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Heptammune: a first-in-class biologic immunomodulator against autoimmune diseases

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Institut d'Investigació Biomèdica de Bellvitge

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4. Partnering Opportunities

1. Our Institution: IDIBELL

IDIBELL is a research centre that integrates the **biomedical research of the Bellvitge University Hospital (HUB), the Catalan Institute of Oncology (ICO), and the University of Barcelona in the Bellvitge Campus (UB)** and the **Viladecans Hospital (HV),** located in south Barcelona

Our mission is to promote and facilitate **translational research of proven scientific excellence**, that integrates innovation and the technological transfer in biomedicine, **generating value for continuous improvement of health** and living standards

Among other facilities, IDIBELL has an animal facility, proteomics unit, genomic lab, molecular interactions arm, biobank, biostatistics department and clinical research and clinical trials support

2. Our goal: PurPose Biotherapeutics

Project origins

IDIBELL Institut d'Investigació Biomèdica de Bellvitge

- Immune-inflammatory Processes and Gene Therapeutics group from IDIBELL
- 20+ years of experience in the field of inflammation
- Scientific team with more than 60 scientific publications in high-impact journals
- More than 20 translational research projects
- Seven patents licensed

Company

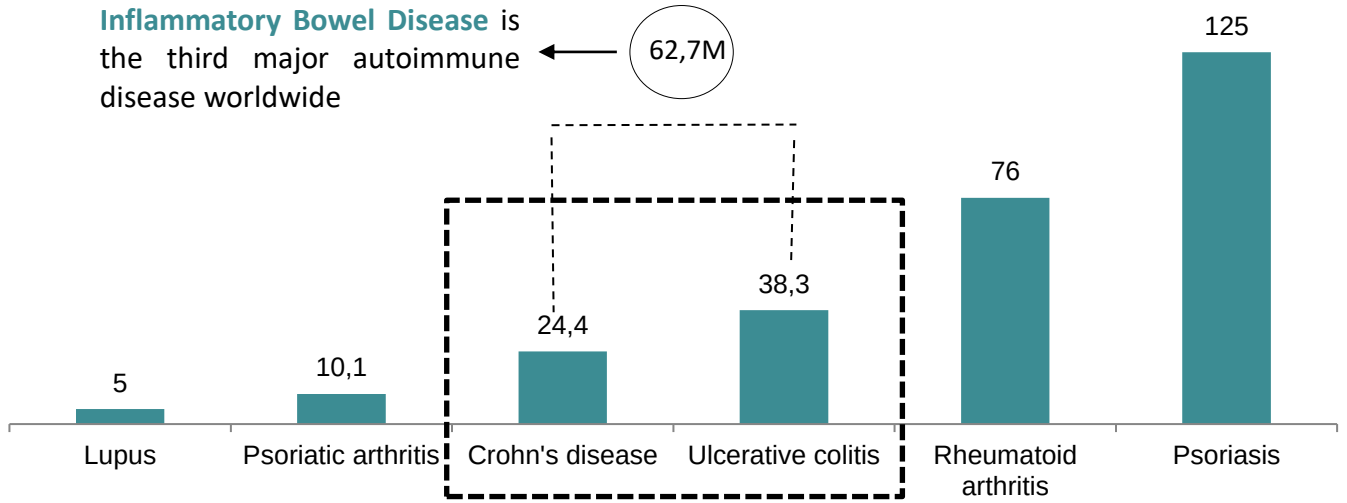
PurPose Biotherapeutics

We envision **PURPOSE** as a Life Sciences company focused on advancing revolutionary therapies for autoimmune diseases

- Company's technology: **development of first-in-class biologics showing high efficacy and no side effects**
- Novel immunomodulatory mechanism: **resetting the immune system and resolving inflammation**
- The company initially **targets Ulcerative Colitis and Crohn's Disease.** Pipeline expansion into additional indications

- ✓ There are **more than 100 different types of autoimmune diseases**, affecting approximately 5-10% of the population in Europe and North America
- ✓ In Europe alone, **57–70 million people** are affected by auto-immune diseases, that's approximately 1 in 10 people – equivalent to the entire UK population

Global prevalence estimates of common auto-immune diseases, million people

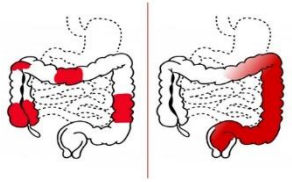


The World Incidence and Prevalence of Autoimmune Diseases is Increasing

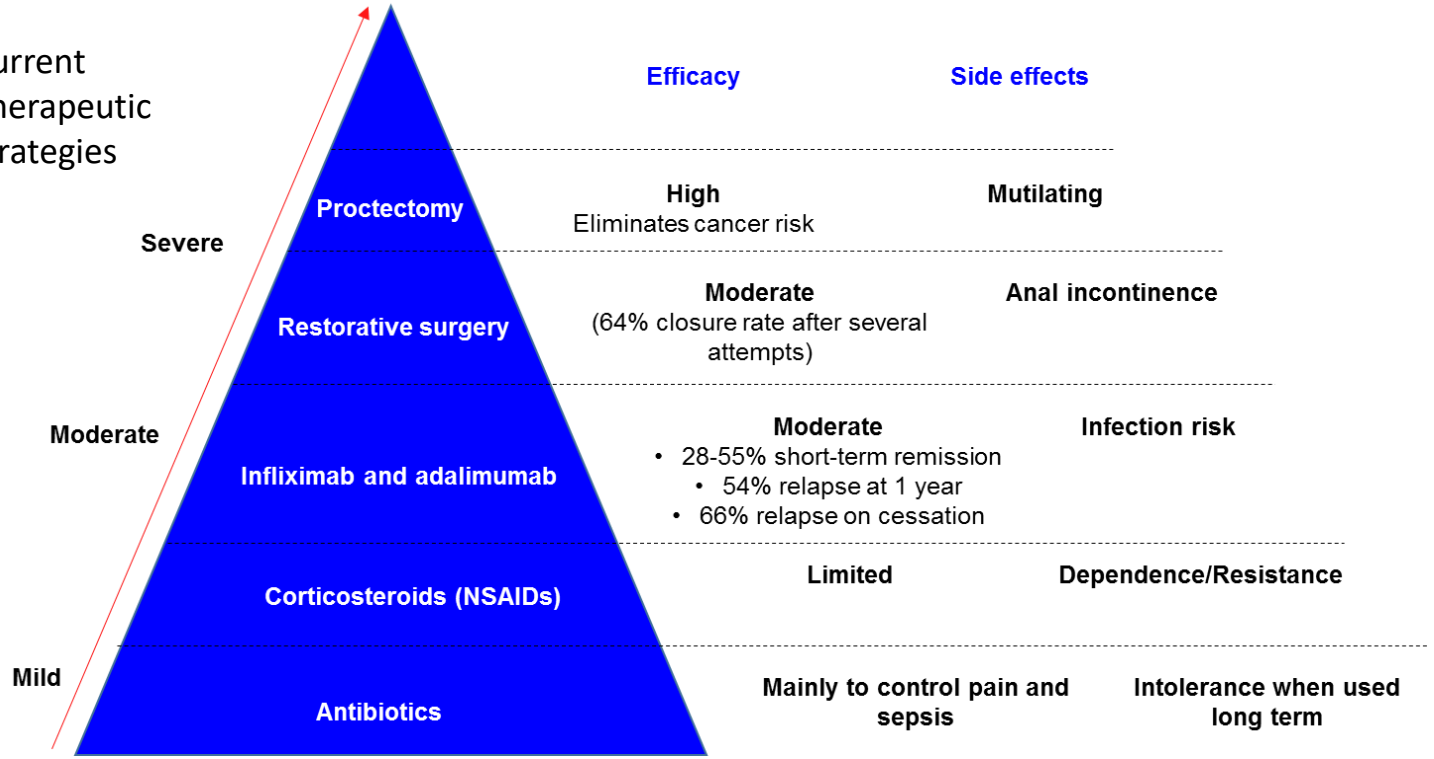
3. Our Product: Heptammune (PRP6-HO7)

MARKET NEED

- ✓ IBD has become a **global disease with accelerating prevalence (62M and increasing)**
- ✓ Two chronic inflammatory disorders of the gastrointestinal tract, **Crohn's disease (CD) and ulcerative colitis (UC)**
- ✓ Life long, relapsing disorders of unknown etiology and **no cure**



CD **UC**



Limitations of Current drugs

- **Limited efficacy**
- **Low safety profiles**
- **Low patient adherence to treatment**
- **Toxicity** (treatment-emergent adverse events)
- **30-40% of patients discontinue the treatment**

Unmet need !!!

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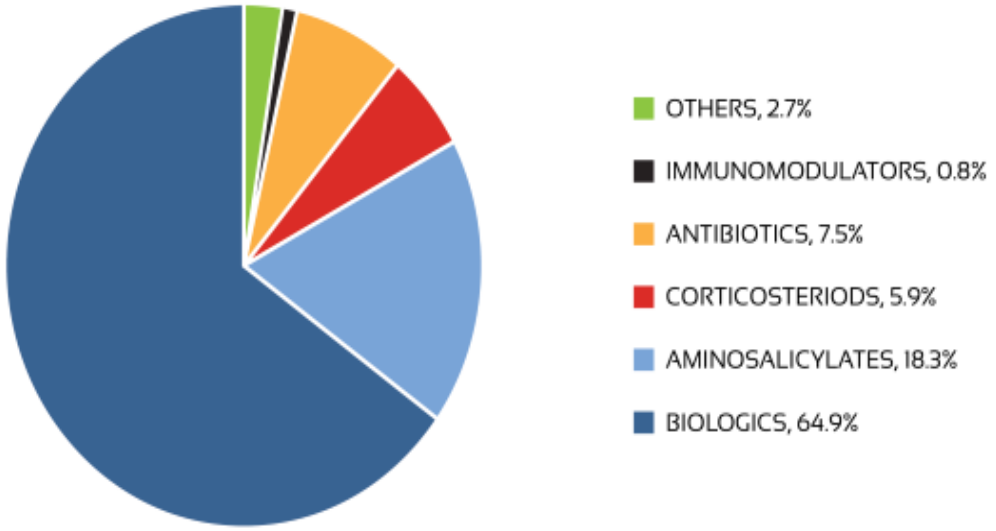
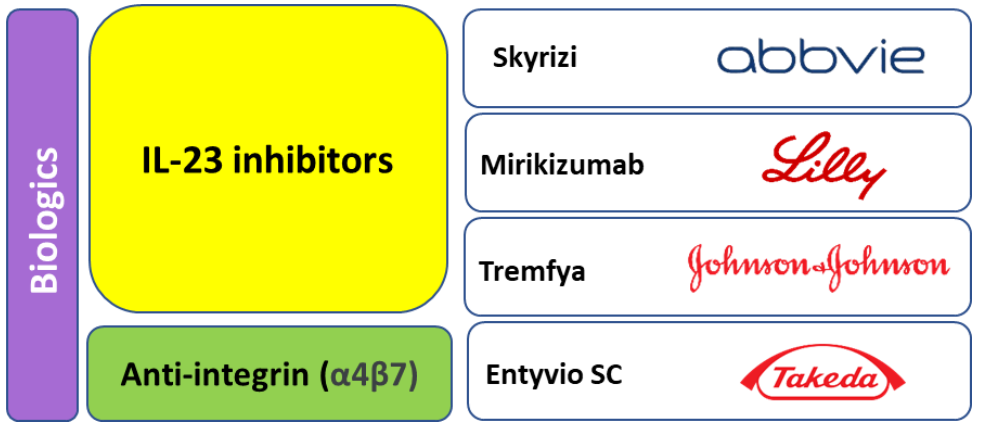
- ✓ **Globally**, about **7.0 M citizens** are affected by **IBD**. (**2.5-3.0 M in Europe**, with a **direct healthcare cost of 4.6-5.6 Bn €/year**)
- ✓ The global **IBD treatment market** is estimated to grow at **CAGR above 4.1 %** over the forecast time frame **2019 to 2026**
- ✓ IBD drugs market is expected to reach **$34.5 Billion in 2031**

World IBD drugs market shares by drug class:



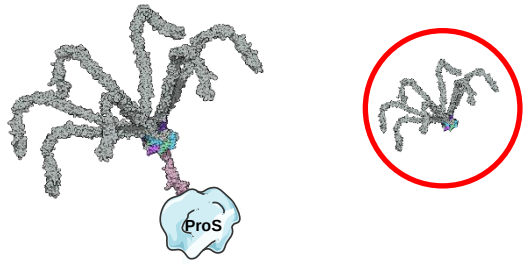
Leading companies that hold major market shares in the **IBD biologic drug industry**:



INNOVATIVE MECHANISM OF ACTION

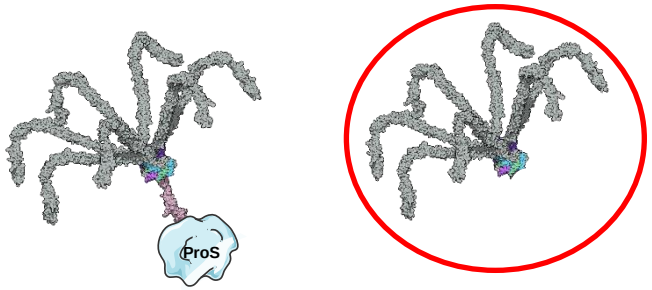
PRP family: C4BP-based first-in-class immunomodulators for autoimmune diseases management

Pysiological conditions:

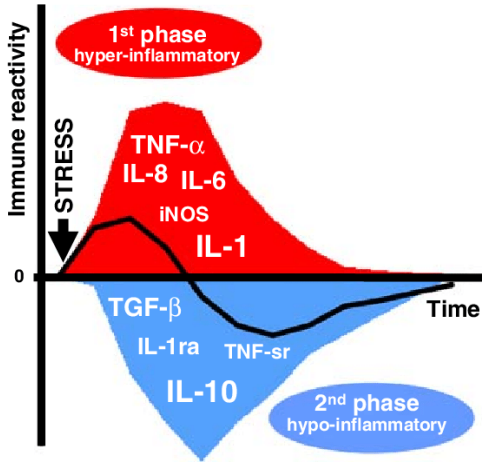


C4BP (β+) (PRP-HE8) (80) : C4BP(β-) (PRP-HO7) (20)

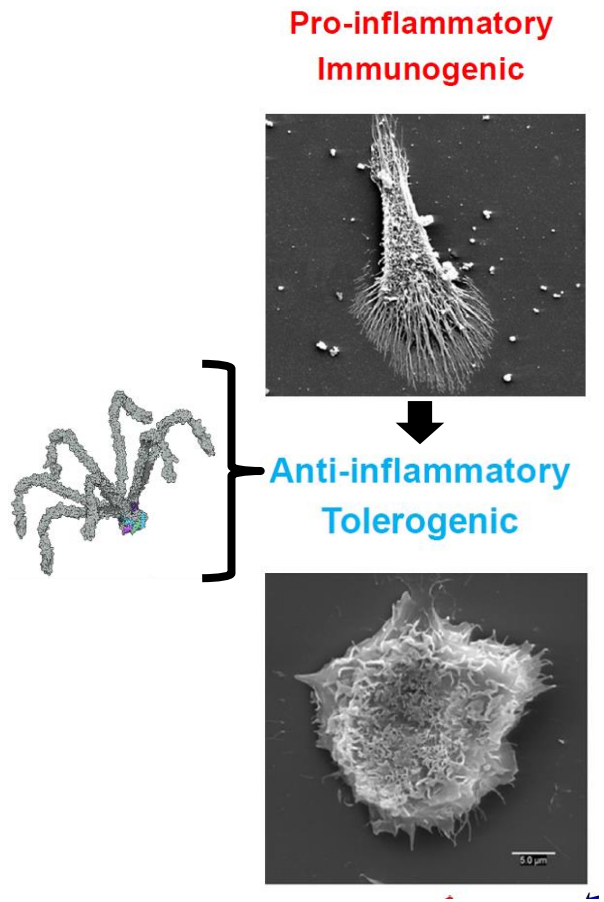
Strong pro-inflammatory conditions (poly-traumatism, sepsis):



C4BP (β+) (PRP-HE8) (50) : C4BP(β-) (PRP-HO7) (50)



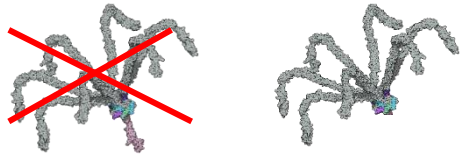
PRP family novel MoA: Immunomodulators able to "*reprogram*" key cells orchestrating the immune response



C4BP(β-): when complement regulation is not enough to control excessive inflammation

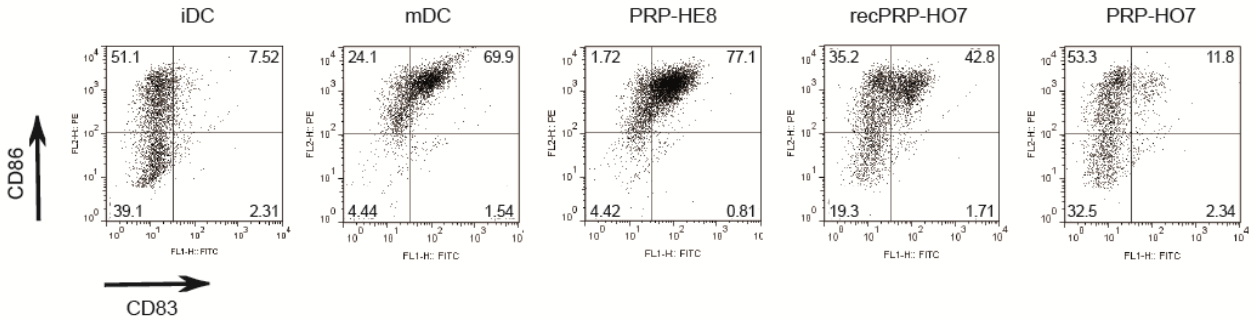
PRP-HO7 (C4BP(β-) isoform induces an anti-inflammatory, tolerogenic state in dendritic cells

PRP-HE8 (C4BP(β+))

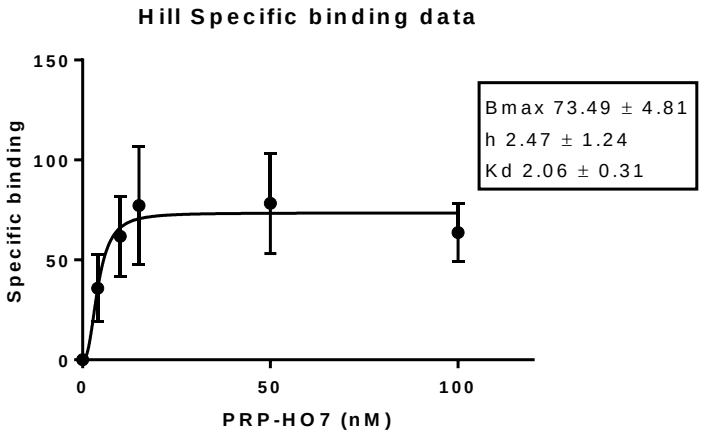


PRP-HO7 (C4BP(β-))

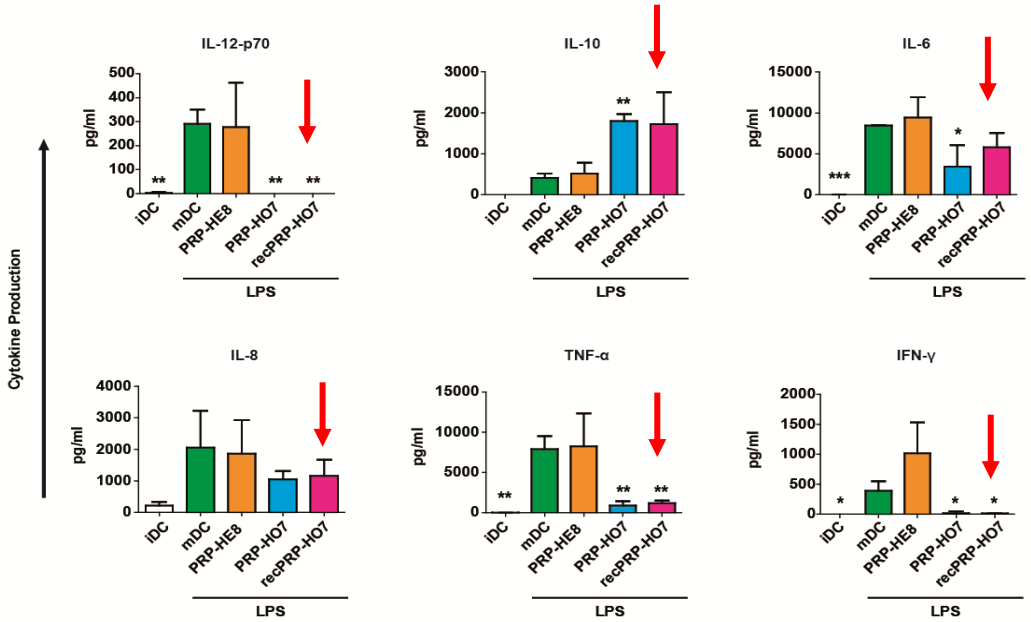
Surface marker expression:



Target binding:

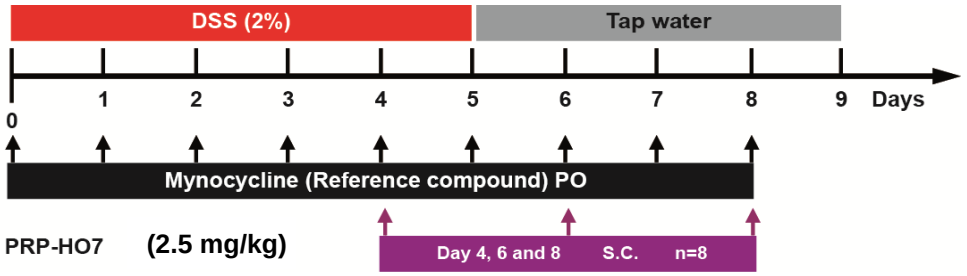


Cytokine production:

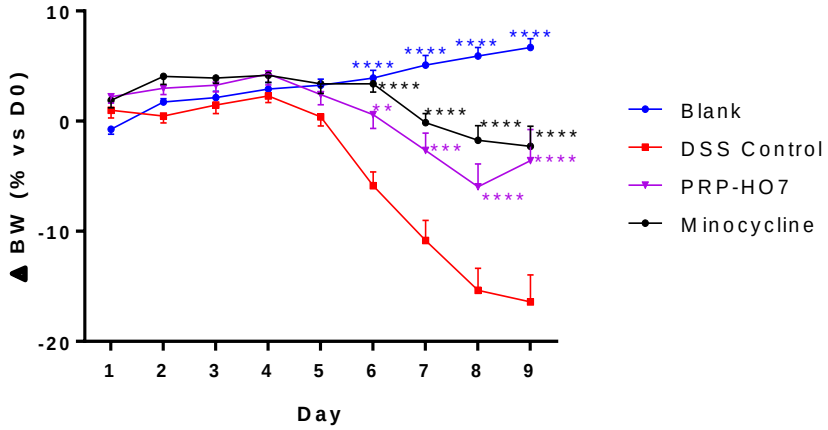


PRP-HO7 in a mouse IBD model

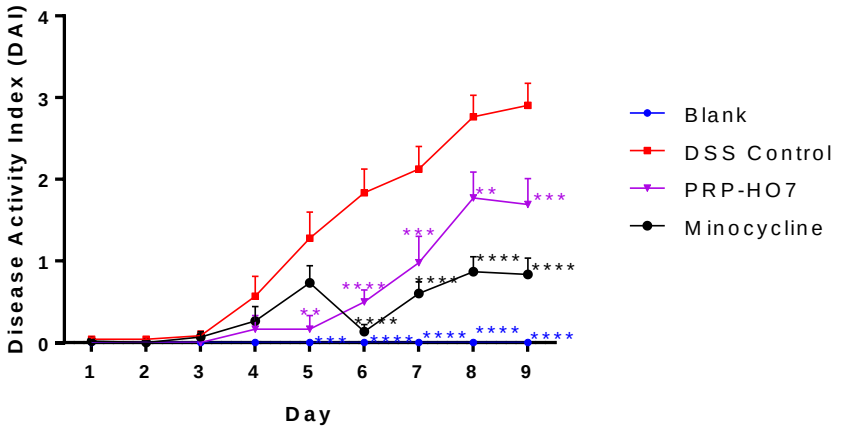
Male C57BL/6
7-8 weeks old



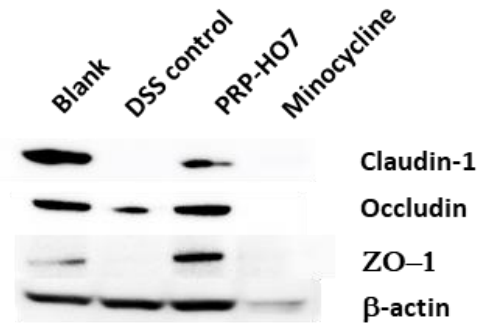
Body weight loss



Colitis evolution

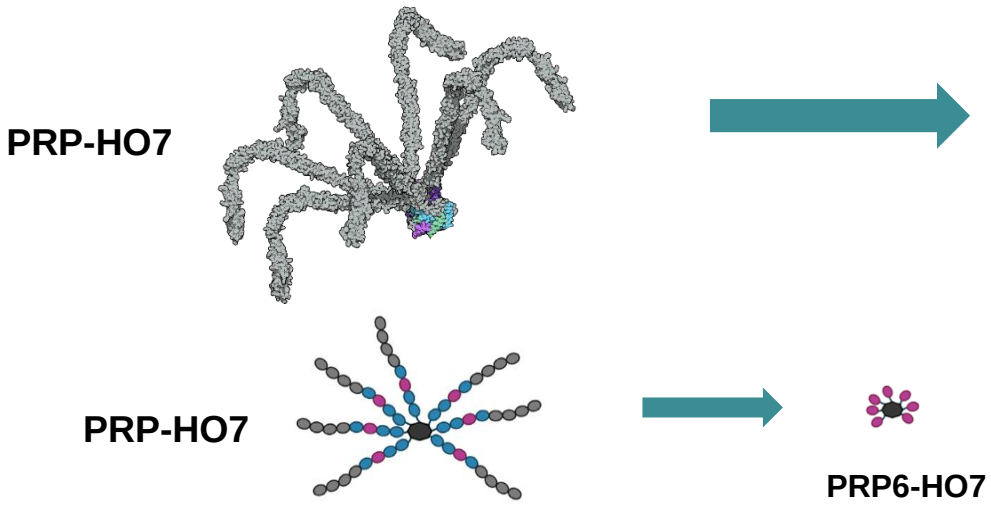


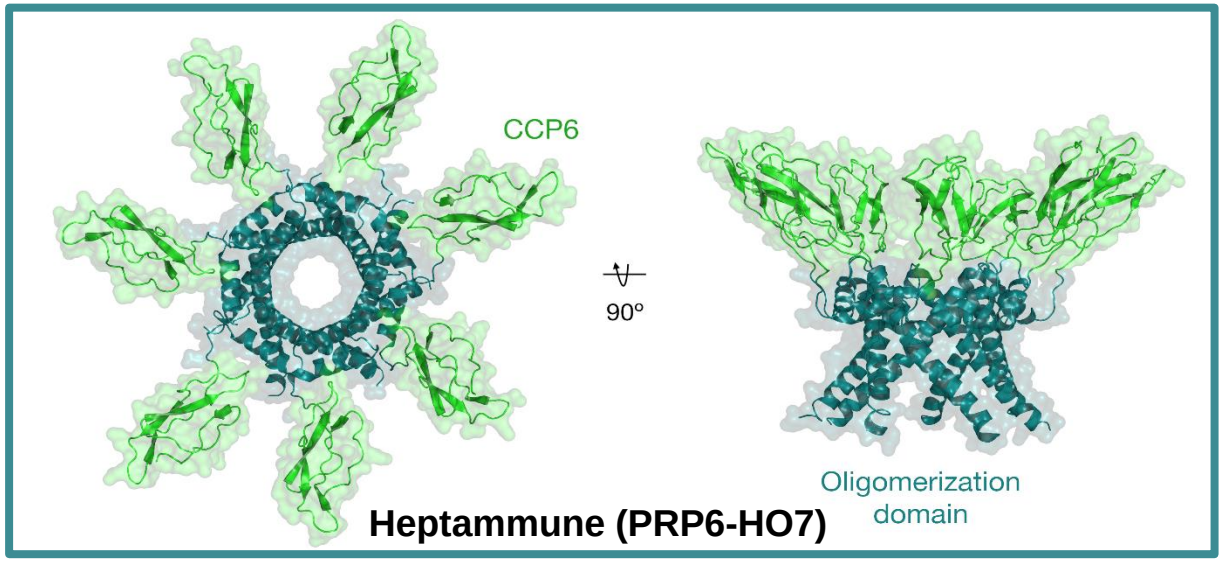
Intestinal epithelium integrity



3. Our Product: Heptammune (PRP6-HO7)

INNOVATIVE MECHANISM OF ACTION

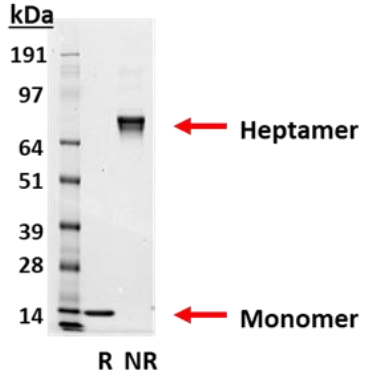




- **Heptammune:**

- ✓ First-in-class biologic
- ✓ Halts inflammatory pathology, restores immunological tolerance and achieves long-term remission of established autoimmune pathologies
- ✓ MoA: Immunomodulation through immune cell "metabolic reprogramming", not immunosuppression
- ✓ 3 times higher efficacy compared to anti-TNF biologics
- ✓ 10 times more specific than CYP (better safety profile)

PRP6-HO7 production



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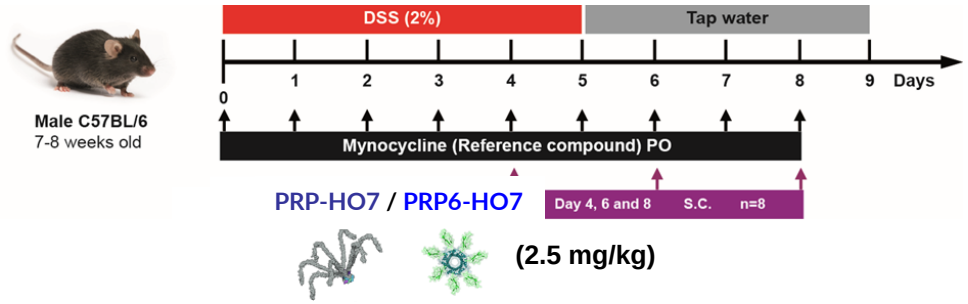
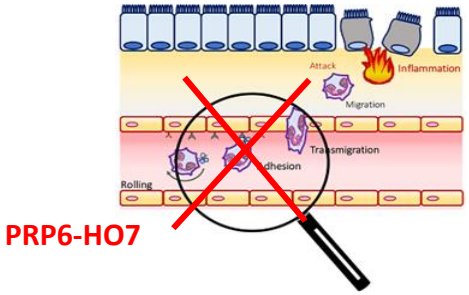
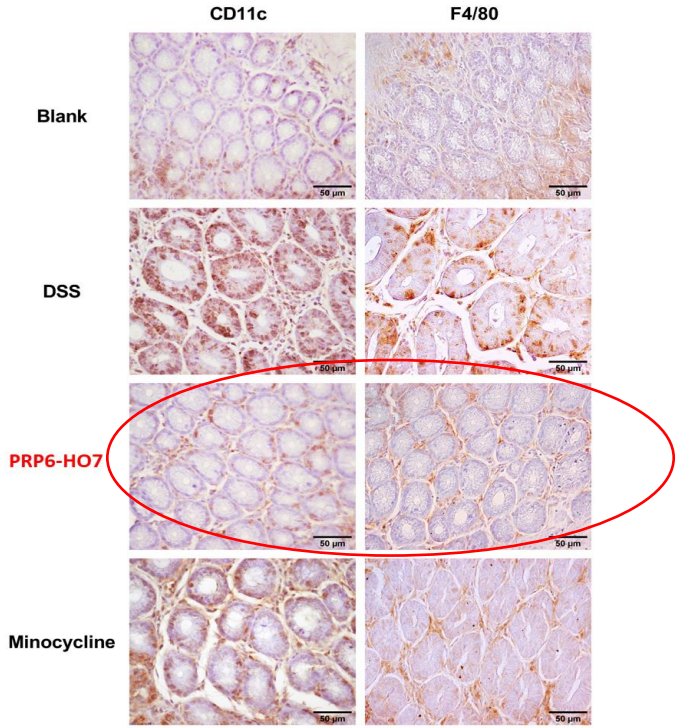
Therapeutic potential of Heptammune in the IBD model: DSS-colitis

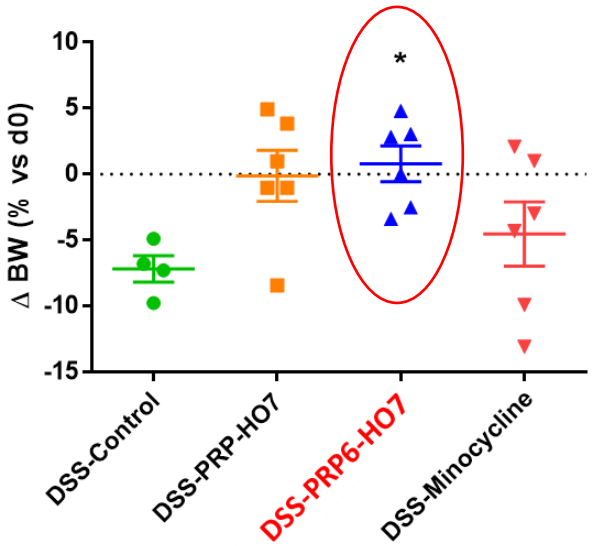


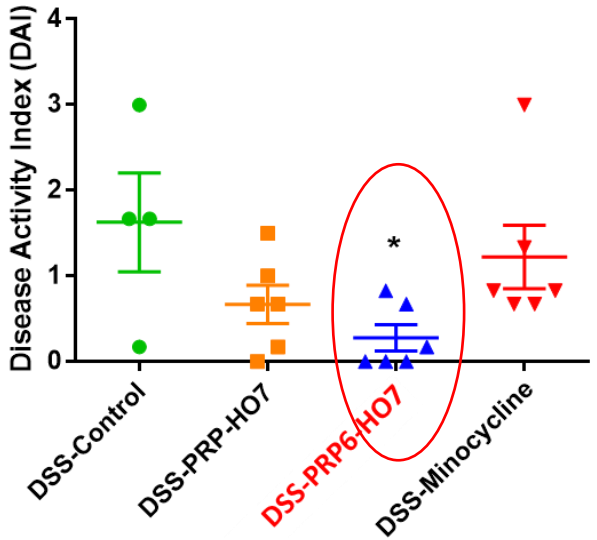


Immune cell infiltration



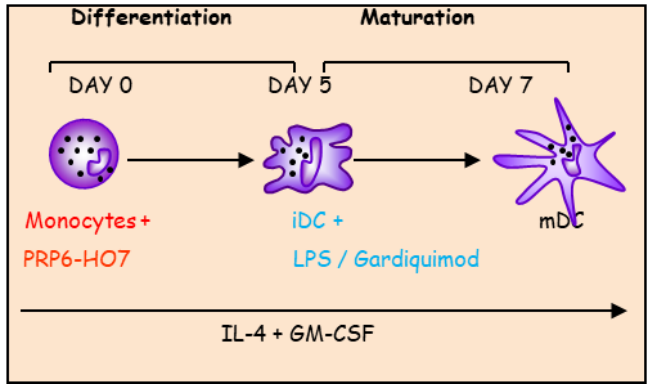
Colitis evolution (day 9)



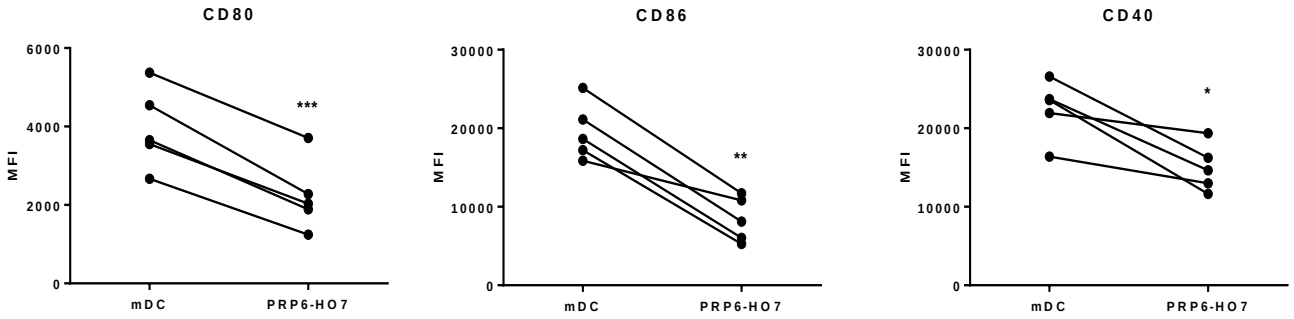


Heptammune as a biomarker for patient stratification and treatment monitoring

Technology:
Easy blood test and exploratory assay differentiating PBMC-isolated monocytes from IBD diagnosed patients and monitoring inflammatory markers after Heptammune *in vitro* treatment



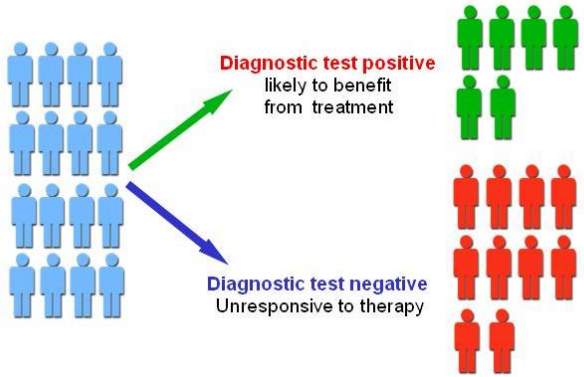
LPS activation



Development status:
Validated in blood samples from Crohn's disease and ulcerative colitis patients

Opportunity: Towards "precision" medicine

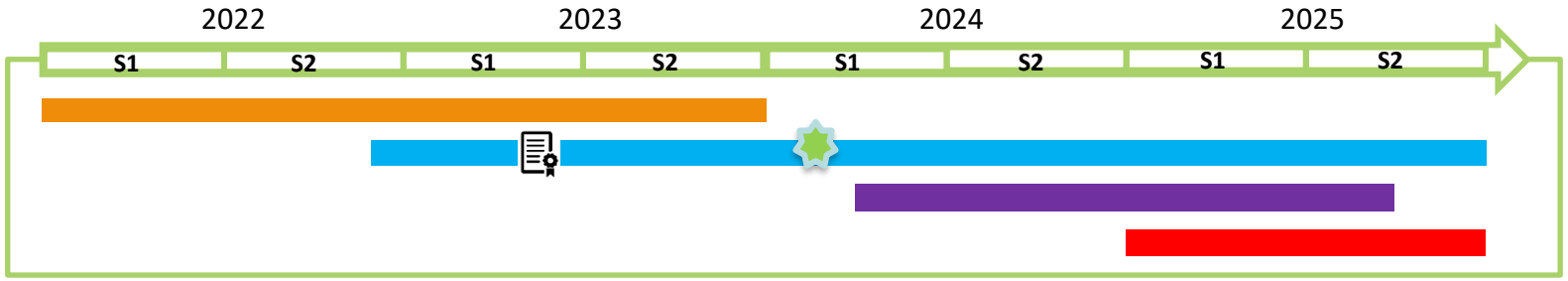
- Predictive efficacy end-point assay for clinical trials to select "responders" from non-responders
- Immunomonitoring and follow-up disease progression in Heptammune-treated IBD patients



Valorisation Plan

How much?	0,4 M €		2,6 M €	2,4 M €
For What?	Non regulatory preclinical trials	Project management	GMP production and scale-up and purification	Regulatory Preclinical studies
To achieve?	Efficacy in a superior *in vivo* model	File new patent (3 IP already filed) Spin off constitution	Manufacturability (outsourced)	Safety and Pharmacology (outsourced)

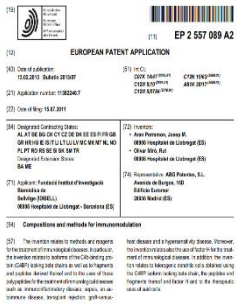
When?



3. Our Product: Heptammune (PRP6-HO7)

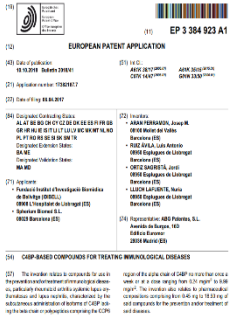
INTELLECTUAL PROPERTY

EP11382240



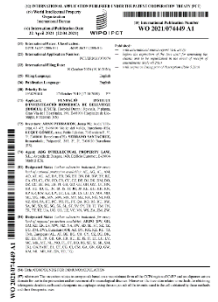
- **Priority date:** 15/07/2011
- **Name**: Compositions and methods for immunomodulation
- **Status**: GRANTED in Europe (Switzerland, Germany, Denmark, Spain, France, UK, Italy, Norway, Poland, Sweden, Turkey), Japan, USA, Australia and Canada
- **Ownership**: IDIBELL (100%)
- **Inventor(s)**: Josep M. Aran and Rut Olivar
- **Scope:** medical use of C4BP isoforms for immunological diseases

EP17382187



- **Priority date:** 06/04/2017
- **Name**: C4BP-based compounds for treating immunological diseases
- **Status**: Currently in national phases in Europe, Japan, Canada, USA and Australia
- **Ownership**: IDIBELL (100%)
- **Inventor(s)**: Josep M. Aran, Luis Ruiz, Jordi Ortiz and Nuria Lluch
- **Scope:** medical use of the C4BP (β-) isoform administered s.c. at a range of doses

EP19382910



- **Priority date:** 17/10/2019
- **Name**: Compositions for immunomodulation
- **Status**: Patent pending in Europe, Japan, Canada, USA and Australia
- **Ownership**: IDIBELL (100%)
- **Inventor(s)**: Josep M. Aran, A. Luque and I. Serrano
- **Scope**: Product claims. Compounds based on a recombinant form of CCP6 region of C4BP (PRP6-HO7)

Potential uncertainty drivers:

Technology.-

Lower efficacy than expected:

- Predictive efficacy endpoint assay for clinical trials developed
- *In vivo* safety and efficacy have been successfully demonstrated in systemic lupus erythematosus, colitis and rheumatoid arthritis mouse models
- Administration in combination with other treatments (drugs, biologics,…) in patients who do not respond to a single therapy
- Possibility to perform pharmacological therapy (direct Heptammune administration), or cell therapy using ex vivo Heptammune-conditioned DCs

GMP Scaling up.-

We have already designed a candidate to be produced in E. coli bioreactors, being fully scalable. Possibility to produce Heptammune in a eukaryotic expression system

Market.-

Although big pharma companies are controlling the market, PurPose Biotherapeutics' pipeline products have a new and distinctive MoA that is of interest for big pharma to consolidate its market share

From the opportunity to the market: Heptammune - optimal cost/benefit

- Market application: Biotechnology / Pharmaceuticals

- Cooperation type:
  - Joint further development (adaptation to specific needs):
    Pre-clinical and clinical co-development
  - License agreement
  - Funding opportunities

The Team

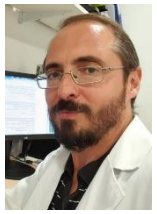
"No one can whistle a symphony. It takes an orchestra to play it" *Halford E. Luccock*

Drug development

M. Cristina Vega (CIB-CSIC)

Clinical collaborators

Jordi Guardiola (CSUB-IDIBELL)



Francisco Rodriguez-Moranta (CSUB-IDIBELL)

Core research team

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Josep M. Aran

External advisors

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Peter F. Zipfel (Hans Knöll Institute, Germany)

Business advisors

Maribel Berges (UPF-BSM / Affirma Biotech)

Laia Traveset (IDIBELL)

Mario De la Cuesta (IDIBELL)

PurPose Biotherapeutics

Immunomodulation for autoimmunity

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