOLUTION	China:200880015680.7	2009.11.11	Pending
8	USE OF BIOLOGICAL SURFACTANT AS ANTI-INFLAMMATORY AGENT AND TISSUE PRESERVATIVE SOLUTION	Japan : 2JP-09092	2009.11.05	Pending
9	USE OF BIOLOGICAL SURFACTANT AS ANTI-INFLAMMATORY AGENT AND TISSUE PRESERVATIVE SOLUTION	USA : 12619644	2009.11.16	Pending
10	USE OF BIOLOGICAL SURFACTANT AS ANTI-INFLAMMATORY AGENT AND TISSUE PRESERVATIVE SOLUTION	EU : EP08753494.7	2009.11.26	Pending
11	USE OF BIOLOGICAL SURFACTANT AS ANTI-INFLAMMATORY AGENT AND TISSUE PRESERVATIVE SOLUTION	India: 4278/KOLNP/2009	2009.12.10	Pending

# 6) Proposal to Global Alliance

## COLLABORATION PROPOSAL

- 1. To develop GPCR131 agonist for overseas clinical development and worldwide marketing.
- 2. To co-develop GPCR131 agonist for various indications including rheumatoid arthritis, atopic dermatitis and Alzheimer's disease etc.

It might be investment, research collaboration or technology licensing.

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