CURNOVA
microRNA Technology

Thanks to a completely new patented therapeutic approach

From Osteoarthritis

CRN-001

Back to a happy & fulfilled live

https://www.gesundheit.com/gesundheit/krankheiten-a-z/1/osteoarthritis-dermatologischer-wirkstoff-bringt-hoffnung

https://lovepik.com/images/photo-jogging-park.html

OSTEOARTHRITIS (OA)

Large unmet medical need to inhibit bone loss and joint pain

- **Affected 57 million in Europe and 650 million people worldwide**
- associated with **chronic pain** and **bone loss**
- **every second women** and **every third men** >65 years of age

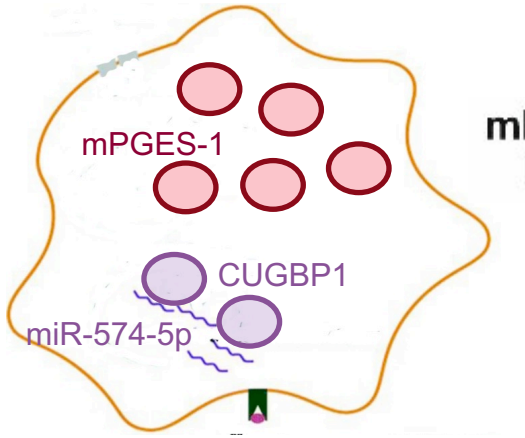
No curative treatment/Disease-Modifying-OA-Drug (**DMOAD**) available

Foto: Fotolia/Sebastian Kaulitzki

INNOVATIVE THERAPEUTIC APPROACH

miRNA-574-5p is an **ideal target** for pharmacological intervention in the treatment of OA

Inflammation & Pain ↑

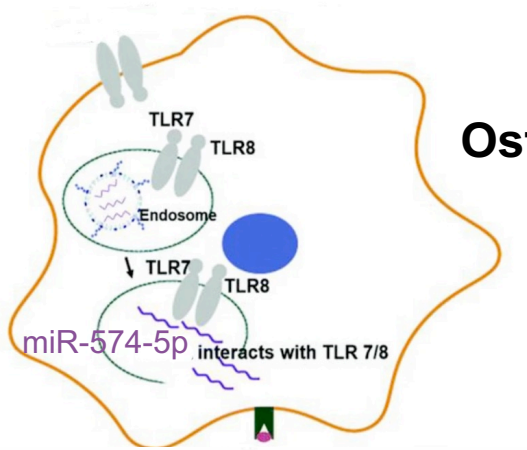


mPGES-1 HIGH
PGE_2 HIGH

miRNA-574-5p Mode of Action

Dual mechanism leading to pain and tissue destruction

Bone resorption ↑



Osteoclast

Osteoclast differentiation HIGH
Bone resorption HIGH

Saul et al., FASEB J (2019); Emmerich et al., Front Pharmacol (2020); Hegewald et al., Front Immunol (2020)

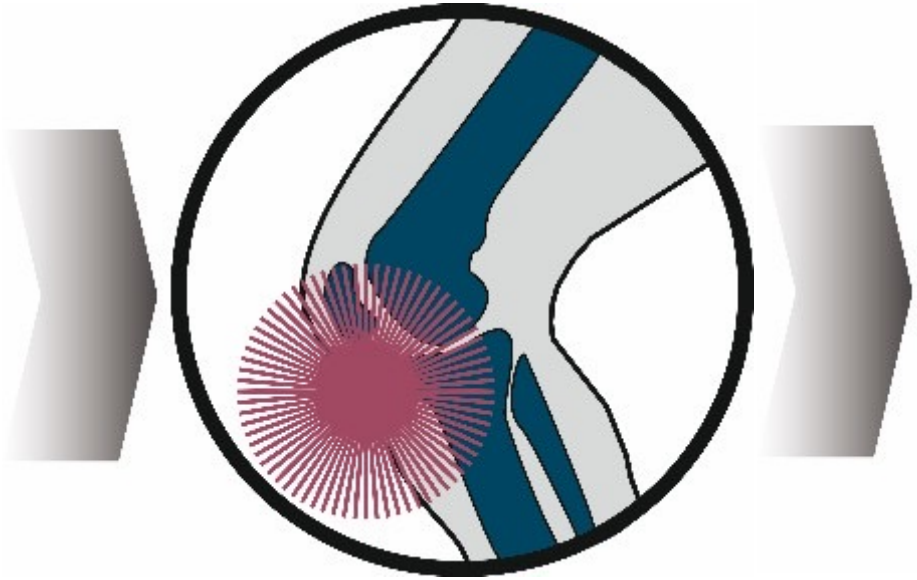
PGE_2 : Prostaglandin E_2, mPGES-1: microsomal prostaglandin E synthase 2; CUGBP1: CUG RNA binding protein 1; TLR: toll like receptor

THE SOLUTION: OUR NEW APPROACH

CURNOVA microRNA Technology

The miRNA-574-5p inhibitor CRN-001 has potential as first in class OA disease modifier

CRN-001



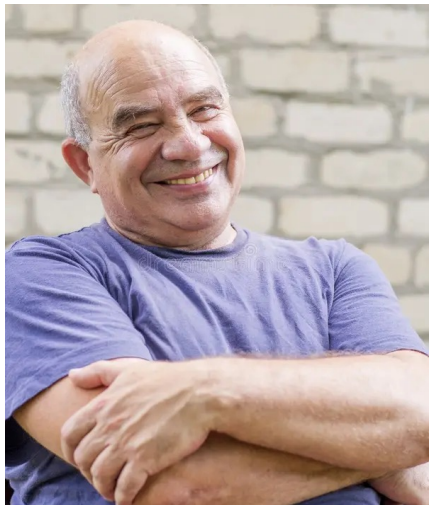
Unique value proposition:

Preserves joint function

Bone Resorption

Inhibits inflammation and pain

Fast track approval



Improves quality of life!

https://Lachender Alter Mann Mit Seinen Armen Gekreuzt Stockfoto - Bild von fällig, erscheinen: 62945608 (dreamstime.com)

CURNOVA (CRN-001) THERAPY ADVANTAGES

Patented drug design for intra-articular application → **Patient benefit**

CELL PENETRATING PEPTIDE (CPP)

PEPTIDE NUCLEIC ACID (PNA)

- Increases PNA solubility
- Efficient membrane permeation
- Cartilage-penetrating
- Long residence time in joint space

- **Directly reaches the site of action**
- **Long-lasting effect**
- **Improves quality of life**

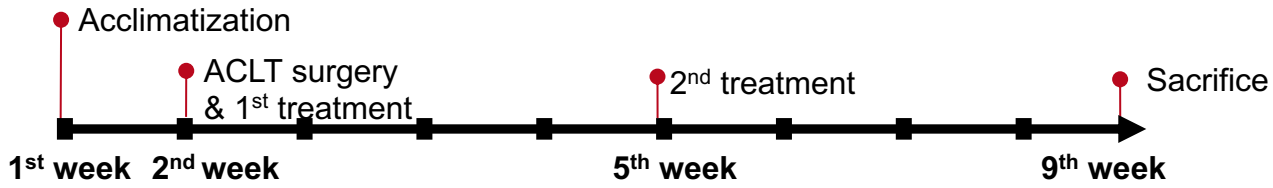
- Highly sequence specific
- Nuclease and protease resistant
- Long half-life

- **Less side effects**
- **Fewer injections (once quarterly)**
- **Functional improvement**

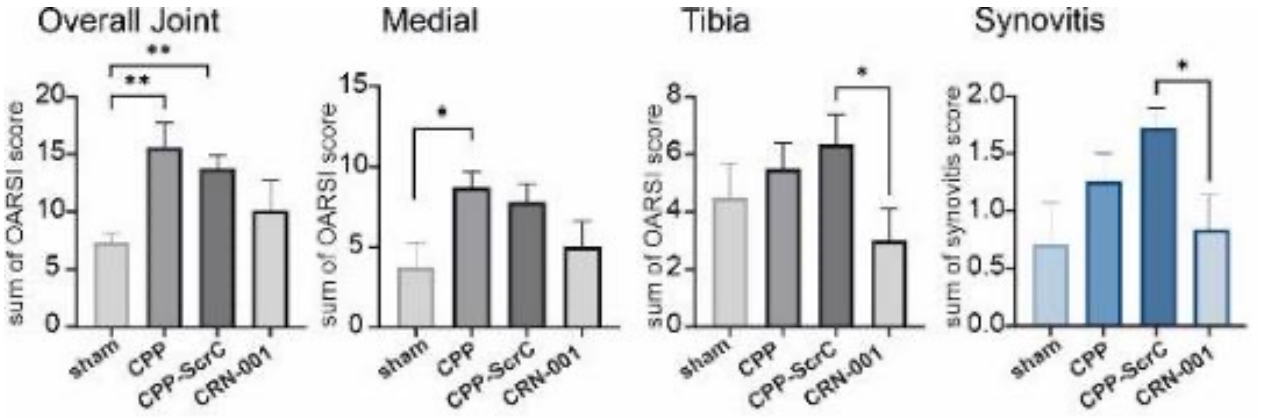
CRN-001

In-vivo proof of concept in a rodent model of OA

***In-vivo* study in anterior cruciate ligament transection (ACLT) mouse model**

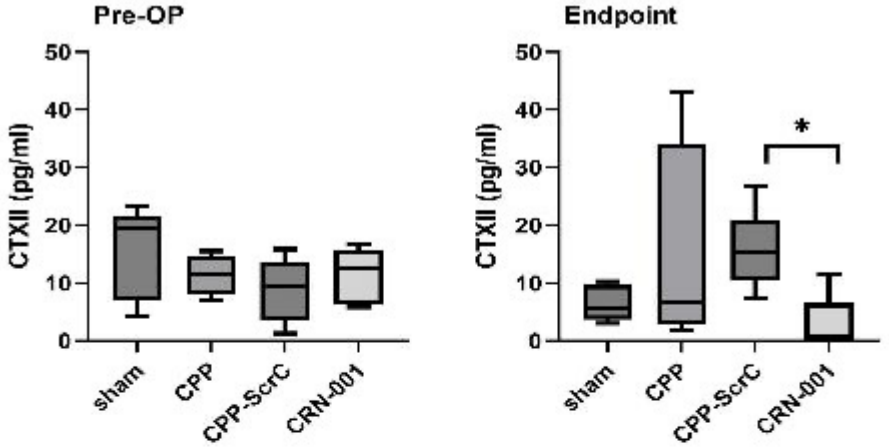


CRN-001 in ACLT mouse model compared with sham-operated, CPP alone, or CPP-coupled to scrambled PNA sequence (CPP-ScrC) treated mice (4 nmol per injection).



→ **OA progression and synovitis is significantly reduced** by CRN-001 (histology analysis)

CTXII measurement in blood samples from in vivo study



→ **Cartilage degeneration significantly reduced** by CRN-001 (CTXII = cartilage degeneration marker in blood)

- *In vitro:* **Dose-dependent reduction of osteoclastogenesis**
- **Low cytotoxicity** even at high concentrations

CRN-001

Unique value proposition

TARGET PATIENT POPULATION

Mid-stage OA (KL grade 2-3, moderate to severe pain) primarily affecting one or two joints and no widespread pain
→Combination of **joint preservation** and **symptom alleviation**

POSITIONING

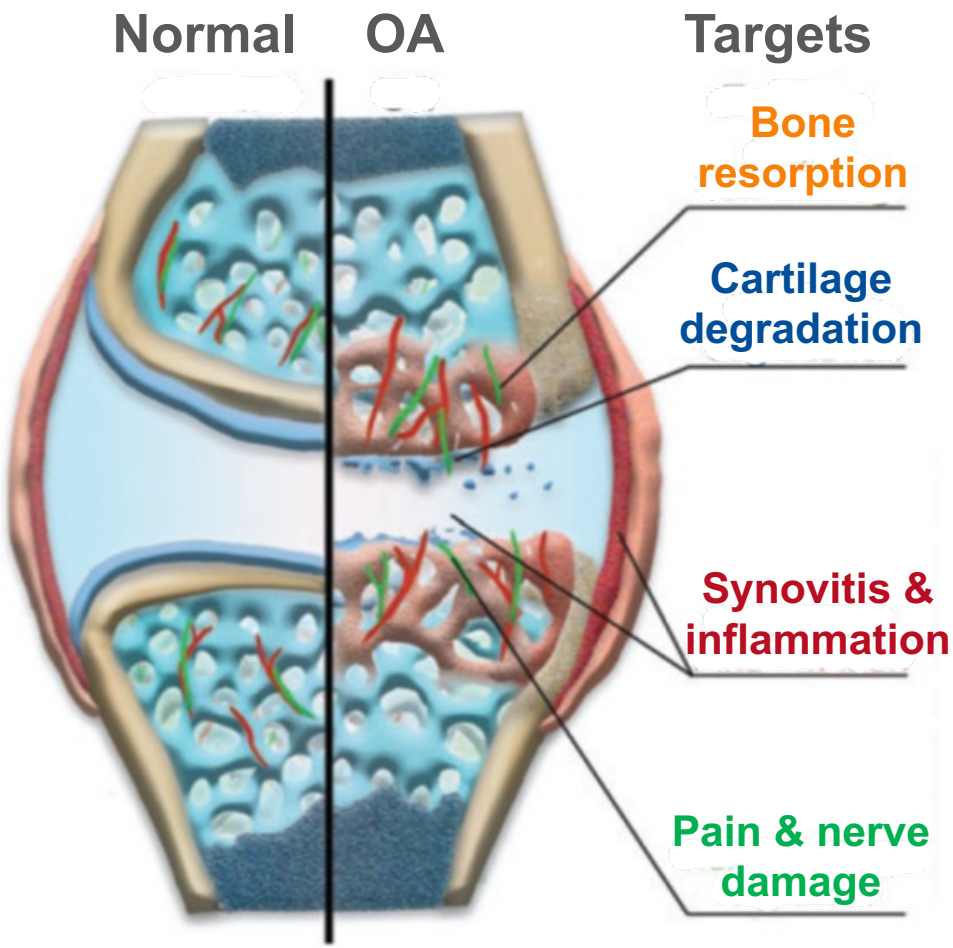
No comparable therapeutic approach on the market or in development
Simultaneously targets two unmet medical needs in OA: Bone resorption and inflammatory pain (structure and symptoms)
Possible biomarker-enabled therapy:
- Circulating miRNA 574-5p as potential biomarker for patient stratification and treatment response (target engagement)
- Use of biomarkers to establish target population with a bone OA phenotype

The present innovation is protected by the following **international patent application and patent:**

I.) "Inhibition of miR-574-5p as novel therapeutic strategy to reduce bone resorption in arthritis disease" (PCT/EP2020/073023)
II.) “MiRNA-574-5p as a biomarker for stratification of prostaglandin E-dependent tumors” (FH59330EP)

One **further patent application** is in preparation.

COMPETITORS I.ART. APPLICATION

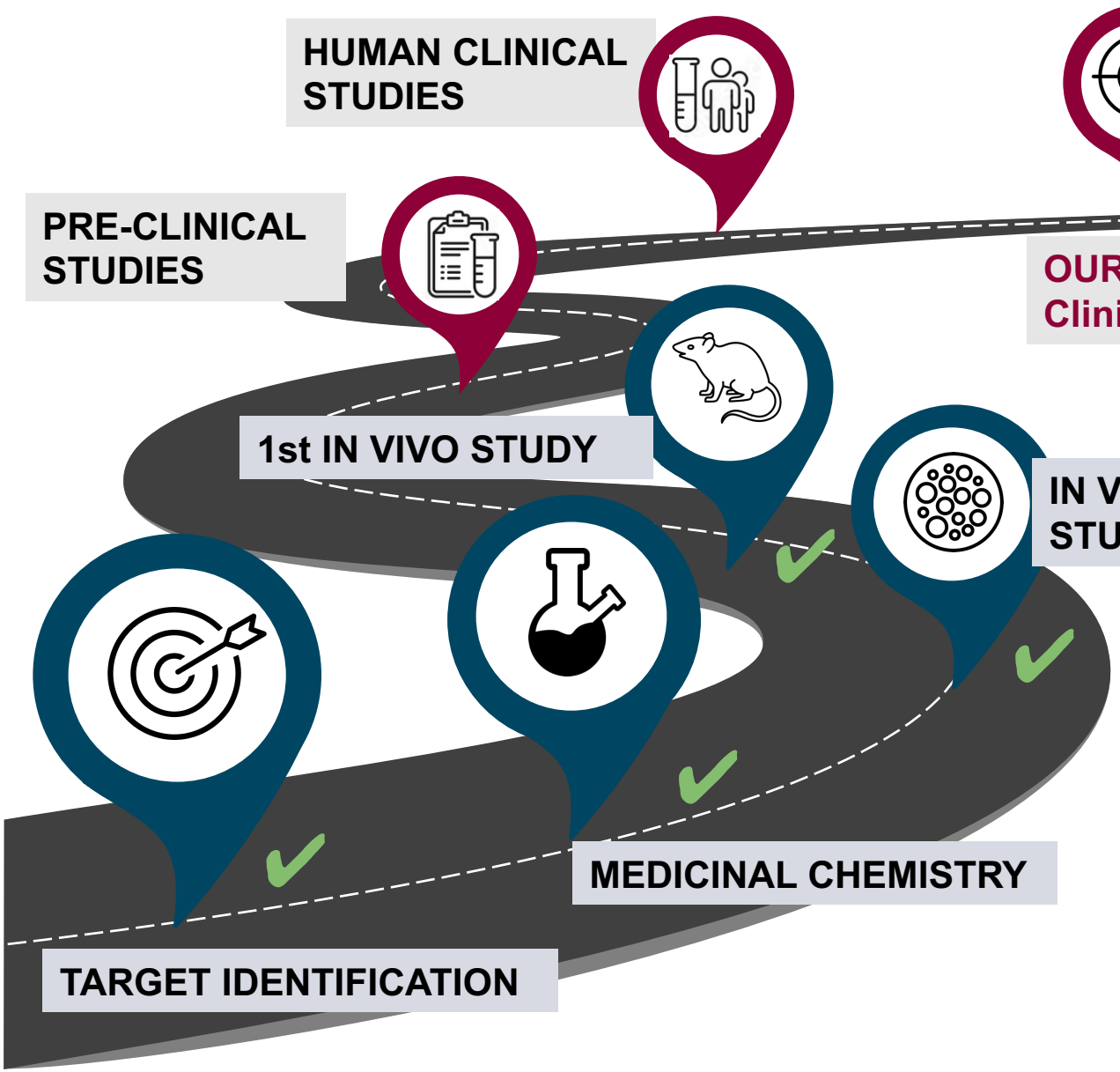


	Bone resorption	Synovitis Inflamma-tion	Pain Nerve damage	Cartilage degeneration
Curnova (CRN-001)	(+)[1]	(+)[3]	(+)[3]	(+)[2]
Bisphosphonates	(+)	(o)	(o)	(o)
Hyaluronic acid	(o)	(o)	(+/-)	(+/-)
Adavivint (Wnt inhibitor)	(o)	(o)	(o)	(+)
GEC-TGFβ1	(o)	(o)	(o)	(+)
Corticosteroids	(-)	(+)	(+)	(-)
Lorecivivint SM04690	(o)	(o)	(+)	(+)

(+) positive effect (o) no effect (-) negative effect

[1] Hegewald et al., Front Immunol (2020); [2]Yue et al., Mol Med Rep (2021); [3]Saul et al., FASEB J (2019);[3]Emmerich et al., Front Pharmacol (2020)

ROAD MAP



Marked development
From 800 M - 2,4 Bn / Year

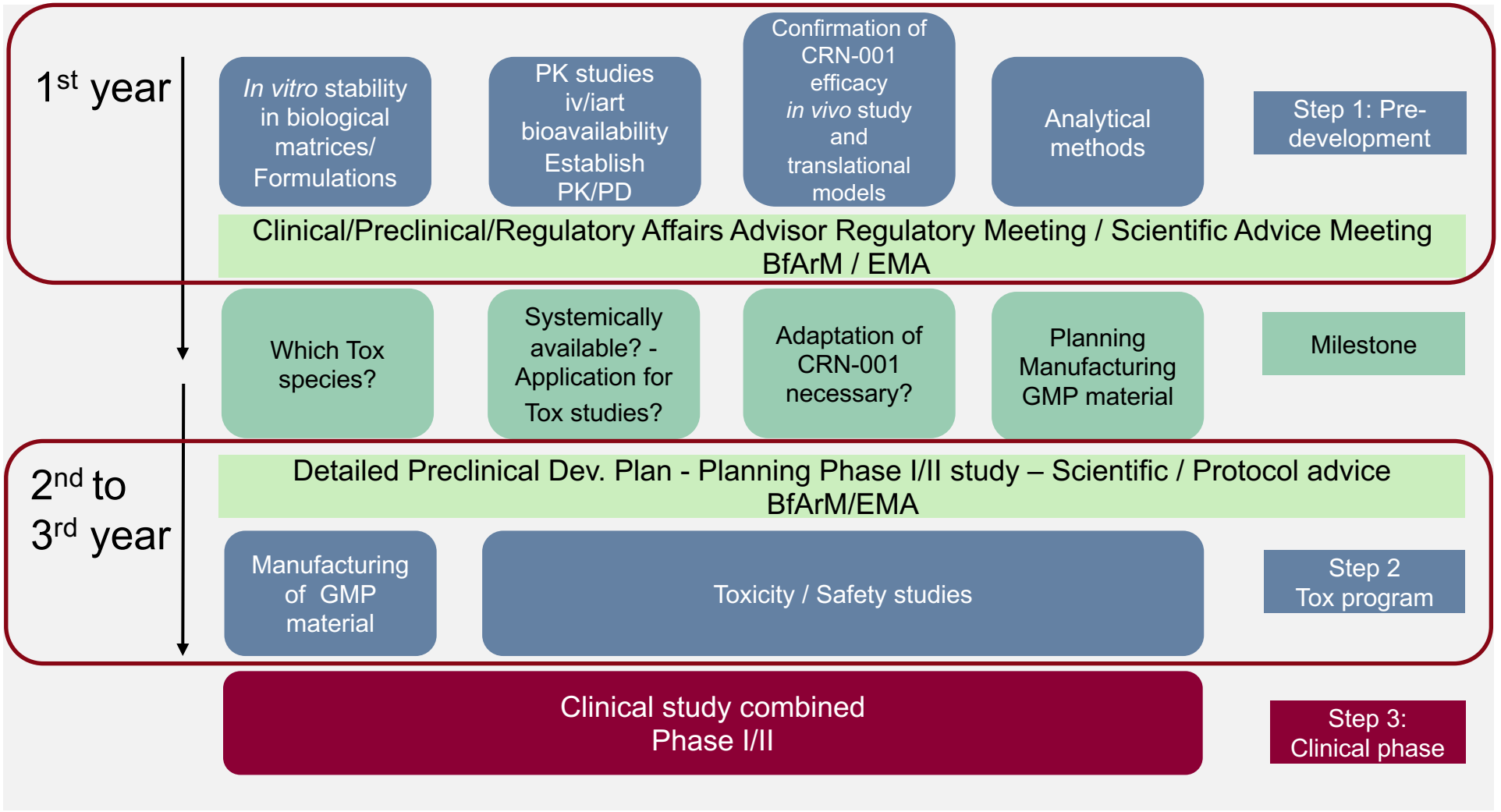
As an IPO or with a joint venture and in cooperation with pharma enterprises

Winner of the
Boehringer Ingelheim Innovation Award 2023

Finalist in the Science Start-ups /
Falling Walls Venture / Global Call 2023

WORK PLAN

Overview



€ 1 - 1.5 M

€ 2 - 5 M*

Possible IPO or joint venture with Pharma Corporate

*Depending on the results of Step 1 and the discussion with the authorities

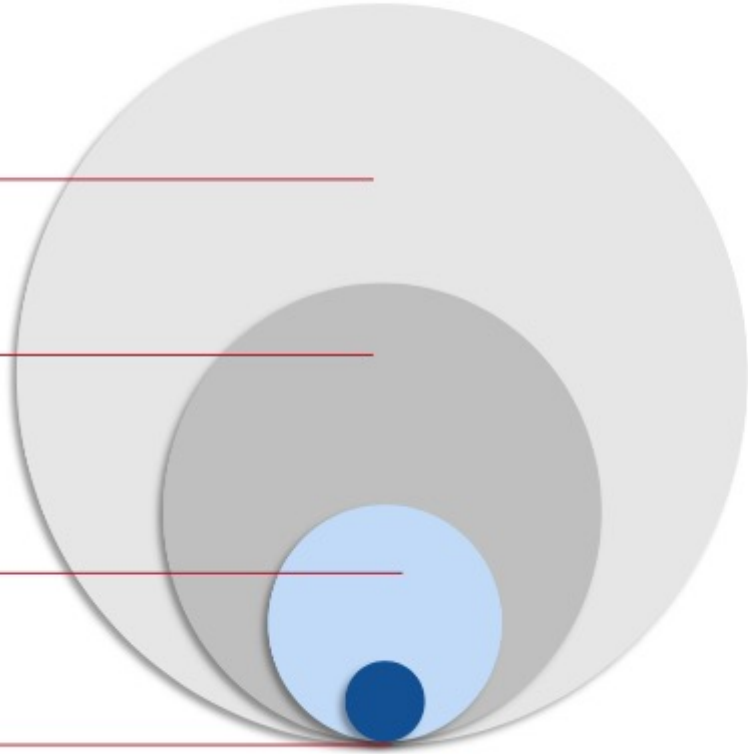
ESTIMATION OF MARKET SIZE AND TURNOVER

Total addressable market: >650M patients with OA world-wide

Addressable market: >100M patients with OA in major markets (US, EU, JP)

Serviceable available market: patients with OA pre-dominantly in one or two joints (>20M patients in major markets)

Serviceable obtainable market: Subgroup characterised by high miR-574-5p levels and bone phenotype biomarkers



Projected sales assuming

- **2%** share of addressable market: >2M patients
- **€100-300** per injection
- **4 injections** per year

→ **€ 800 M-2.4 Bn** per year

OUR TEAM

Complementary team of experts in drug development and business management

PD DR. MEIKE SAUL

CSO

- Discovered miR-574-5p as a therapeutic target
- Conceived the process of CRN-001 development

DR. DOROTHEE KRONE

CEO/CFO

- Expert in business management
- Founding of a start-up and successful merger
- Expert in preclinical/clinical analytics and ADME (ASTA Medica)

PD DR. AIMO KANNT

Scientific Advisor

- Expert in drug research and development (Sanofi)
- Expert in pharma project management

PROF. DR. DIETER STEINHILBER

Scientific Advisor

- Expert in pharmacology
- Identified with Dr. Saul the regulatory mechanism of miR-574-5p on PGE_2 synthesis
- Founding of a start-up and successful exit

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