Organogenesis

# ReNu®

## CUTTING EDGE
## **OA SYMPTOM RELIEF.**

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# ReNu®

ReNu® is a cryopreserved amniotic suspension allograft that may be used as a single-injection treatment for the symptoms of osteoarthritis. ReNu consists of amniotic fluid cells and micronized amniotic membrane, and contains three key factors:

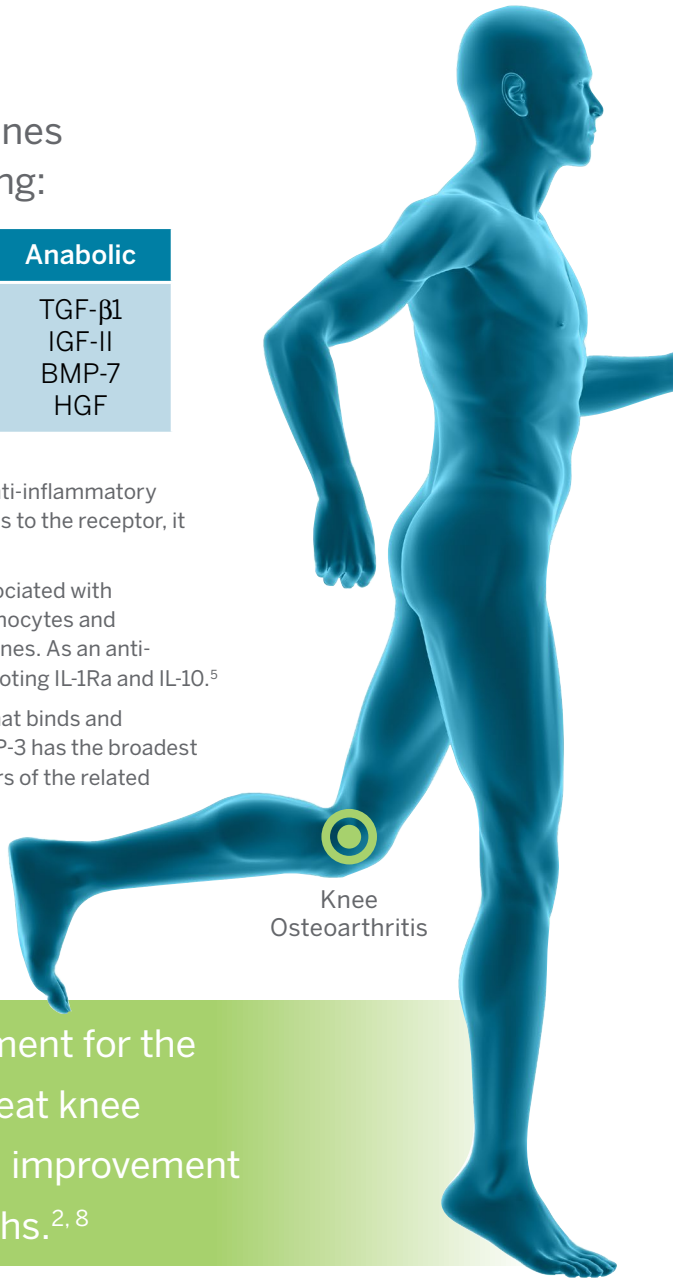
1. Extracellular matrix (ECM) particles, including hyaluronic acid[1]
2. Amniotic fluid cells[1]
3. A rich supply of anti-inflammatory cytokines and regenerative growth factors[1], including:

| Protease Inhibitors | Inflammation Modulation | Anabolic |
|---|---|---|
| TIMP-1<br>TIMP-2<br>TIMP-3 | IRAP/IL-1Ra<br>IL-6<br>IL-1F5 | TGF-β1<br>IGF-II<br>BMP-7<br>HGF |

**IRAP/IL-1Ra:** Interleukin-1 receptor antagonist (IL-1Ra or IRAP) is an anti-inflammatory cytokine that competitively binds to the IL-1 receptor. When IL-1Ra binds to the receptor, it prevents the pro-inflammatory signaling cascade of IL-1.[4]

**IL-6:** Interleukin-6 (IL-6) is a dual pro-/anti-inflammatory cytokine associated with osteoarthritis (OA). As a pro-inflammatory cytokine, IL-6 activates monocytes and macrophages, which then signal downstream pro-inflammatory cytokines. As an anti-inflammatory cytokine, IL-6 inhibits IL-1 and TNF-α activity, while promoting IL-1Ra and IL-10.[5]

**TIMP-3:** Tissue inhibitor of metalloproteinase 3 (TIMP-3) is a protein that binds and inhibits the activity of various matrix metalloproteinases (MMPs). TIMP-3 has the broadest inhibitory profile, being able to inhibit not only MMPs, but also members of the related families of a disintegrin and metalloproteinases (ADAMs) and ADAMs with thrombospondin motifs (ADAMTSs). TIMP-3 acts as an anti-inflammatory by preventing further tissue damage and the subsequent downstream release of pro-inflammatory cytokines.[6] Decreased levels of TIMP-3 are present in degraded human osteoarthritis cartilage compared to normal cartilage.[7]



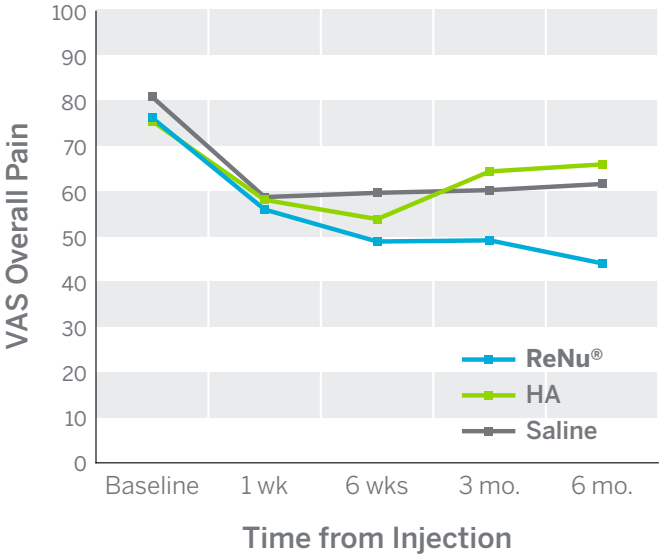

ReNu® is an innovative, single-injection treatment for the symptoms of osteoarthritis. When used to treat knee osteoarthritis, clinical studies have shown an improvement in pain and function scores for up to 12 months.[2, 8]

# Response to ReNu®: Clinical Evidence

In a multicenter, 200 patient, randomized controlled clinical trial, ReNu® was evaluated in patients with documented Kellgren-Lawrence Grade 2 and 3 OA of the knee, which represents a moderate stage.[1, 8]

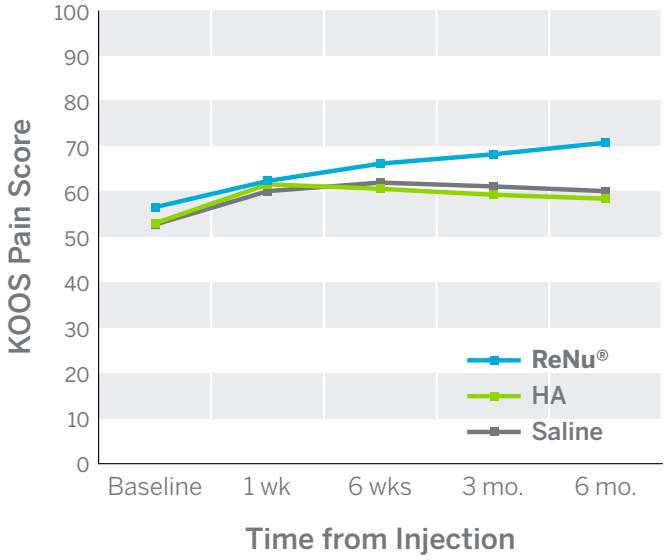
Patients were blinded to their allocation and were randomized 1:1:1 to one of three treatment arms: a single injection of ReNu®, a single injection of a commercially available hyaluronic acid (HA), or a single injection of saline.[8]

**At 6 months, ReNu® treatment resulted in significantly greater improvements in pain scores compared with both HA and saline.[8]**




VAS Overall Pain (Visual Analog Scale) is a patient-reported outcome measurement used to assess patients' opinions regarding their current level of pain.

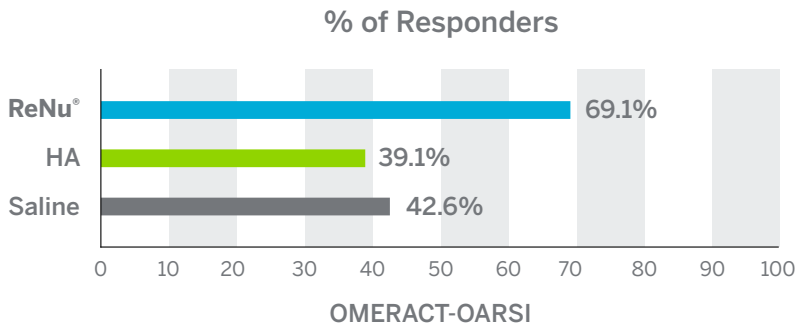
**At 6 months, ReNu® group showed significantly greater improvement compared with both HA and saline groups in the KOOS pain subset.[8]**




KOOS Pain (Knee Injury Osteoarthritis Outcome Score) is a patient-reported outcome measurement used to assess the patient's opinion about knee-associated problems and changes induced from treatment.

## Responder Analysis

At 6 months, the responder rates for the ReNu® treatment group were significantly higher than those for the saline and HA groups.[8]



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## Safety Profile

The tissues in ReNu® are collected from fully consented mothers undergoing scheduled caesarean section births of full-term healthy babies. Donors are tested for relevant communicable diseases by an FDA registered laboratory, and Organogenesis only releases tissue for transplantation that has negative or non-reactive results for the following[3]:

- **anti-HIV-1 and anti-HIV-2**
- **HIV-1/HBV/HCV NAT**
- **Hepatitis B surface Antigen (HBsAg)**
- **Hepatitis B Core total antibody (anti-HBc)**
- **Hepatitis C anti-body (anti-HCV)**
- **WNV**
- **Syphilis**
- **HTLV I/II**

After screening, the amniotic tissue is aseptically processed in a controlled, clean environment following strict technical quality assurance standards[3].

## Sizing

ReNu® is available in a variety of sizes.

| Product Code | Product Description/Size |
|---|---|
| **RN-1000** | ReNu Small 0.5cc |
| **RN-1001** | ReNu Medium 1.0cc |
| **RN-1002** | ReNu Large 2.0cc |


**References: 1.** Data on file, Organogenesis Inc. **2.** Vines JB, Aliprantis AO, Gomoll AH, Farr J. Cryopreserved Amniotic Suspension for the Treatment of Knee Osteoarthritis. J Knee Surg 2016; 29:443-450. **3.** ReNu Allograft Tissue Information and Product Preparation Insert. **4.** Jacques C, Gosset M, Berenbaum F, Gabay C. The role of IL-1 and IL-1Ra in joint inflammation and cartilage degradation. Vitamins and Hormones 2006:74;371-403. **5.** Wong PKK, Campbell IK, Egan PJ, Ernst M, Wicks IP. The role of the interleukin-6 family of cytokines in inflammatory arthritis and bone turnover. Arthritis & Rheumatism 2003:48(5); 1177-1189. **6.** Scilabra SD, Pigoni M, Pravata V, Schatzl T, Muller SA, Troeberg L, Lichtenthaler SF. Increased TIMP-3 expression alters the cellular secretome through dual inhibition of the metalloprotease ADAM10 and ligand-binding of the LRP-1 receptor. Scientific Reports 2018:8(14697). **7.** Morris, K.J., Cs-Szabo, G. & Cole, A.A. Characterization of TIMP-3 in human articular talar cartilage. Connect Tissue Res 51, 478-490 (2010). **8.** Farr J, Gomoll AH, Yanke AB, Strauss EJ, ASA Study Group, Mowry KC. A randomized controlled single blind study demonstrating superiority of amniotic suspension allograft injection over hyaluronic acid and saline control for modification of knee osteoarthritis symptoms. J Knee Surg. 2019, In press.

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