

IDEA<sup>2</sup> October 2021

# Liposphere – Enabling smooth articulation of joints

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**Liposphere**  
*Revolutionizing biolubrication.*

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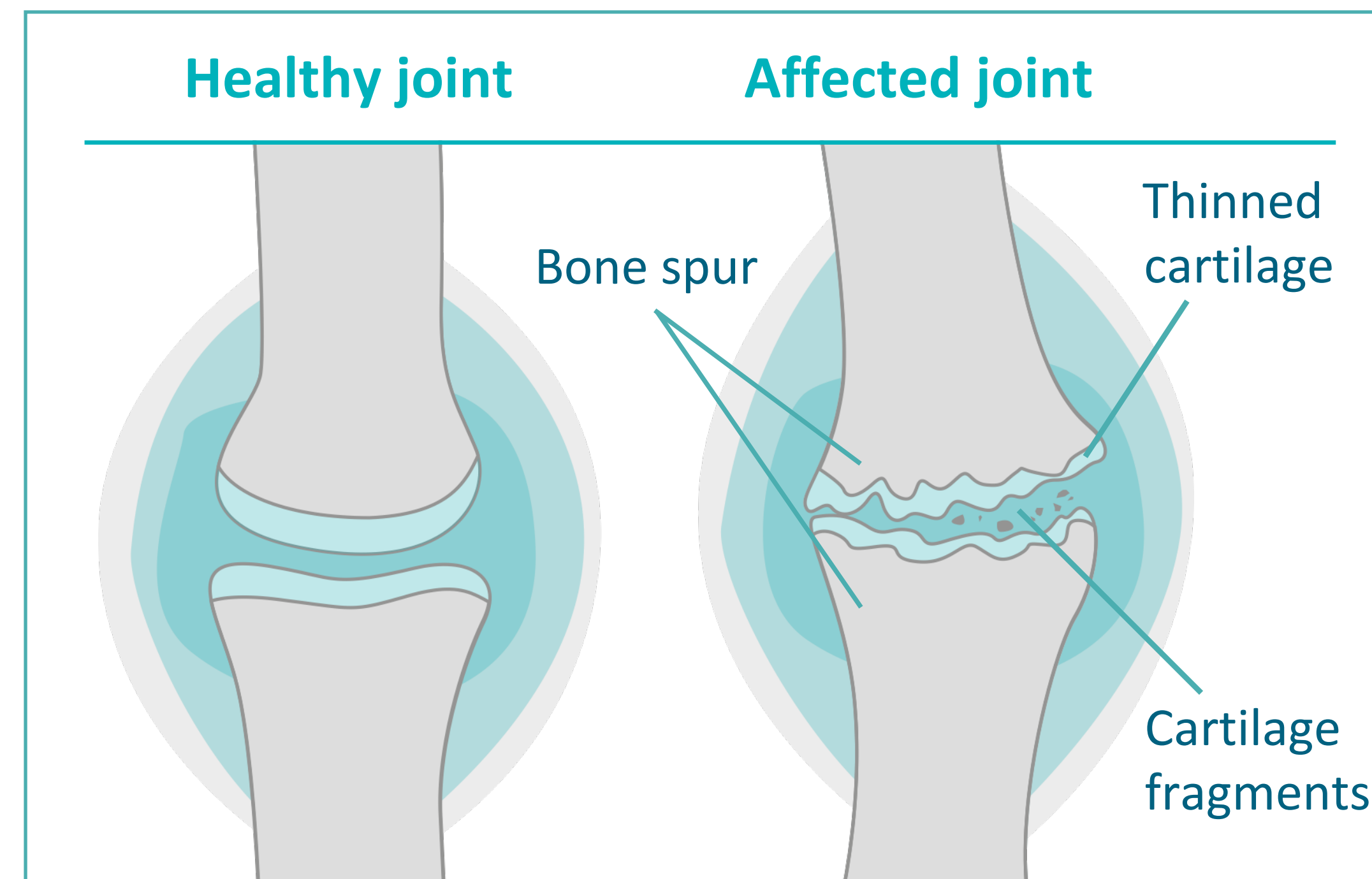
Pinpointing the problem

## Osteoarthritis

// Degenerative Joint Disease

- > Progressive breakdown/loss of cartilage
- > Pain and limitation of active lifestyle

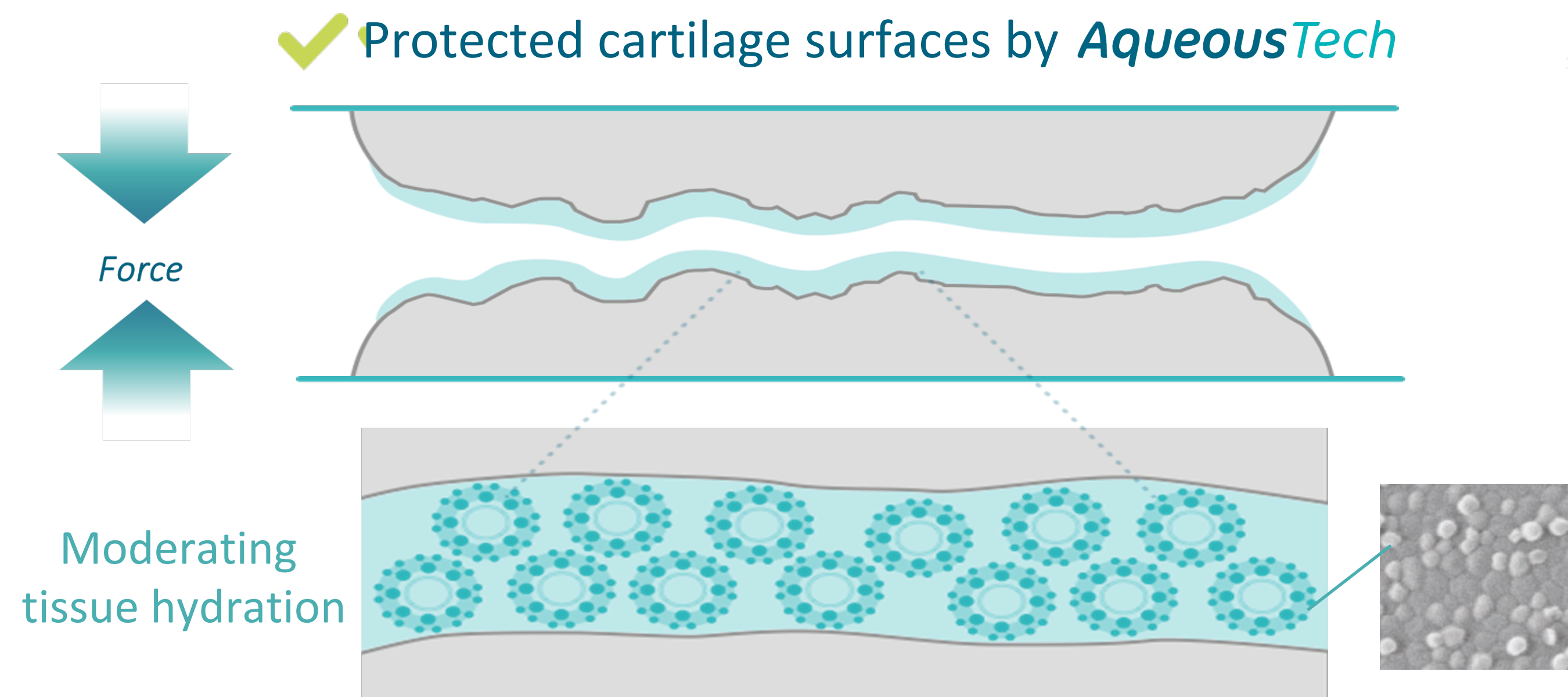
// Current treatment solutions:  
partially beneficial and time-limited



*Over 300M people globally suffer from Osteoarthritis.*

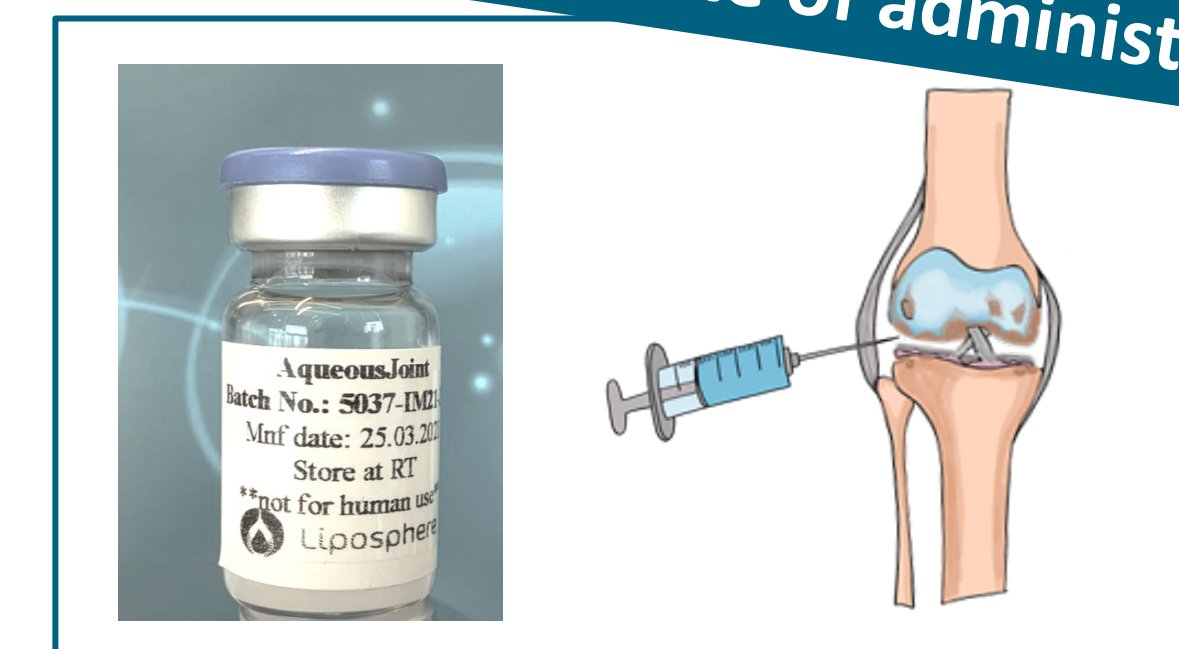
## AqueousJoint Our Solution

“A revolutionary, water-based, biocompatible  
knee joint articulation compound to restore cartilages’ natural mechanical properties.”



- ✓ Long shelf stability
- ✓ Scalable for mass production
- ✓ Encapsulation potential

Ease of use  
➤ Established route of administration



**Mode of Action: Hydration Lubrication Mechanism <sup>4</sup>**



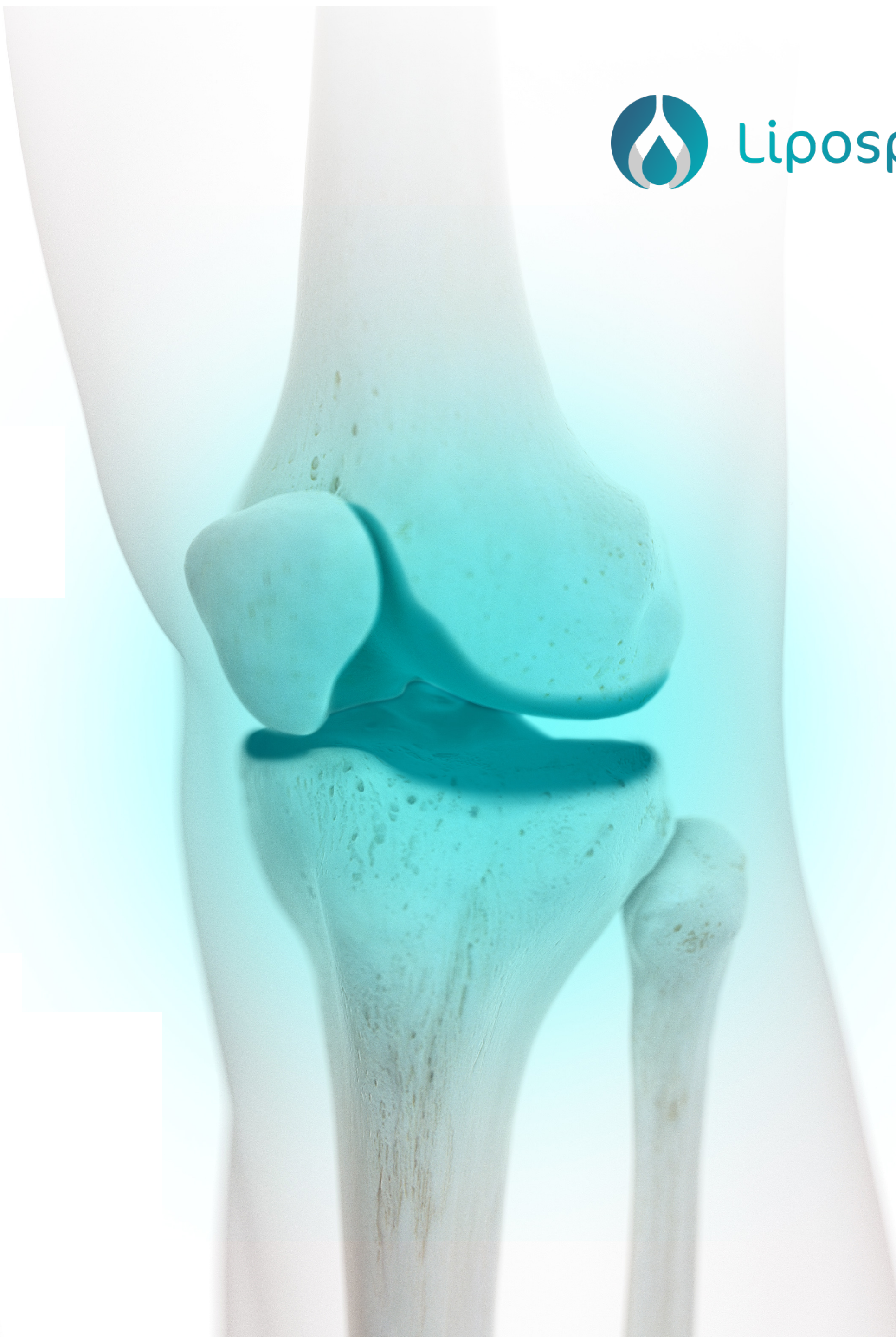
Liposphere's orthopedic product

## ***AqueousJoint***

...forms a hydrated, **protective coating** on cartilage to treat **Osteoarthritis** as a **local knee injectable**.

### **Anticipated patient benefits**

- ✓ **Reduction of pain by protecting cartilage**
- ✓ **Delaying surgery** and improve dosing schedule.
- ✓ **Resume normal activities.**





Liposphere's orthopedic product

## Why AqueousJoint?

The Theory

Why and how should a lubricant work?

Osteoarthritis and Cartilage 21 (2013) 1660–1667

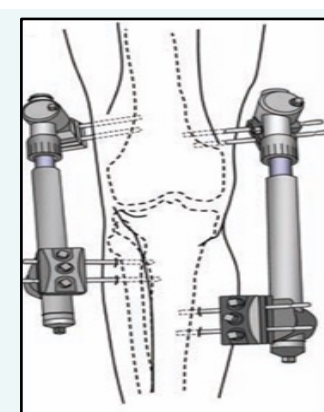
### Osteoarthritis and Cartilage



Sustained clinical and structural benefit after joint distraction in the treatment of severe knee osteoarthritis



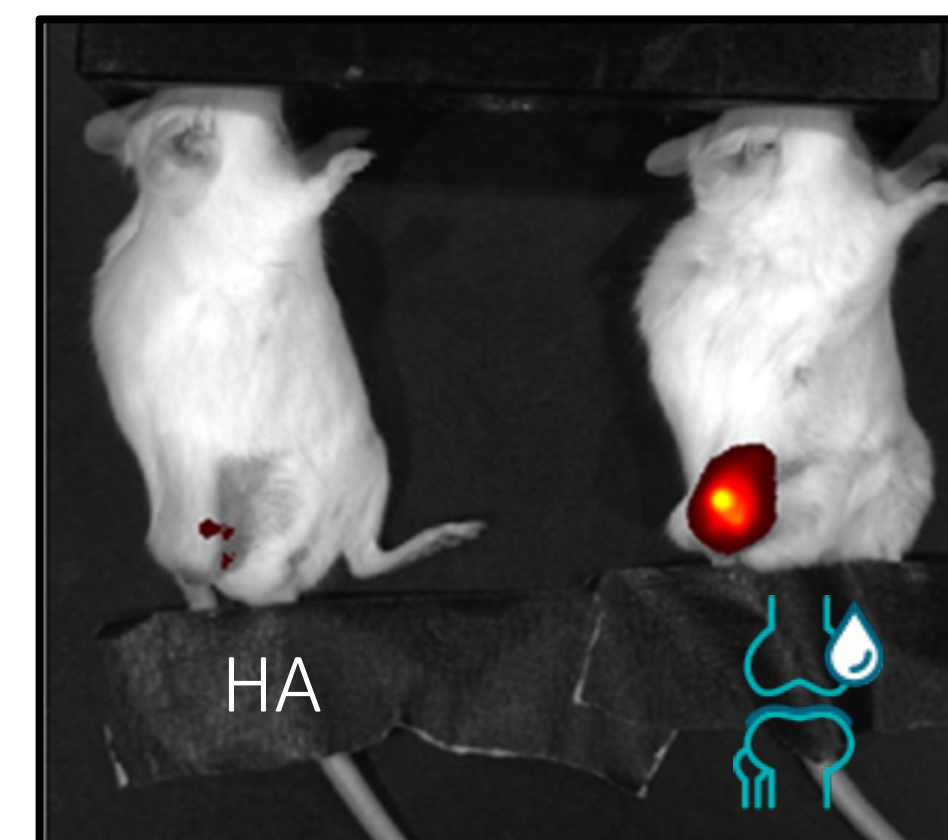
K. Wiegant<sup>†‡</sup>, P.M. van Roermund<sup>‡</sup>, F. Intema<sup>†</sup>, S. Cotozana<sup>§</sup>, F. Eckstein<sup>§</sup>, S.C. Mastbergen<sup>†</sup>, F.P.J.G. Lafeber<sup>†\*</sup>



*“... It is hypothesized that temporary joint distraction prevents mechanical stress on the cartilage, prevents further wear and tear and allows tissue repair to begin.”*

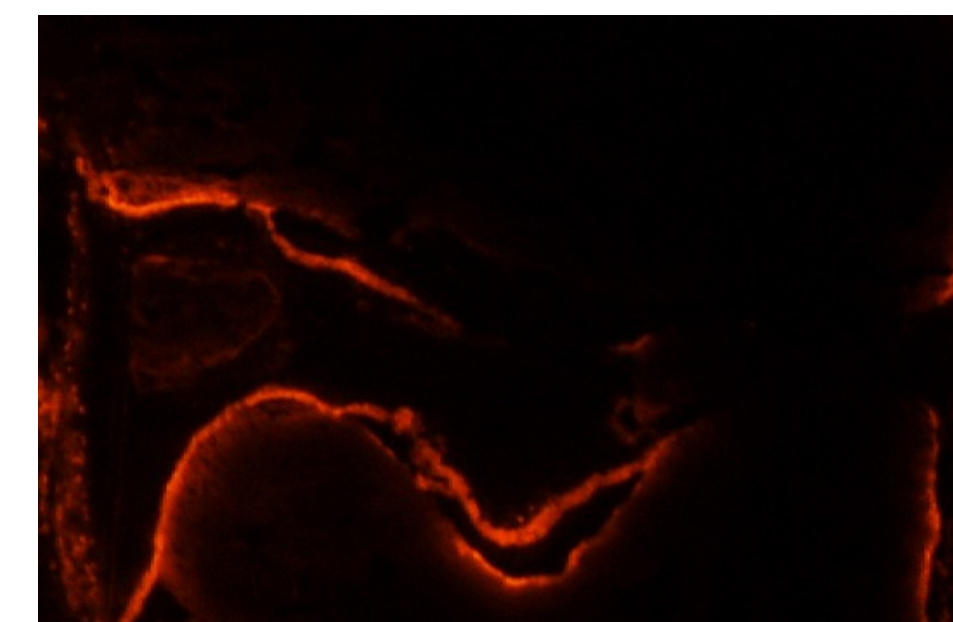
Boundary lubricants could potentially initiate tissue repair

### Retention time study in mice



T = 72 hours post-injection.

In Practice



Coating cartilage

### Efficacy study\* in mice

Intra-articular injection of phospholipid-based lubricant reduces shear-responsive inflammatory genes in the superficial layer of cartilage post joint destabilization.

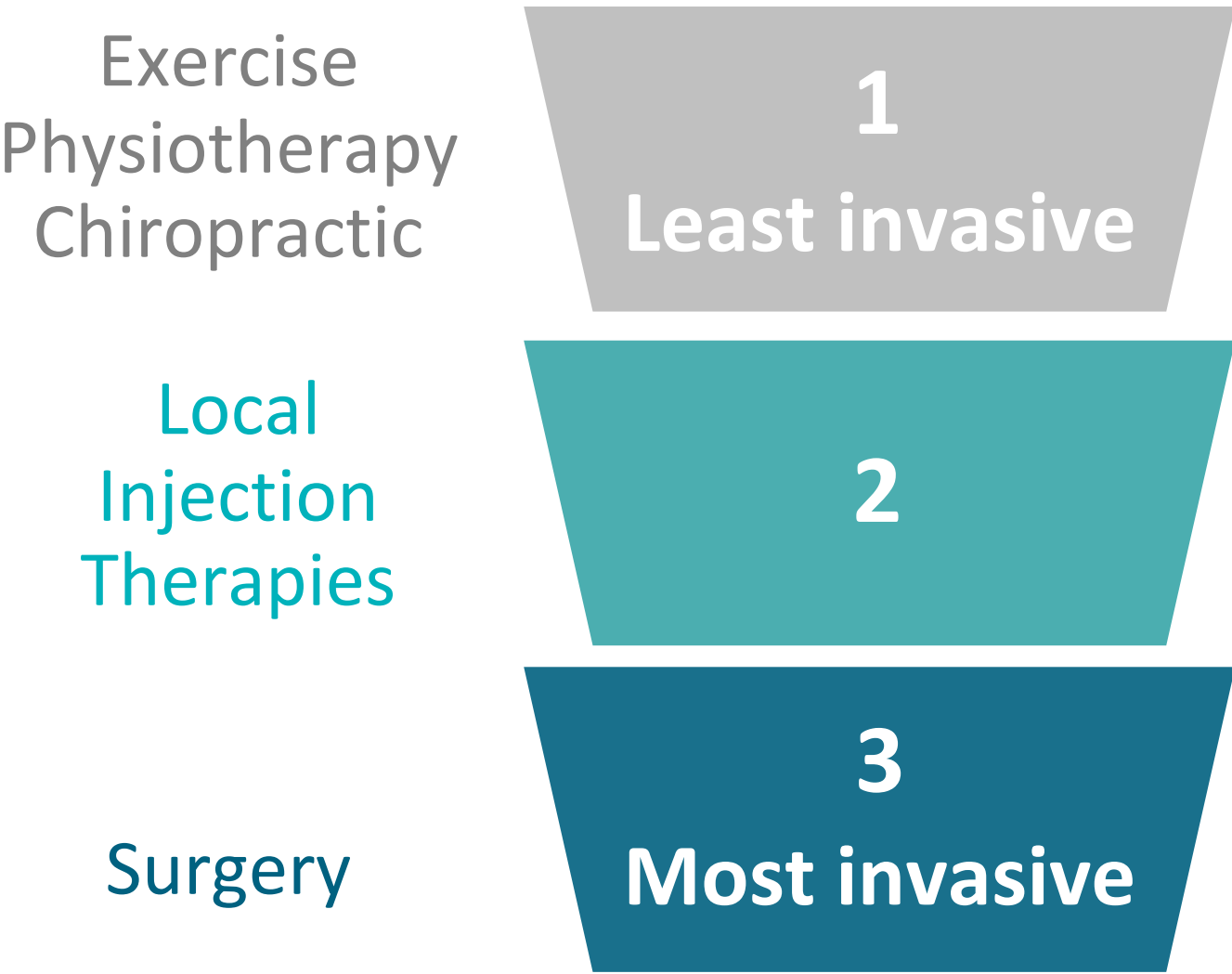
\* Collaboration Prof Jacob Klein Weizmann Institute/Prof. Tonia Vincent Oxford University



Osteoarthritis

Current solutions

Stage II – local injectables



Corticosteroids	Hyaluronic acid-based
Drug	Visco-supplement
// anti-inflammatory, pain relief // acts rapidly // short-term effect // Side effect: cartilage damage // restricted to 3-5x per year	// delayed pain relief effect, but up to 6 months // controversial clinical benefit // less effective in older adults and severe cases

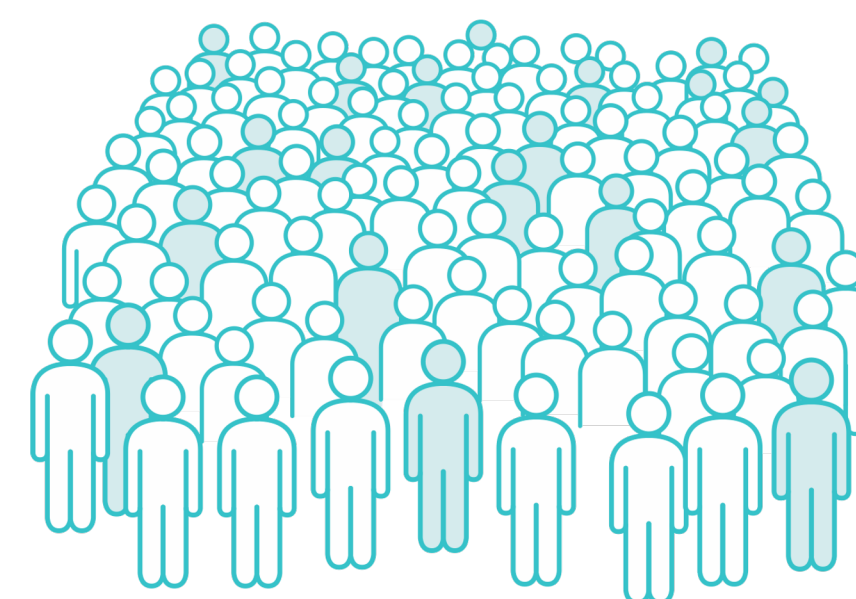
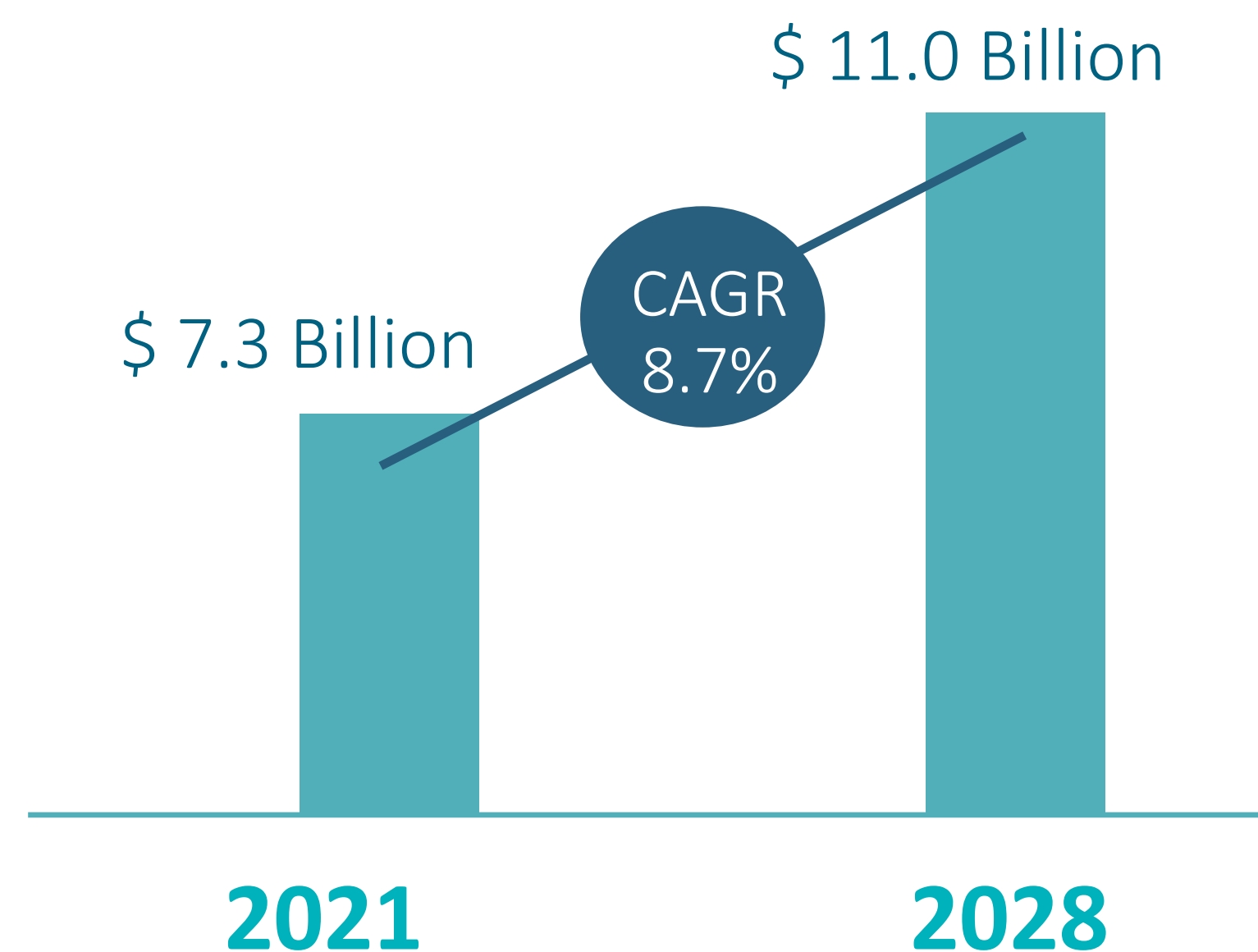
We focus on Stage 2 treatment aiming to delay Total Knee Replacement.



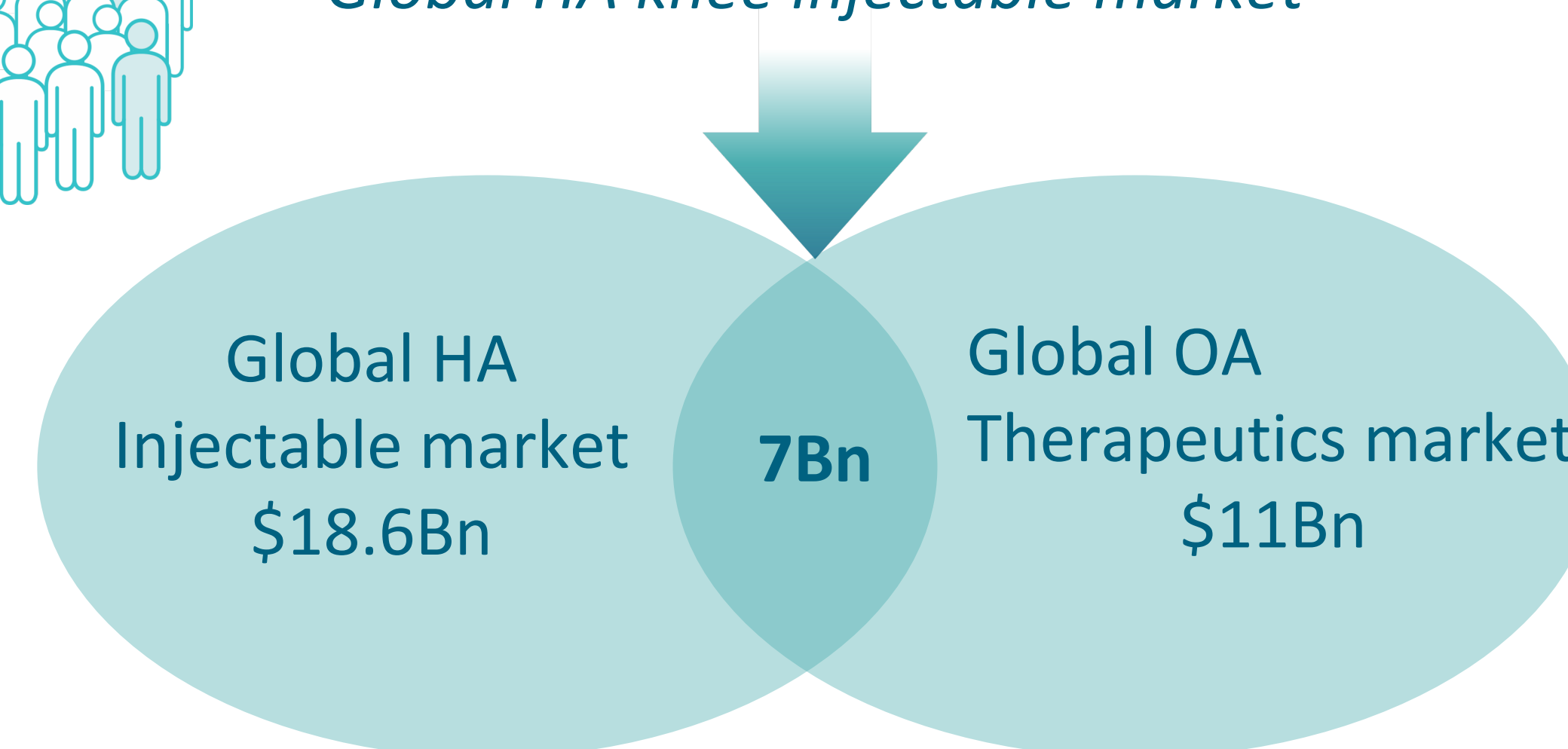
*AqueousJoint*

# Market and Competition

## Global Osteoarthritis Therapeutics Market



Customer target segment  
Global HA knee injectable market





**Key players:** Sanofi, Ferring, Fidia, Seikagaku, Anika Therapeutics, Zimmer Biomet, Fidia...



A comparison

## Why AqueousJoint?

	 <b>AqueousJoint</b>	<b>Hyaluronic acid-based</b> <i>Market standard injectable</i>
<b>Protection against wear and tear</b>	// High  Lubrication capability clearly <b>outperforms</b> HA.	// Low
<b>Mode of Action</b>	// Boundary lubricant	// Viscosity enhancement
<b>Retention time</b>	// > 50x longer than HA	// rapid metabolic turnover



## Key metrics

# Accomplished Milestones

### *Preclinical/clinical milestones*

- ✓ Tech transfer to own facility
- ✓ ISO 13485:2016 certification
- ✓ Upscaled in-house manufacturing
- ✓ Retention time study in-vivo
- ✓ Preclinical biocompatibility
- ✓ In process of 2 in-vivo efficacy studies
- ✓ Submission ethical application FIH study

### *Strategic and business milestones*

- ✓ Established IP license (TTO Weizmann, Yeda)
- ✓ Raised seed-funding (USD 7.3M):  
private and Israel Innovation Authority
- ✓ Finalist MassChallenge accelerator, Spinoff Prize
- ✓ Participant MIT IDEA<sup>2</sup> program
- ✓ Winner AO development incubator
- ✓ In discussions with potential strategic partners



An outlook

## Next steps *AqueousJoint*

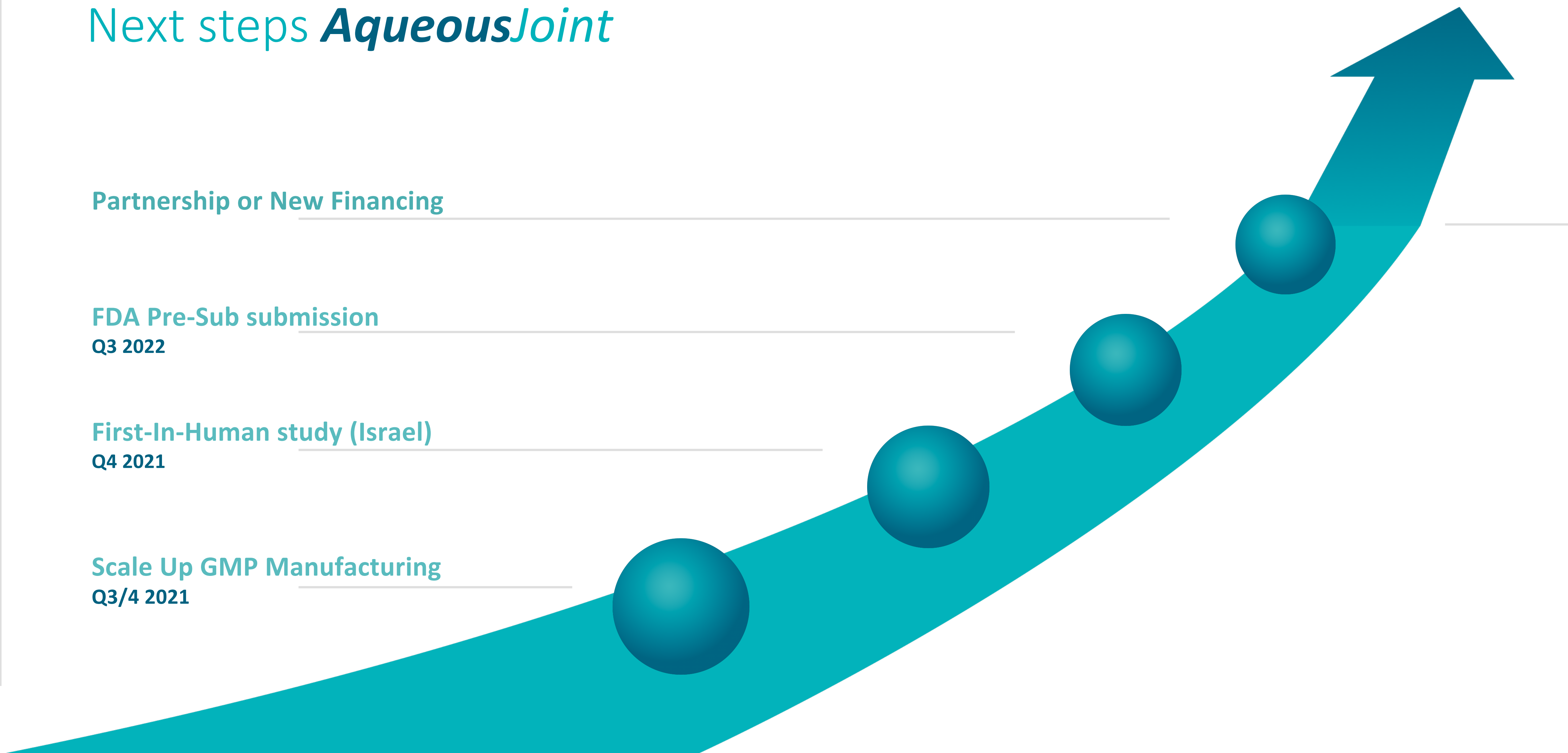
Partnership or New Financing

FDA Pre-Sub submission  
Q3 2022

First-In-Human study (Israel)  
Q4 2021

Scale Up GMP Manufacturing  
Q3/4 2021

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Who we are

## Liposphere's IDEA<sup>2</sup> Team

**Ronit Goldberg**

Co-Founder, CEO

PhD in Chemistry  
Weizmann Institute



**Sabrina Jahn**

Co-Founder,  
Business Development

PhD in Physics  
University of Cambridge



*„ We founded **Liposphere** as a **spin-off** from the **Weizmann Institute of Science (Israel)** in 2019  
after having worked several years together in an academic setting.”*

**Advisory**

**Scientific:** Prof Jacob Klein (Weizmann); **Clinical:** Dr Gabi Agar, Asaf Harofeh Hospital,  
**Business:** Yael Baratz (Pearl Cohen Baratz), Keren Haruvi-Snir, President Sandoz North America



## What happened since June Update

### // Key accomplishments

- *Clinical:* Submission FIH trial request
- *Developmental progress:* Large animal safety, Ex-vivo on cartilage and wear efficacy, analytics
- Filing *patent* protecting *product manufacturing method*
- *Company structure:* hired 4 new employees, IAA granted 3<sup>rd</sup> year of funding
- Business: Winner of AO incubator program

### // Key communication: what did we learn?

- *Orthopaedic clinicians:* willingness to evaluate AqueousJoint, retention time as crucial measure
- *Potential investors:* understanding interest of investing





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*AqueousJoint*

## Impact Statement

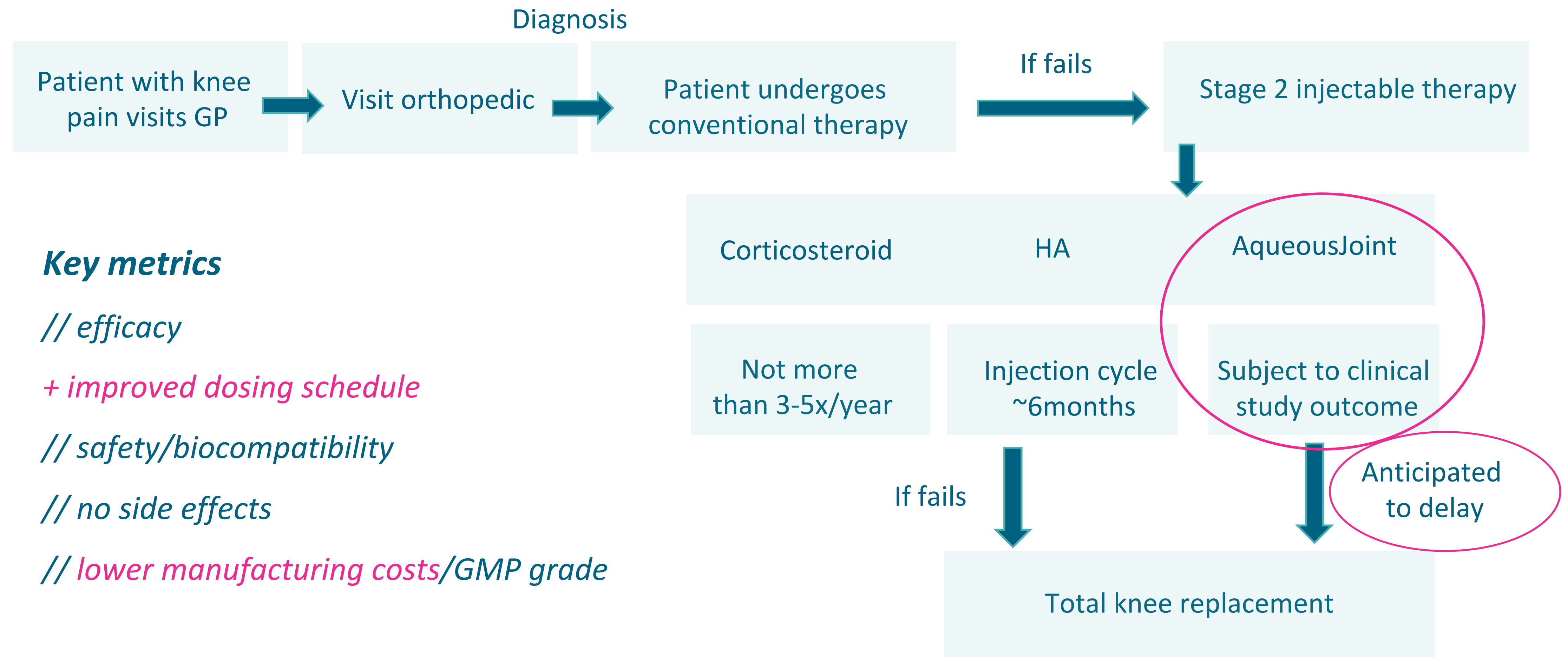
For Osteoarthritis patients with chronic knee pain, it's a challenge to maintain an active, pain-free life-style. Today, their best options are regular local injections of hyaluronic acid or corticosteroids which, because of poor long-term effectiveness yields continuing pain, frequent visits to the doctor with painful injections. Thus, there is a need to extend the effectivity of the injectables to treat OA patients which, if solved, will improve the quality of life by reducing pain enabling normal activities.

Solving this need can be achieved by the use of our long lasting, patented joint articulation compound AqueousJoint that will restore the natural lubrication properties of cartilage and will be demonstrated by the reduction of knee pain.



## AqueousJoint

# Today's workflow + AqueousJoint



*AqueousJoint*

## References

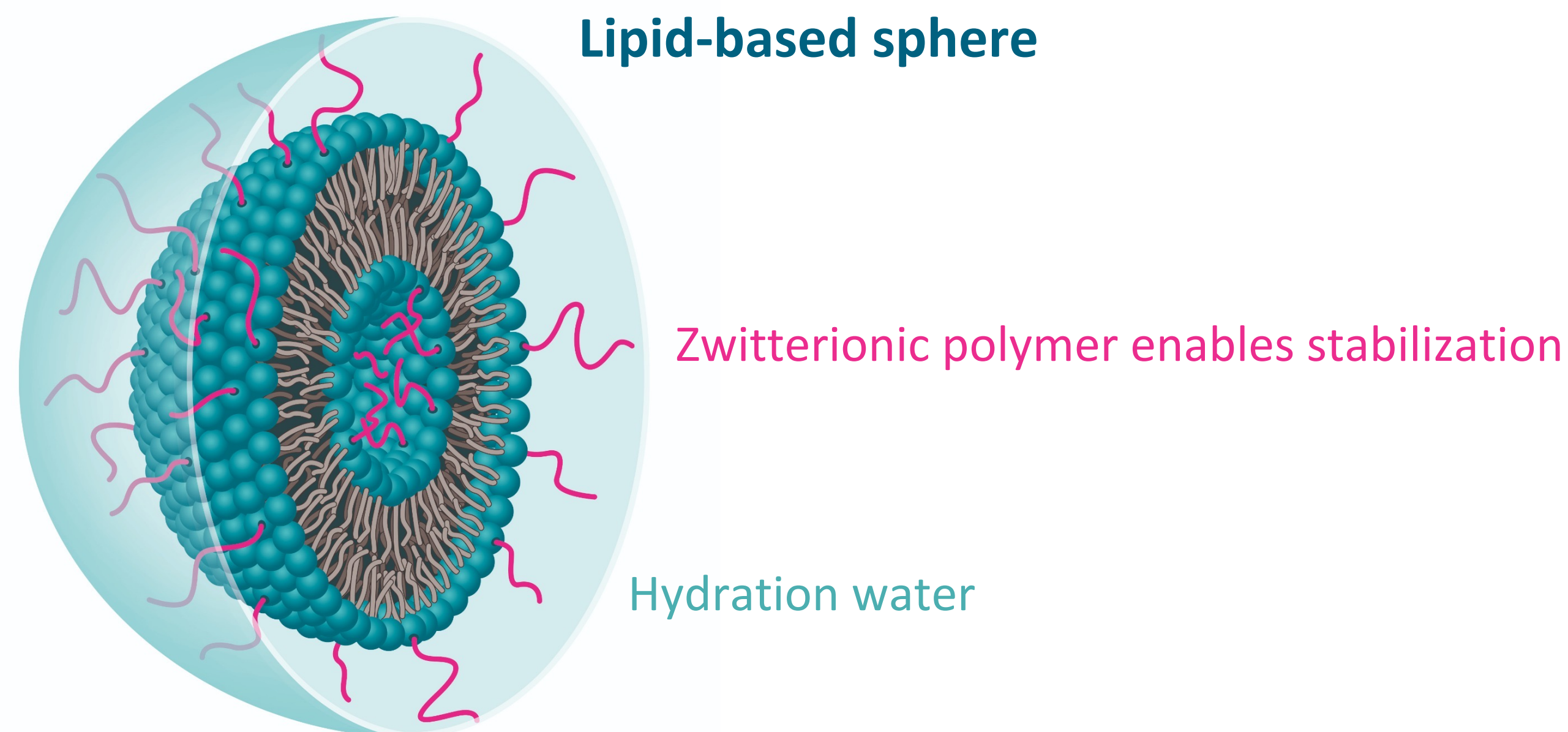
1. Osteoarthritis Therapeutics Market - Global Forecast to 2025 | Markets and Markets
  2. Hyaluronic Acid Market Size | Industry Analysis Report, 2020-2027 (grandviewresearch.com)
  3. Hyaluronic Acid Injection Market Ravishing USD 18.6 Bn by 2028| Corneal (Allergan), Galdermal (Q-Med), LG Life Science, Bohus BioTech, IMEIK,
  4. Raviv U, Laurat P, Klein J. Fluidity of water confined to subnanometre films. Nature. 2001;413(6851):51-54.
- Goldberg R, Schroeder A, Silbert G, Turjeman K, Barenholz Y, Klein J. Boundary lubricants with exceptionally low friction coefficients based on 2D close-packed phosphatidylcholine liposomes. Adv Mater. 2011;23(31):3517-3521.
- Jahn S, Seror J, Klein J. Lubrication of Articular Cartilage. Annual review of biomedical engineering. 2016;18:235-258.



AqueousJoint technology

## Liposphere's joint articulation compound

- ✓ Efficient at high-loads
- ✓ Reduces wear and friction
- ✓ Provides superior lubrication
- ✓ anticipated to be classified as medical device

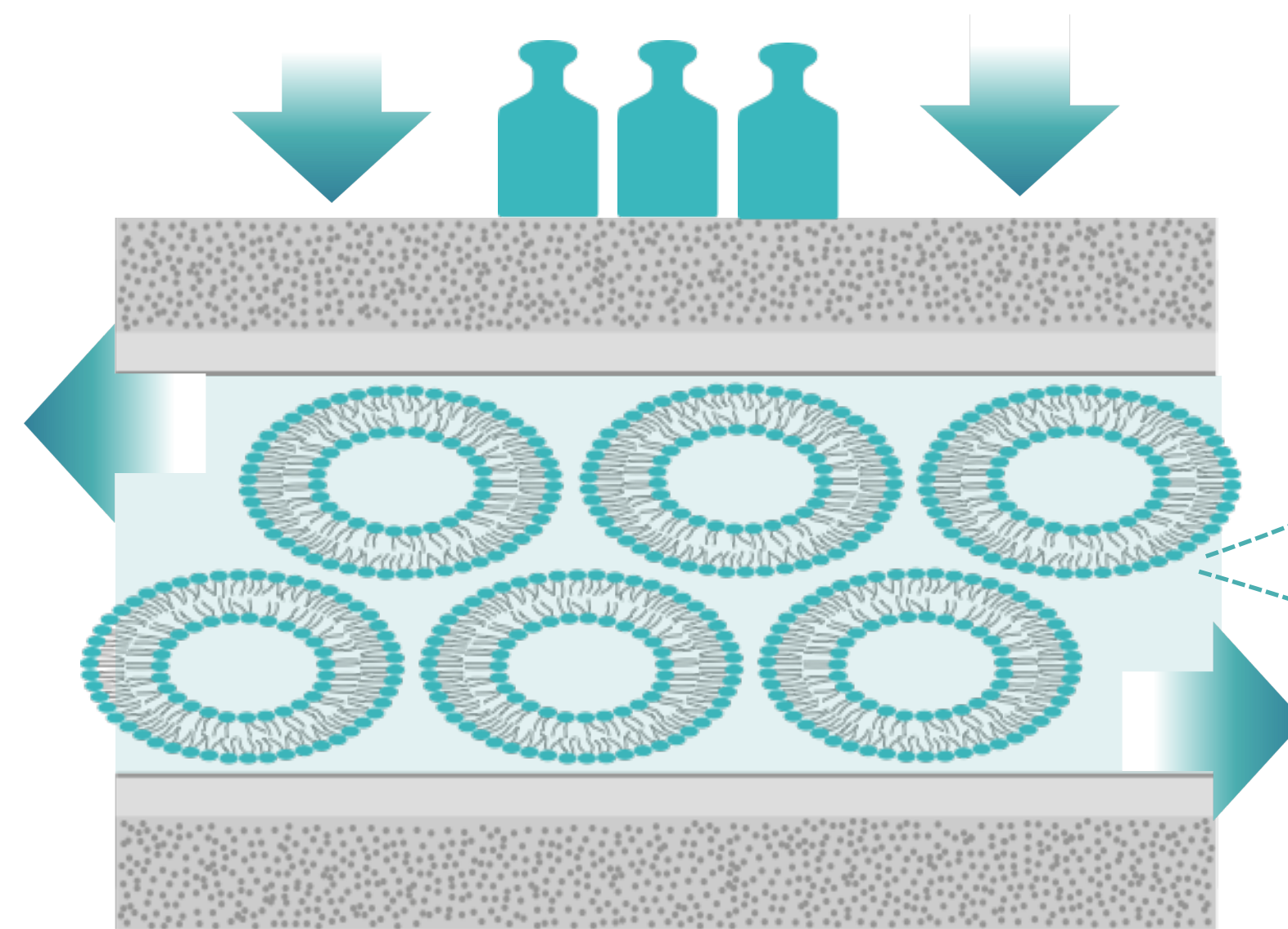


***Formulations hold water in the most efficient way.***

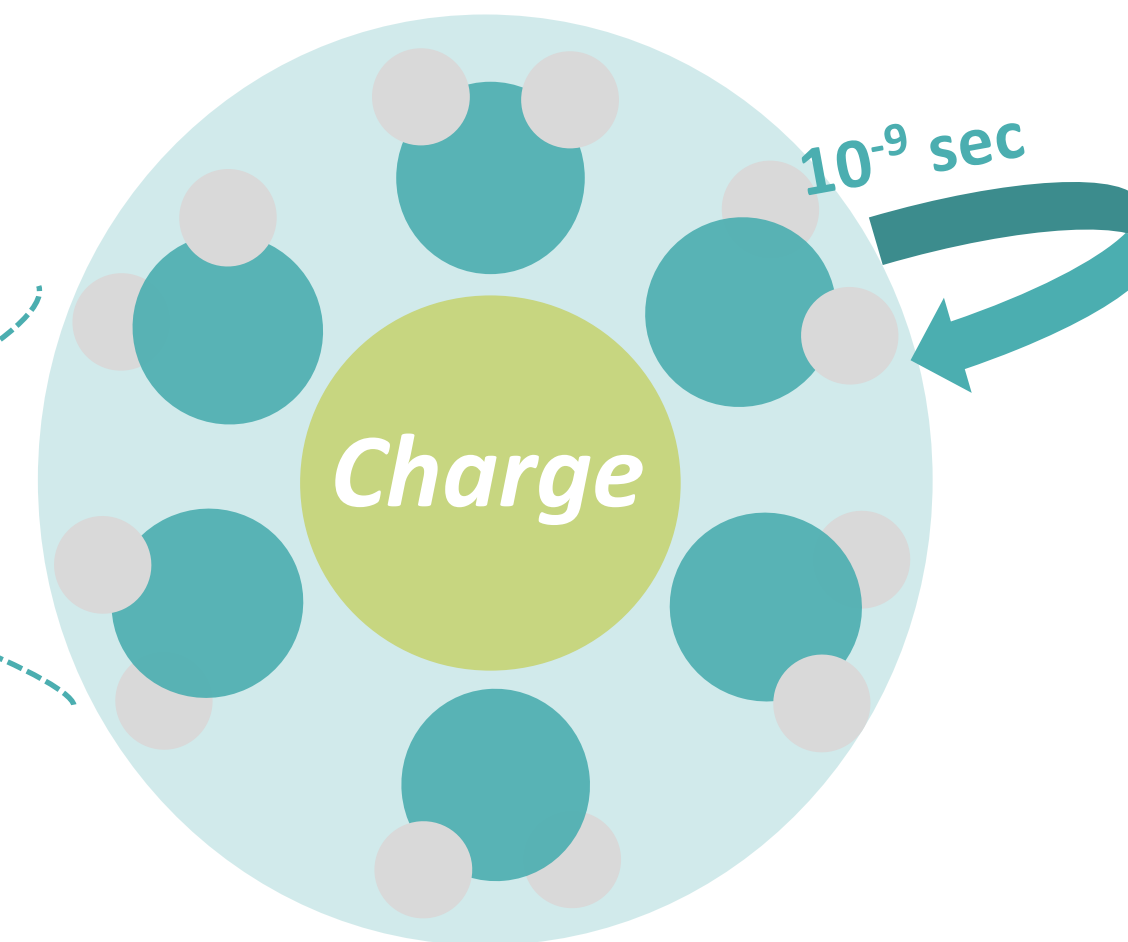
***Water acts as the lubricating element.***

How does it work?

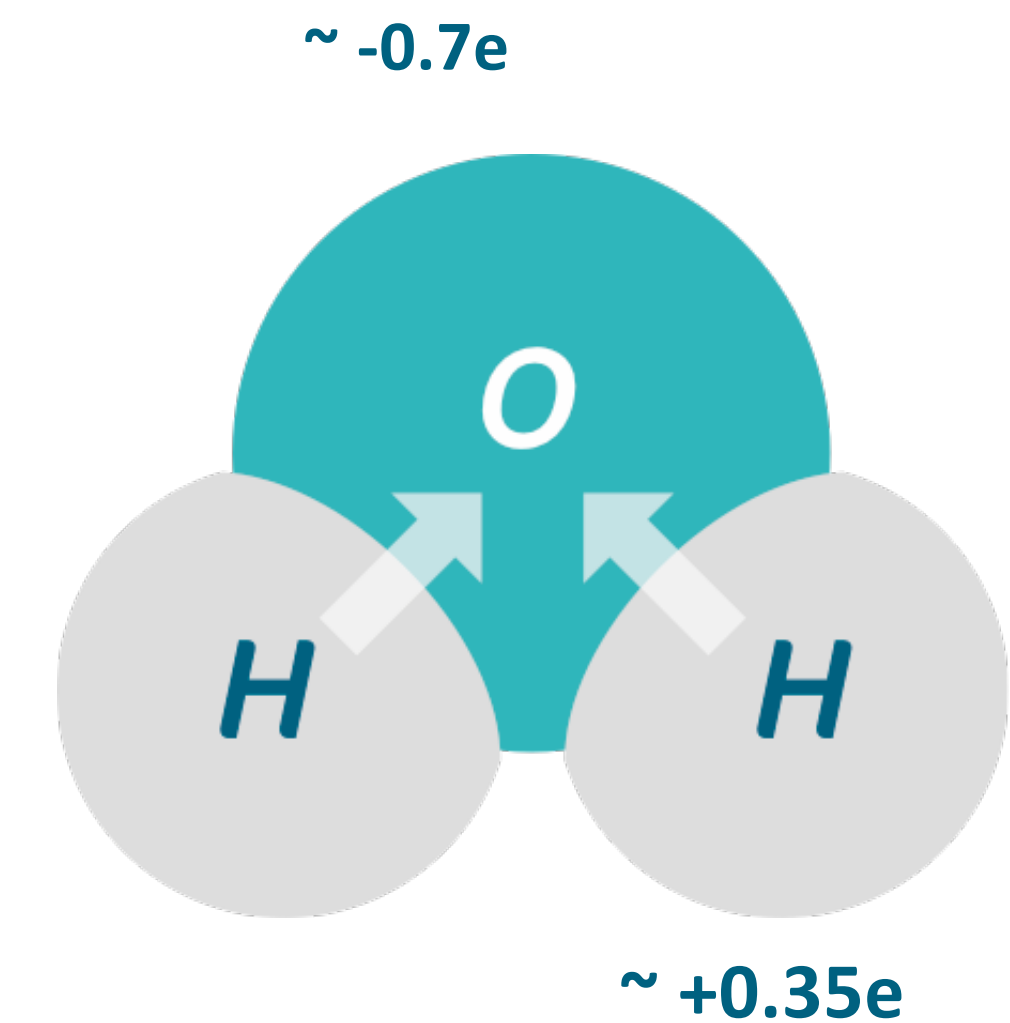
## AqueousJoint's surface action



*AqueousJoint protecting cartilage surfaces*



*Hydration water surrounding charged elements of AqueousJoint*



*Water molecules are the actual lubricating elements.*