Partnering Opportunity / HS-101 – rhHAPLN1

First-in-class Disease-Modifying Osteoarthritis Drug

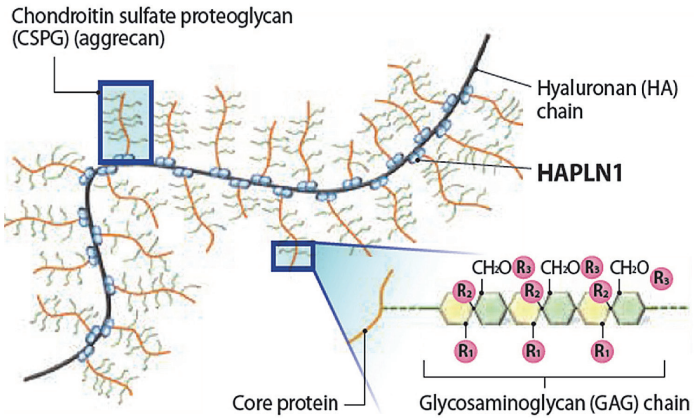
- **HS-101 has the potential to regenerate cartilage, improve ECM structure, restore joint homeostasis and reverse OA progression, as well as relieve symptoms.**
- **Cartilage repair has been successfully demonstrated in small and large animal models.**
- **Excellent preliminary safety and tox profile in early rodent studies. Large mammal studies are ongoing.**

Pharmacological and Structural MoA

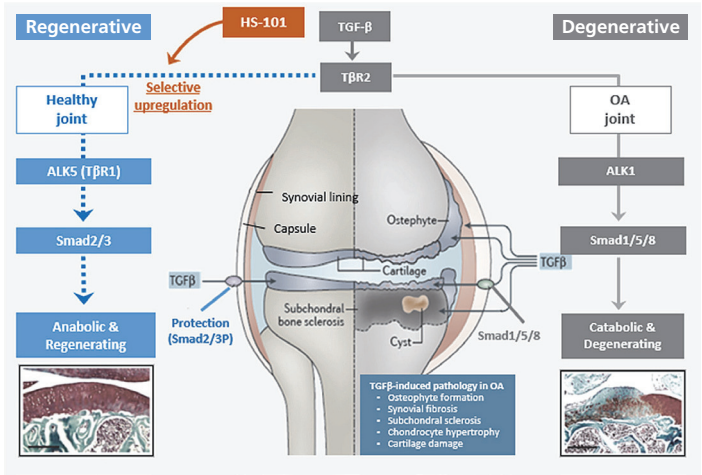
HS-101 (rhHapln1) is a recombinant form of the endogenous human Hyaluronan and Proteoglycan Link Protein 1 (HAPLN1) which is thought to be a potential rejuvenation factor for aging cells and relevant to multiple indications including Osteoarthritis.[1]

HAPLN1 is a hinge-like protein that structurally links aggrecan with hyaluronan in the cartilage ECM. The hyaluronan component binds with CD44 receptors on the cell surface, forming clusters in the pericellular matrix.

The concentration of HAPLN1 in fibroblasts of people aged >55 is 36x lower than in people aged <45.[2] Both the protein and mRNA forms of HAPLN1 are significantly reduced in the cartilage of OA patients receiving joint replacement surgery.[3]



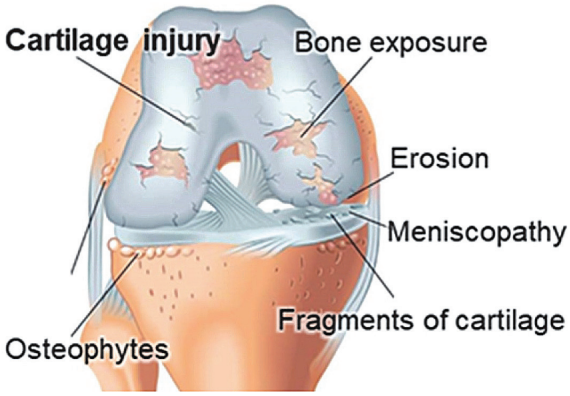
The TGFßR1 (ALK5)-Smad2/3 pathway is a key mechanism in cartilage regeneration and its homeostasis. Data from *in vitro* experiments indicate that HS-101 selectively upregulates TGFßR1, driving the equilibrium towards cartilage regeneration rather than cartilage destruction.



Modified from Van der Kraan (Nat Rev Rheumatol 2017)

High Unmet Need

OA affects approximately 300 million people worldwide, or 15% of the adult population.[4] This is expected to rise to over 350 million people by 2025. An annual cost burden of over 15 billion USD, alongside almost one million hospitalisations, highlights the urgent and pressing need for better treatment options. Unfortunately, options for OA patients are severely limited.

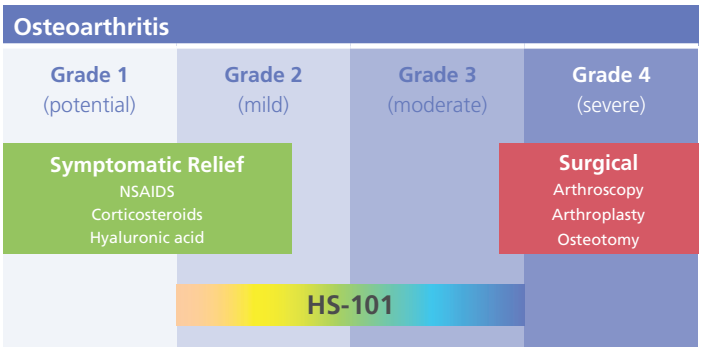


A Lack of Disease Modifying Therapies

- Currently, none of the pharmacotherapies available on the market provide disease-modifying effects. There exists a clear gap in options between current first-line therapies, which provide temporary symptom reduction (NSAIDs, steroids, hyaluronic acid & analgesics), and expensive, invasive surgical interventions.
- Consequently a significant unmet need exists for pre-surgical OA patients with mild to moderate OA (65% of all OA patients).

HS-101 Market Positioning

HS-101 will be positioned as a first-line therapy for patients with K&L grade 2-3 osteoarthritis, as an intra-articular injection. Based on its pre-clinical profile, HS-101 is expected to be a chronic treatment with initial recovery of joint homeostasis followed by maintenance doses at 2-3 monthly intervals.



1 European Spine Journal (2011) 20:4; 572-577. doi: 10.1007/s00586-010-1598-0

2 Cancer Discovery (2019) 9:1; 64-81. doi: 10.1158/2159-8290.CD-18-0193

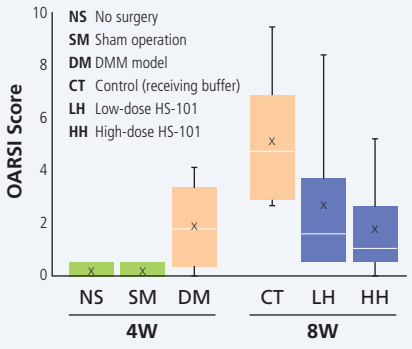
3 International Orthopaedics (2013) 37:10; 2051-2059. doi: 10.1007/s00264-013-1937-y

4 Centers for Disease Control. cdc.gov/arthritis/data_statistics/cost

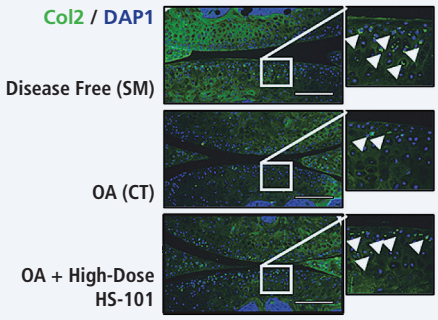
In-vivo Efficacy Data – Clear Improvement With Cartilage-Repairing Effects

Mouse Model Study

Study with destabilized medial meniscus (DMM) mouse model showed a significant dose-dependent improvement in OARSI score when treated with HS-101 via intra-articular (IA) injection.

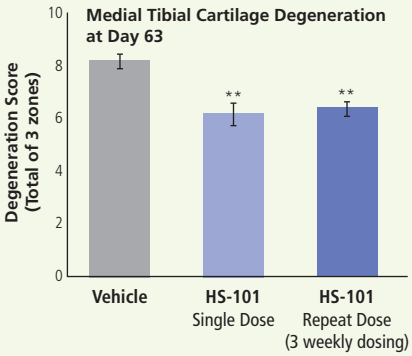


Recovery of collagen-producing chondrocytes

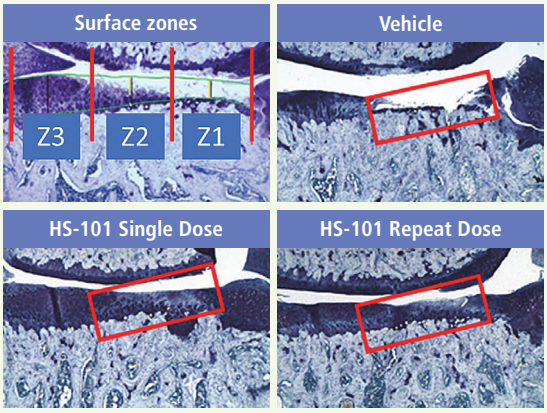


Rat Model Study

No toxicity observed at 140x single effective dose with NOAEL 7.0 mg/kg for male and female. Efficacy shown at 6wk (Day 63) post-treatment even with a single injection of nano gram dosing.

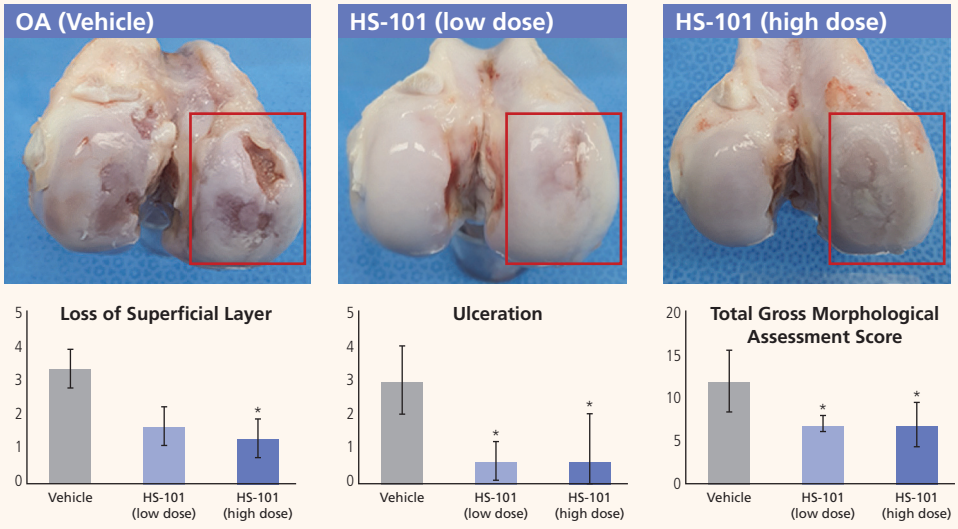


** p < 0.01 K-W test (Dunn's post-hoc) vs. vehicle



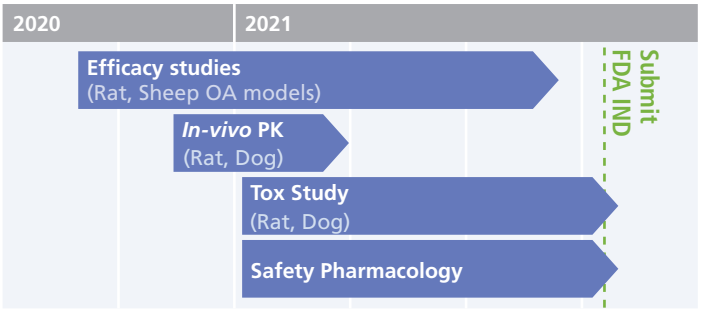
Goat Model Study

Both low- and high-dose IA HS-101 show a clear improvement in cartilage surface ulceration & damage compared to OA model animals treated with vehicle alone. The positive effect of HS-101 on the joint is clearly visible to the naked eye, whilst scoring of surface damage shows a significant improvement. These clear improvements are observed even at 6 weeks post-treatment.



* Statistically significant compared with OA group (*P < 0.05)

IND-Enabling Study Programme



Partnering Objectives

HaplnScience is a Korean Biotech focused on developing anti-aging therapies to improve the health of the growing elderly population. In addition to OA, the HaplnScience portfolio includes potential therapies for COPD, skin aging, hair loss.

HaplnScience is currently looking for a global development and commercialisation partner for HS-101 in the treatment of Osteoarthritis and other Osteochondral defects.

Intellectual Property

HS-101 is covered by method of use patents that are currently pending in the US, Europe, China, Korea, and Japan. HaplnScience is currently working to build up a supporting patent estate composed of process and formulation patents.

Further Information

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HAPLN SCIENCE

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