PRP-HO family: novel biologic immunomodulators

PurPose Biotherapeutics

IDI BELL

Madrid, 29 de octubre de 2019

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   g) Pitfalls & Risks to be considered
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1. The Institution

IDIBELL, biomedical and biotechnology cluster in the life and health sciences sector

biopol'H

ICO
Institut Català d'Oncologia

UNIVERSITAT DE BARCELONA

IDIBELL
Institut d'Investigació Biomèdica de Bellvitge

Bellvitge Hospital

Hospital de Viladecans

Ajuntament de L'Hospitalet

2. The Research Group

"No one can whistle a symphony. It takes an orchestra to play it"

Halford E. Luccock

PIITG Group
(Molecular Genetics Lab- IDIBELL)

Ana Luque

Inmaculada Serrano

Javier Checa

Alejandro Cuenca

Marta Guevara

Bryan Herrera

Andreja Anžič

Zhara Mohammadkarimi

COLLABORATORS AND ADVISORS:

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(Nephrology Unit, CSUB-IDIBELL)

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(CIB, CSIC, Madrid)

Prof. Anna M. Blom
(Lund University, Sweden)

Prof. Peter F. Zipfel
(Hans Knöll Institute, Germany)

GOBIERNO DE ESPAÑA MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES

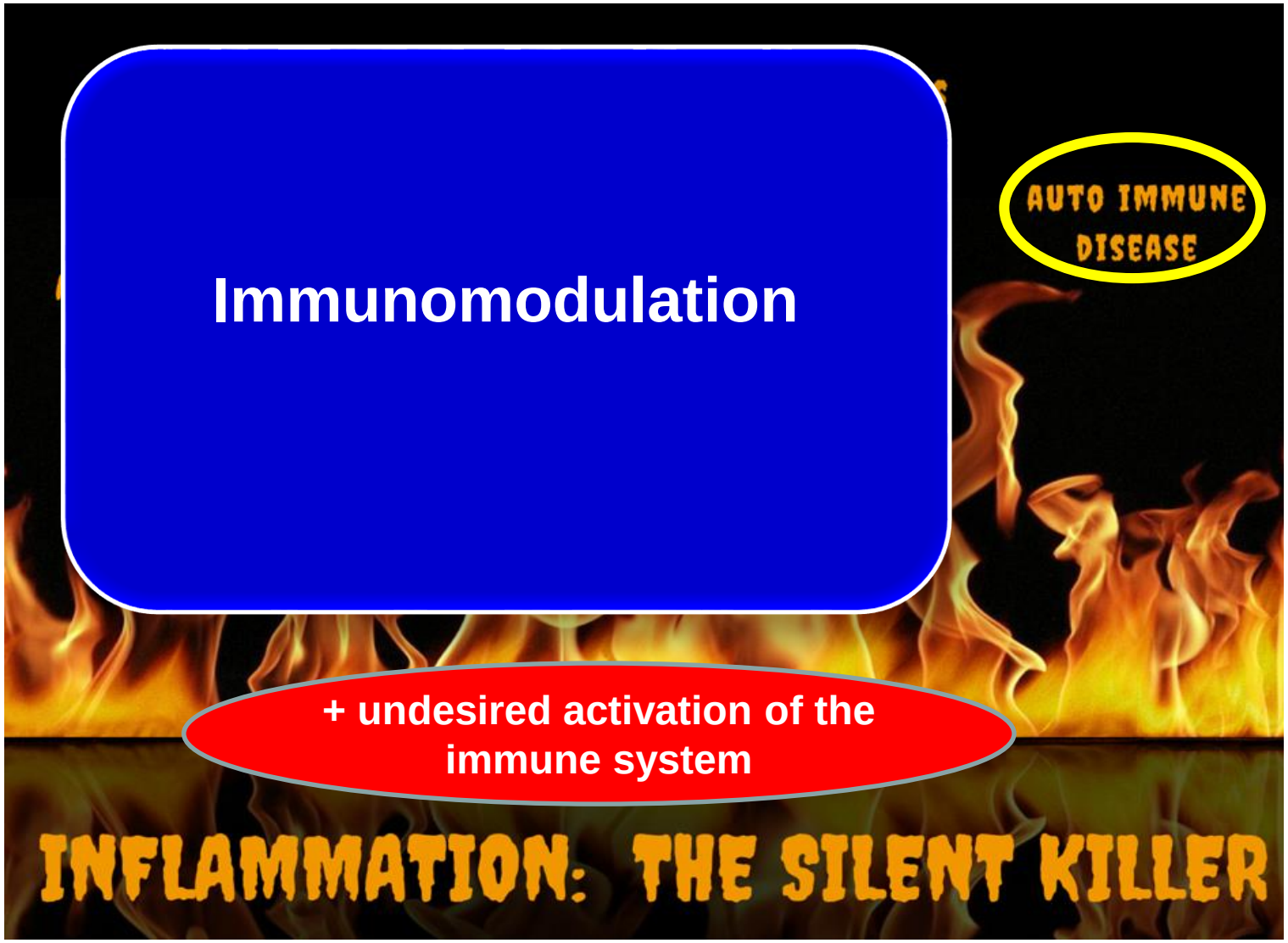
MEDICAMENTOS INNOVADORES
Plataforma Tecnológica Española

IDI BELL

PurPose Biotherapeutics

farmaindustria

3. The Product (Background)



3. The Product (Target Indications)

Autoimmune Diseases

Brain
Multiple Sclerosis
Guillaun-Barre Syndrome
Autism

Thyroid
Thyroiditis
Hashimoto's Disease
Graves' Disease

Blood
Leukemia
Lupus Erythematosus
Hemolytic Dysglycemia

Bones
Rheumatoid Arthritis
Ankylosing Spondylitis
Polymyalgia Rheumatica

GI Tract
Celiac's Disease
Crohn's Disease
Ulceratic Colitis
Diabetes Type I

>100 Autoimmune Diseases

Muscles
Muscular Dystrophy
Fibromyalgia

Nerves
Peripheral Neuropathy
Diabetic Neuropathy

Lung
Fibromyalgia
Wegener's Granulomatosis

Skin
Psoriasis
Vitiligo
Eczema
Scleroderma

3. The Product (Differential Features Facing the Market)

GLOBAL
AUTOIMMUNE
DISEASE
THERAPEUTICS
MARKET

OPPORTUNITIES AND FORECASTS, 2018-2025

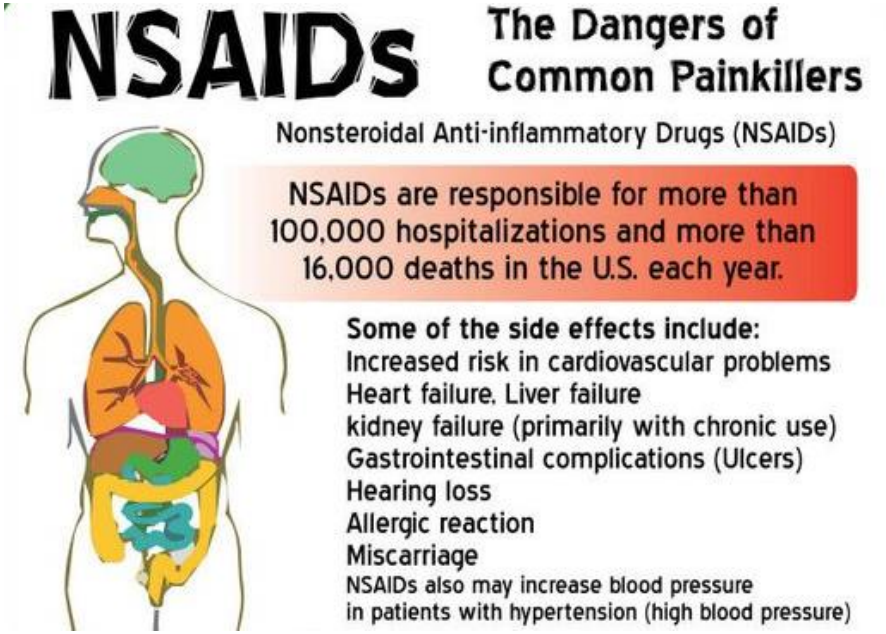
Global Autoimmune Disease Therapeutics market is expected to reach **$153,320 million** by 2025.

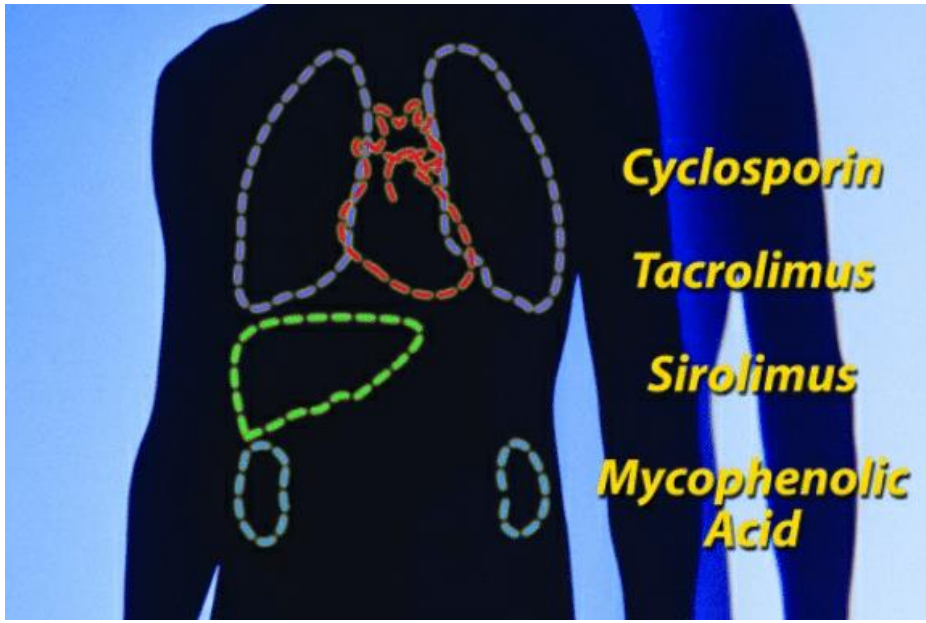
Growing at a **CAGR of 4.2%** (2018-2025)

©Allied Market Research

Present anti-inflammatory and immunosuppressive drugs

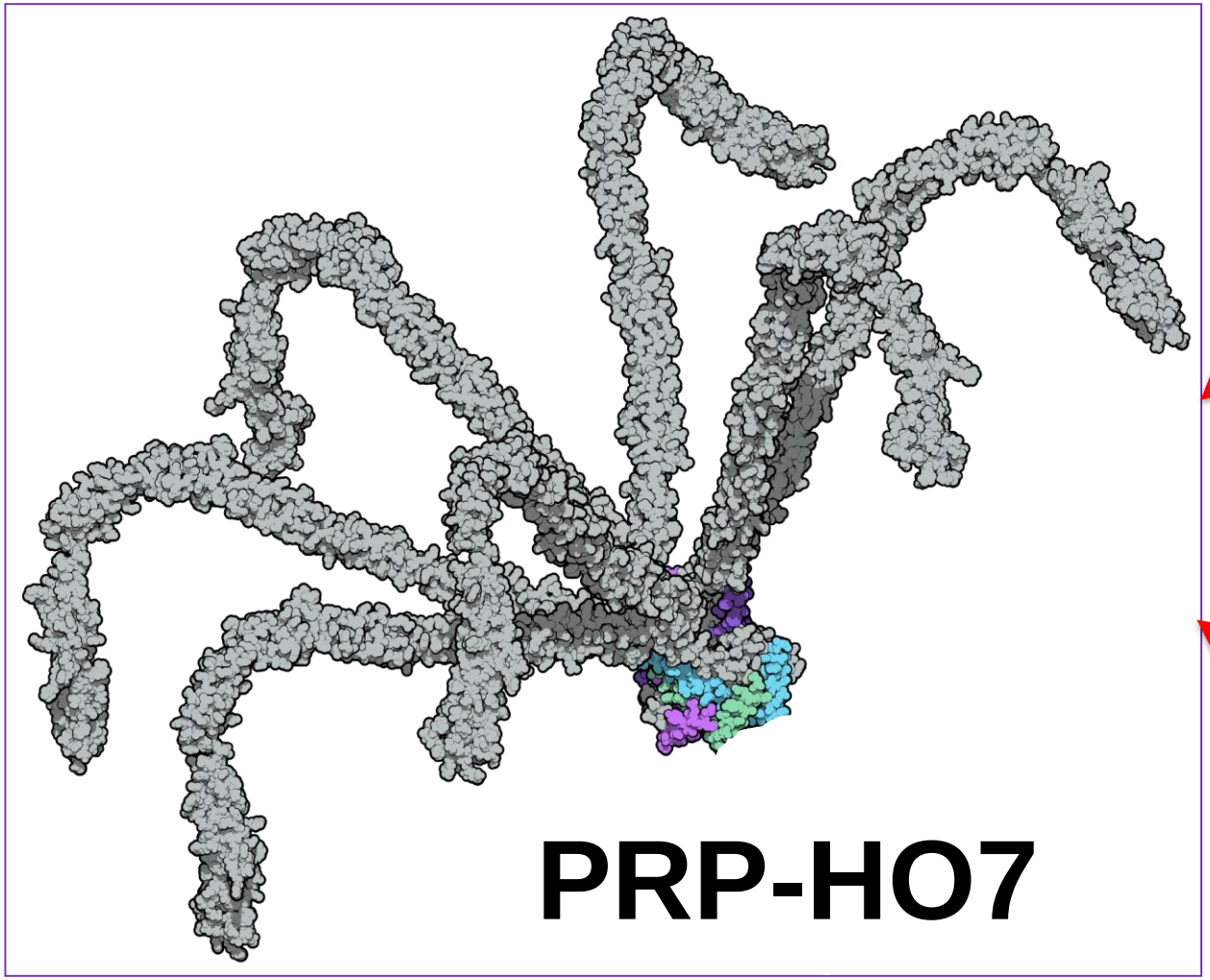
- **Low efficacy**
- **Relevant and non-specific adverse events**



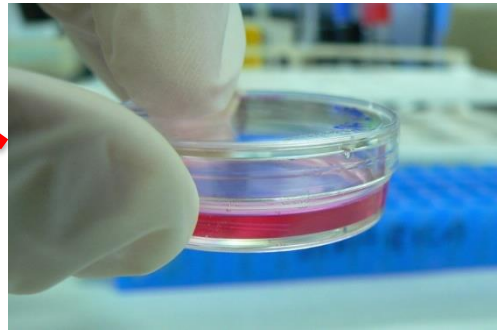


3. The Product (Innovative Mechanism of Action)

Hit molecule: Immunomodulatory naturally occurring blood protein



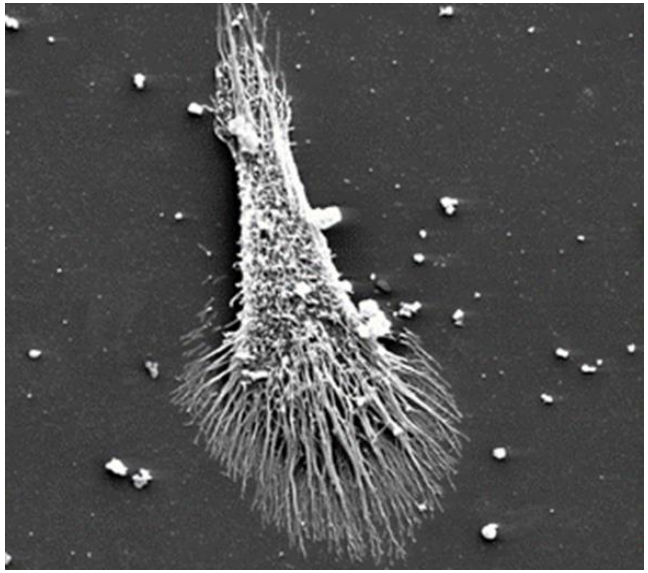
-Olivar et al. (2013) ***J Immunol.*** 190: 2857-72.
-Olivar et al. (2016) ***J Immunol.*** 196: 4274-90.
-Serrano et al. (2018) ***Front Immunol.*** 9: 892.
-Luque et al. (2019) ***Semin Cell Dev Biol.*** 85: 143-52.
-Luque et al. (2019) ***Kidney Int.*** In Press.

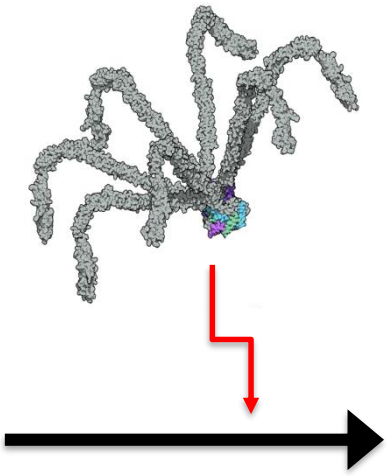


PRP-HO7 novel mechanism of action: Immunomodulator able to "*reprogram*" key cells orchestrating the immune response

Pro-inflammatory

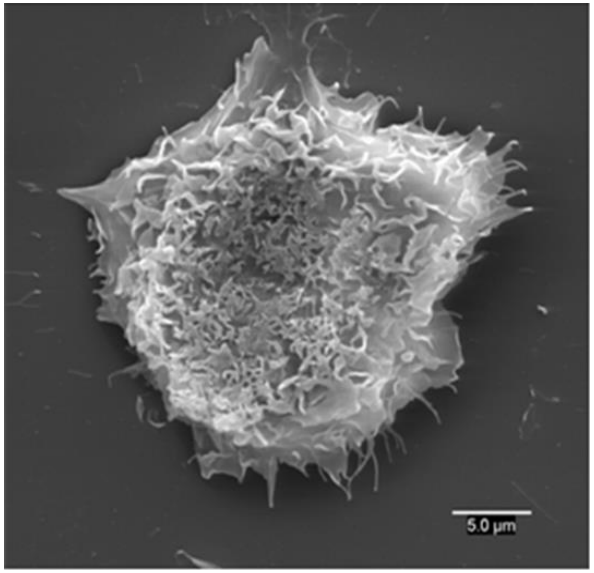
Immunogenic





Anti-inflammatory

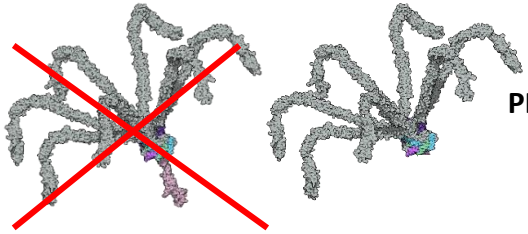
Tolerogenic



3. The Product (Innovative Mechanism of Action)

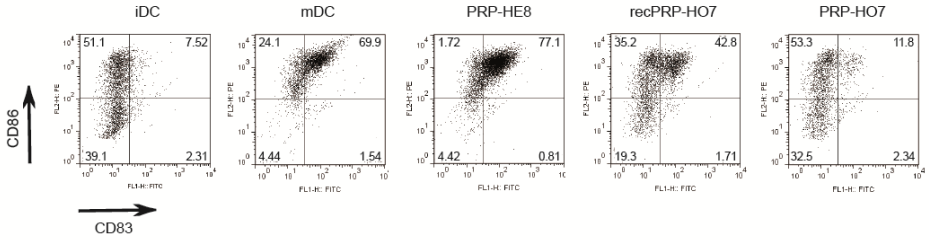
PRP-HO7 isoform induces a anti-inflammatory, tolerogenic state in dendritic cells

PRP-HE8

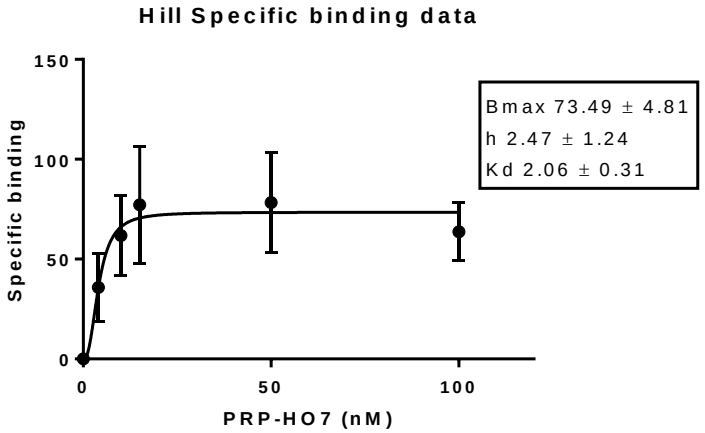


PRP-HO7

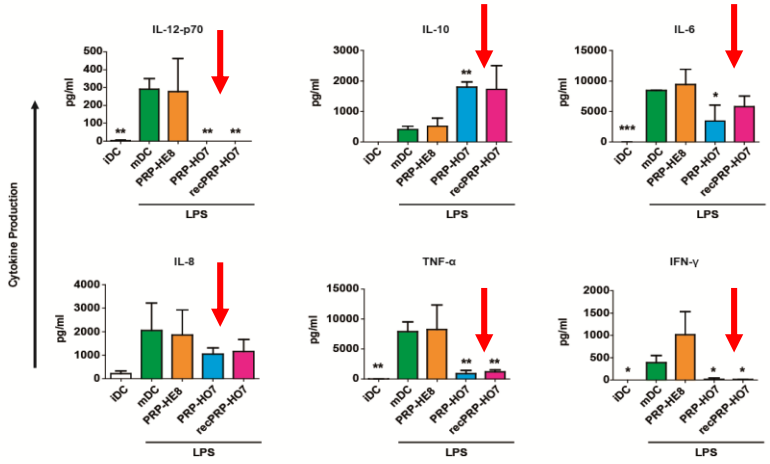
- Surface marker expression:



- Target binding:



- Cytokine production:



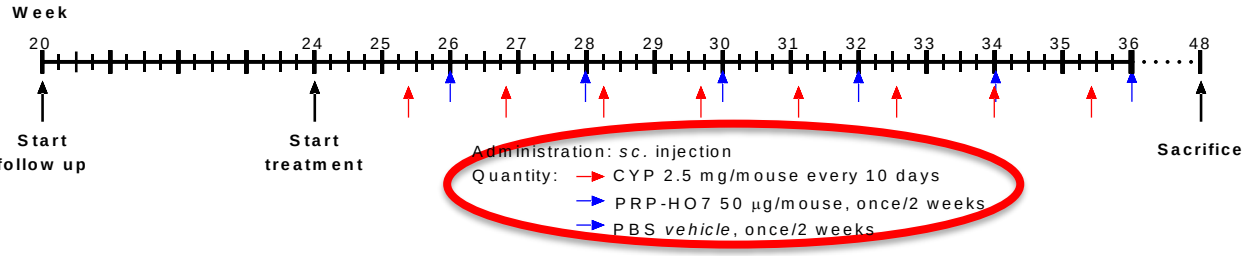
- Olivar et al. (2013) ***J Immunol.*** 190: 2857-72.

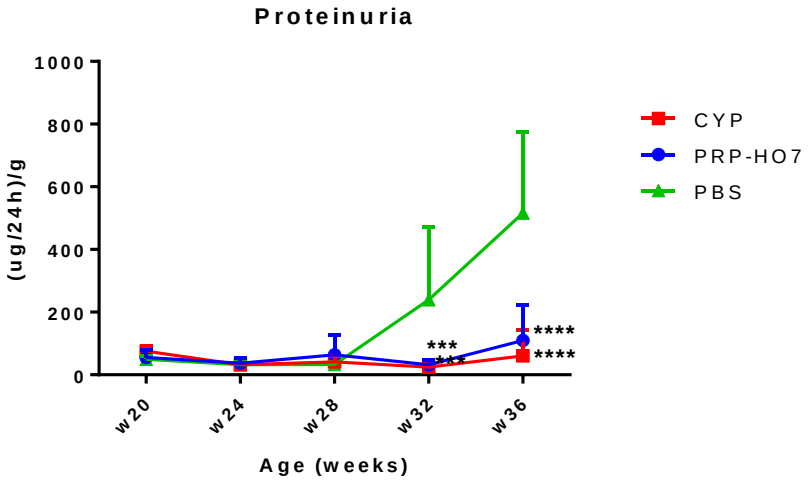
Pre-clinical efficacy (I)

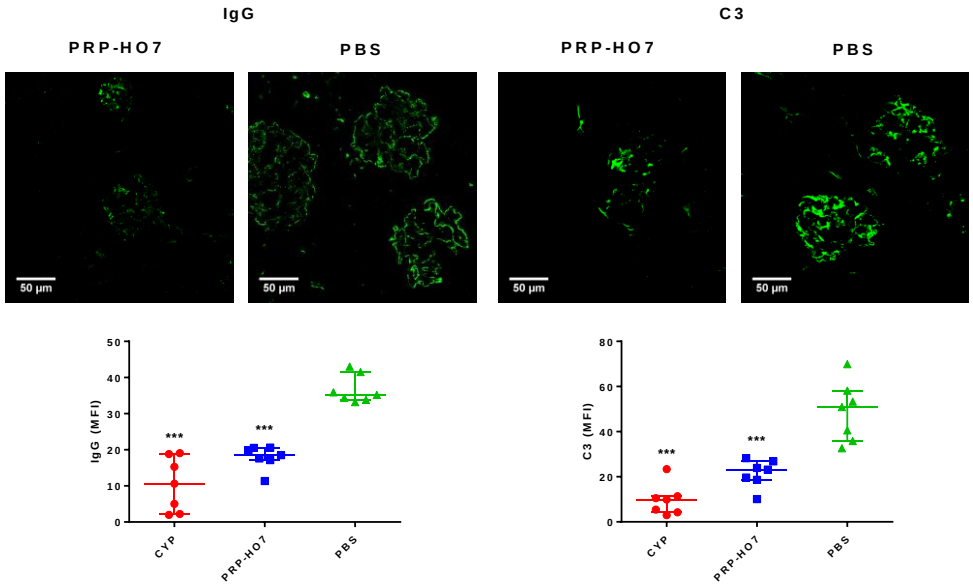
Systemic Lupus Erythematosus (SLE)

Lupus Nephritis

Female **NZBW F1**





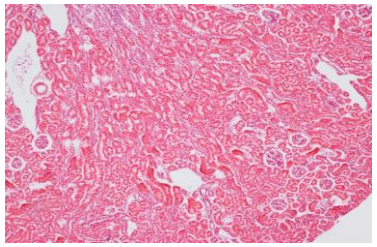


-Luque et al. (2019) ***Kidney Int.*** In Press.

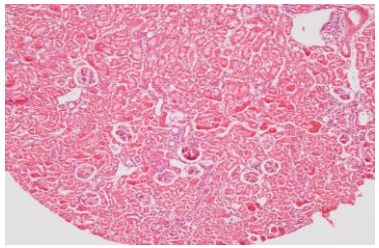
Pre-clinical efficacy (I)

Systemic Lupus Erythematosus (II)

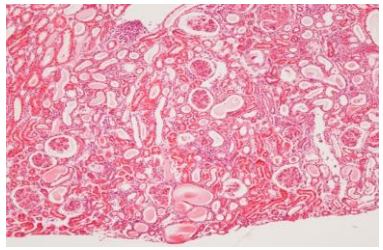
Comparative transcriptional profile of CYP- and PRP-HO7-treated lupus nephritis kidneys



CYP

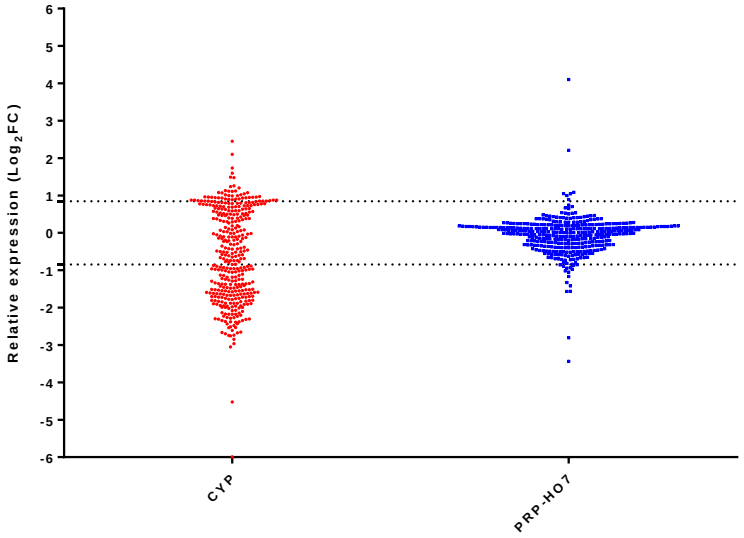


PRP-HO7



PBS

H&E (100x)



PRP-HO7 vs. CYP:

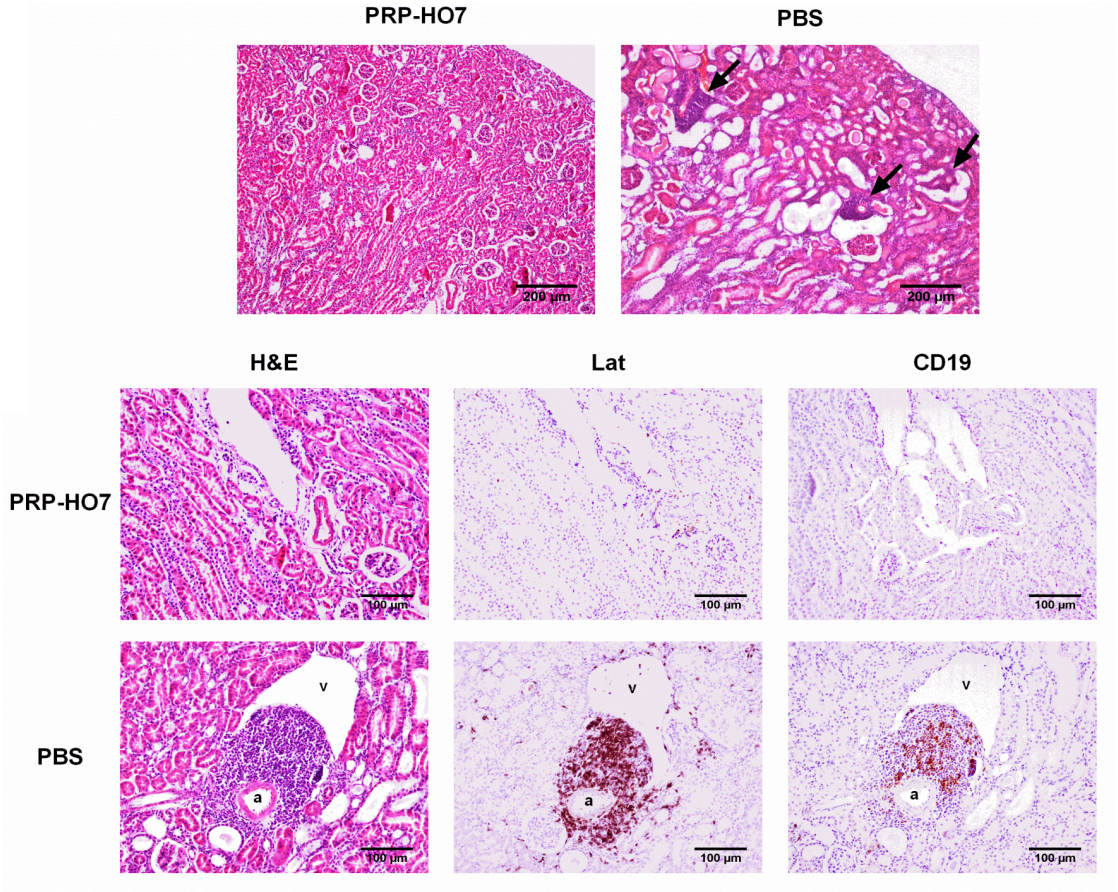
-Specificity ↑

-Toxicity ↓

-Luque et al. (2019) ***Kidney Int.*** In Press.

Pre-clinical efficacy (I)

Systemic Lupus Erythematosus (III)



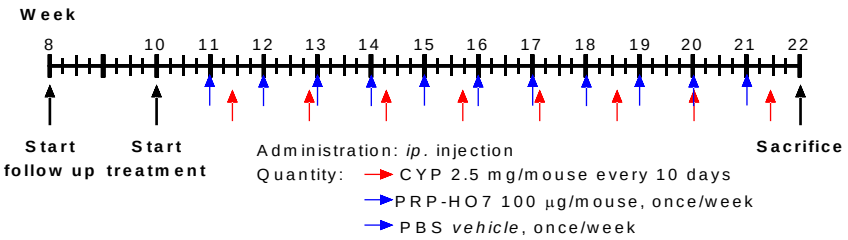
PRP-HO7 prevents ectopic lymphoid structures development in autoimmune lupus nephritis

-Luque et al. (2019) ***Kidney Int.*** In Press.

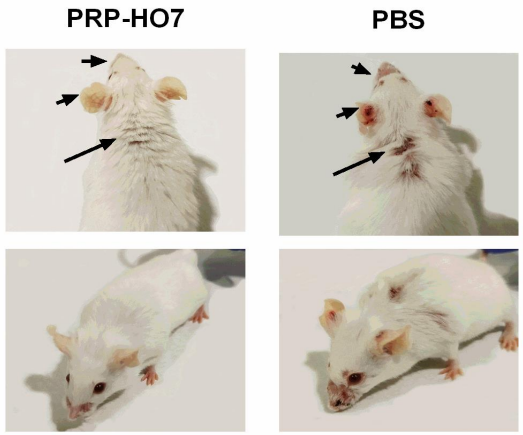
Pre-clinical efficacy (I)

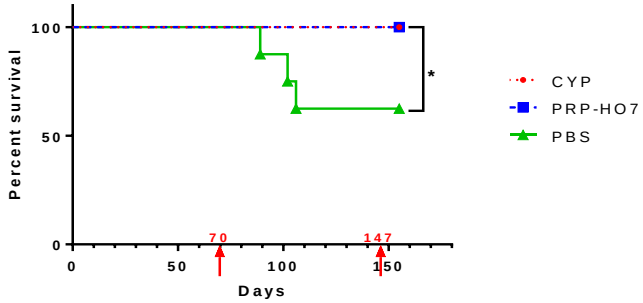
Systemic Lupus Erythematosus (IV)

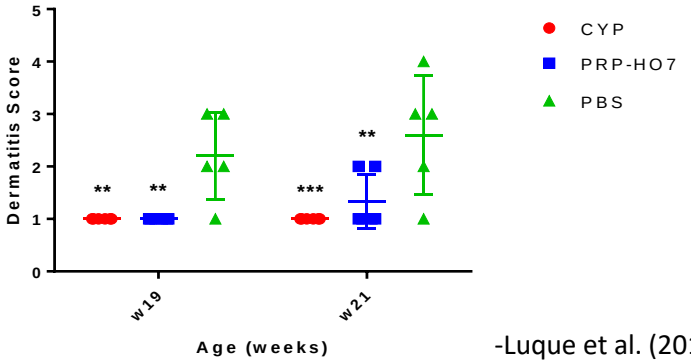
Female **MRL/lpr**



Facial rash





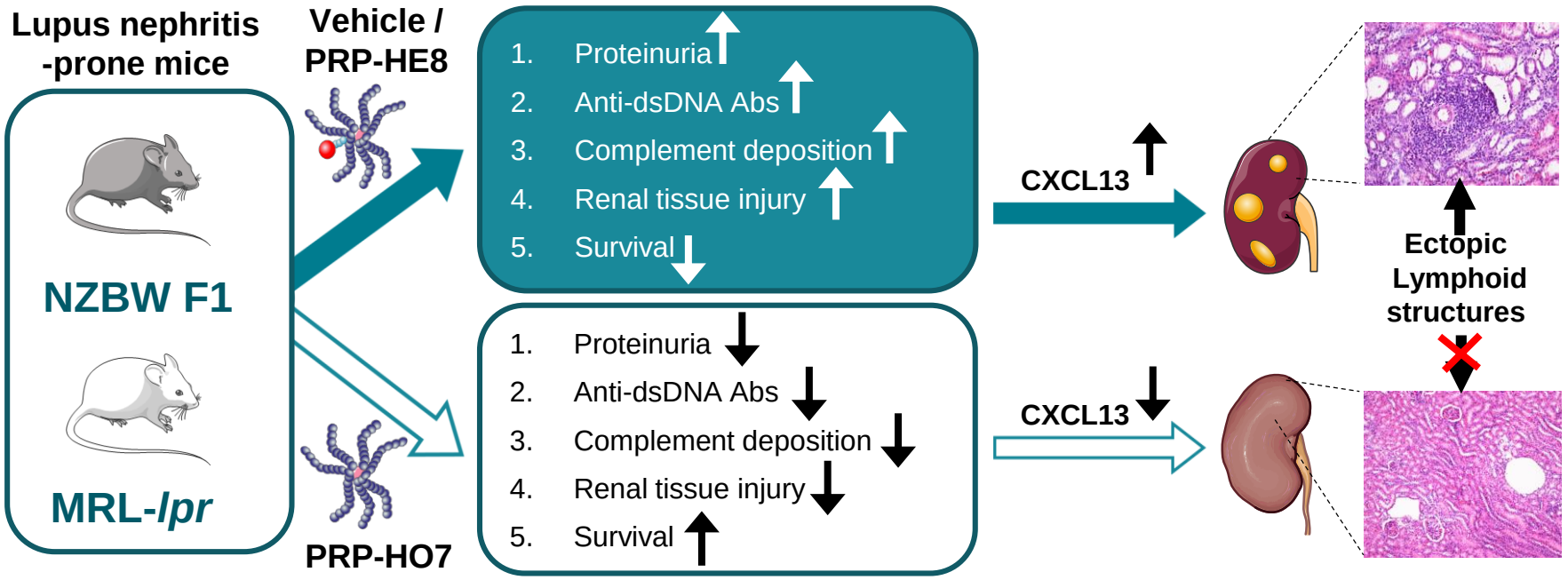


-Luque et al. (2019) ***Kidney Int.*** In Press.

Pre-clinical efficacy (I)

Systemic Lupus Erythematosus (V)

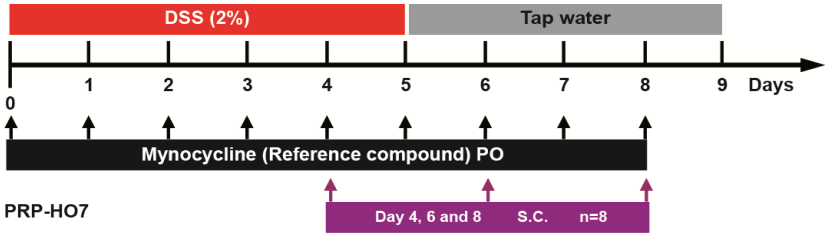
The anti-inflammatory and tolerogenic functions of PRP-HO7 restore immune homeostasis and improve autoimmune lupus pathology.

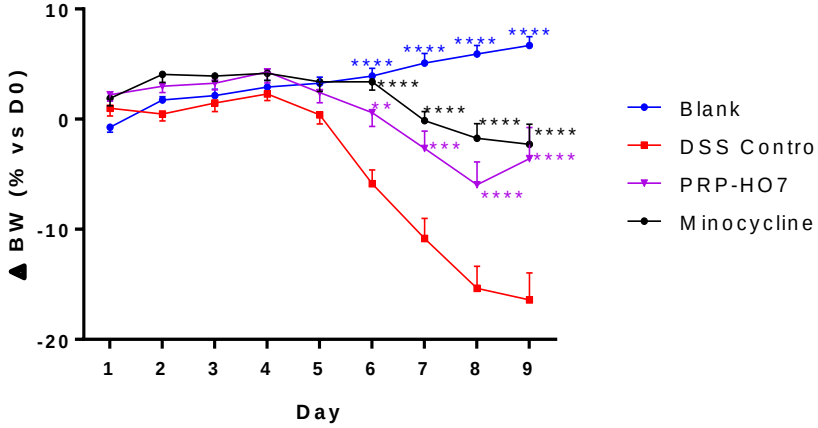


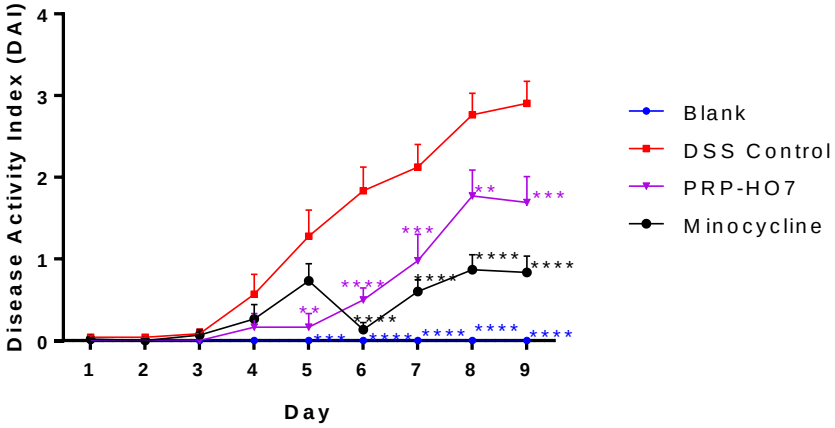
Pre-clinical efficacy (II)

Inflammatory Bowel Disease

Male C57BL/6
7-8 weeks old



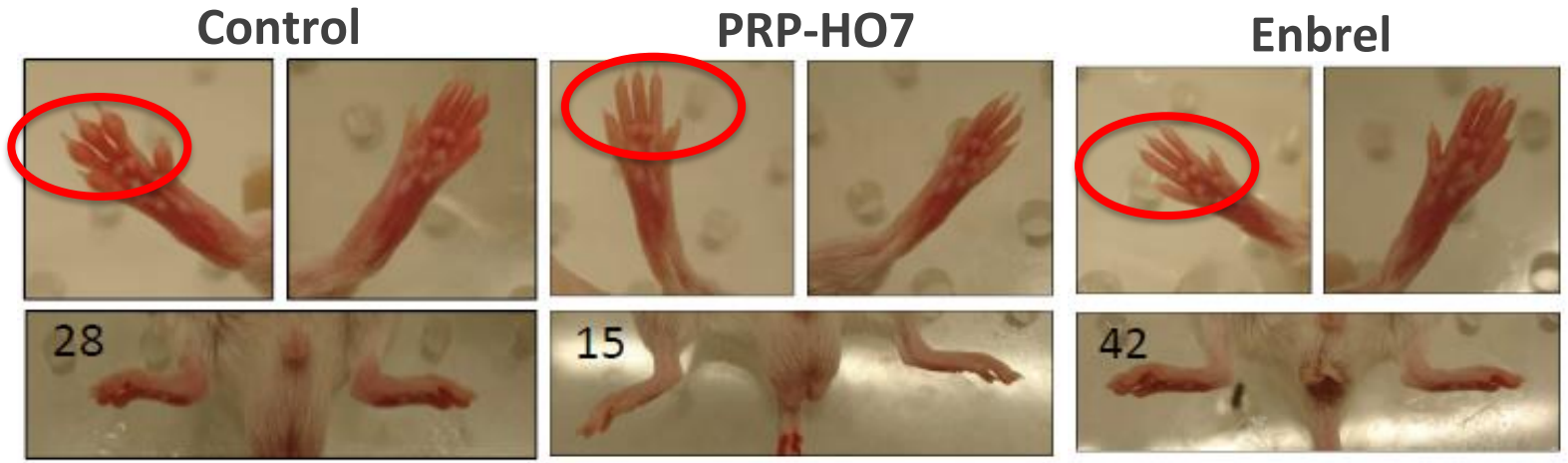




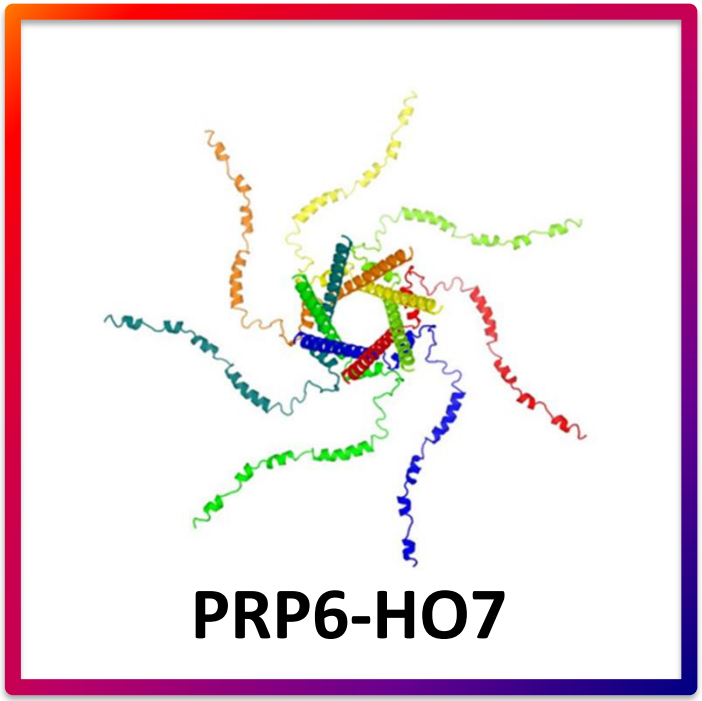
Pre-clinical efficacy (III)

Rheumatoid Arthritis

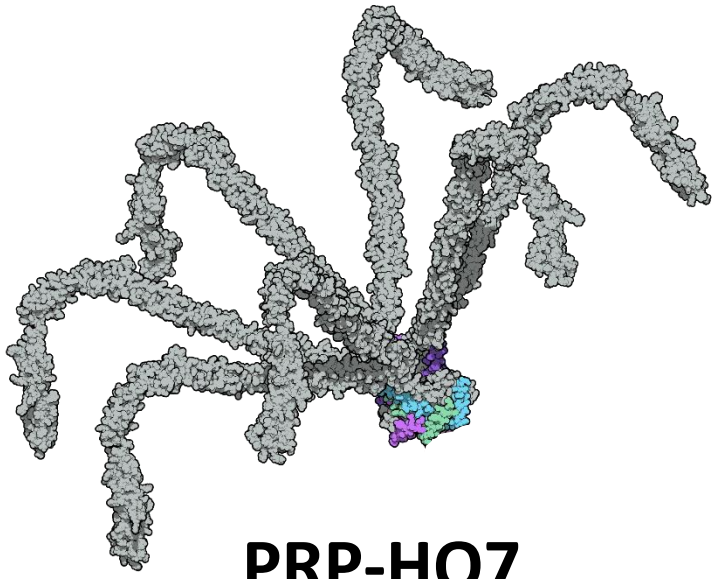
Hindlimbs (End of study)



3. The Product (Current Status of Development)



PRP6-HO7



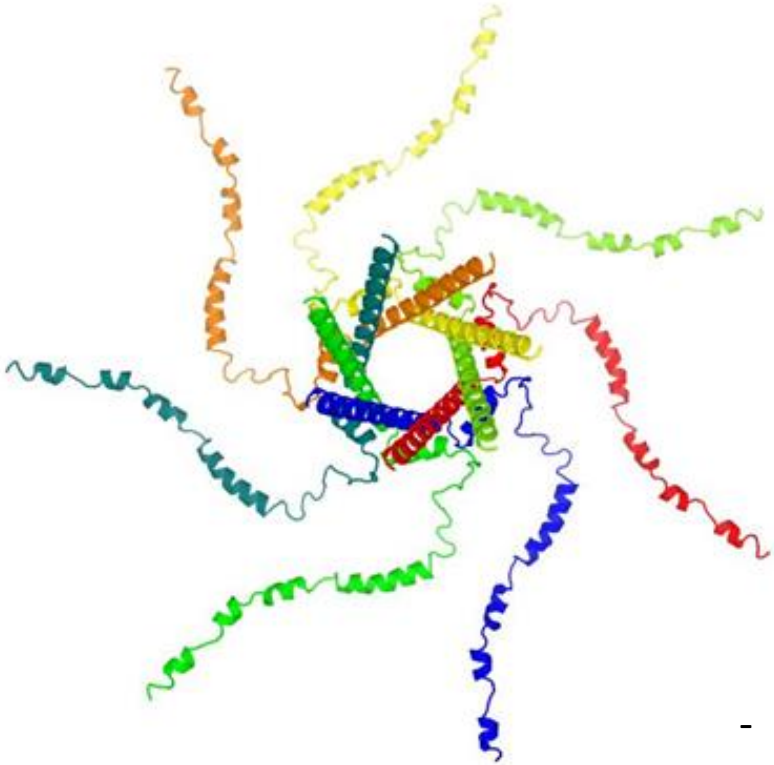
PRP-HO7

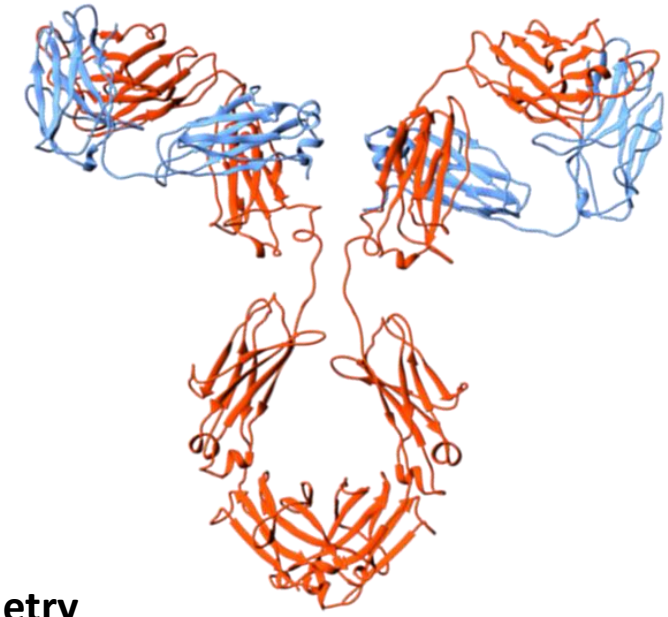
H2L: PRP6-HO7 - Improved biologic

- **Smaller than a MoAb (< 100 kDa)**
- **Same immunomodulatory activity and stability tan PRP-HO7**
- **Non-glycosylated**
- **Scalable and cost-effective recombinant protein production in *E. coli***

3. The Product (Current Status of Development)

Structural features of PRP6-HO7 vs. Monoclonal antibodies

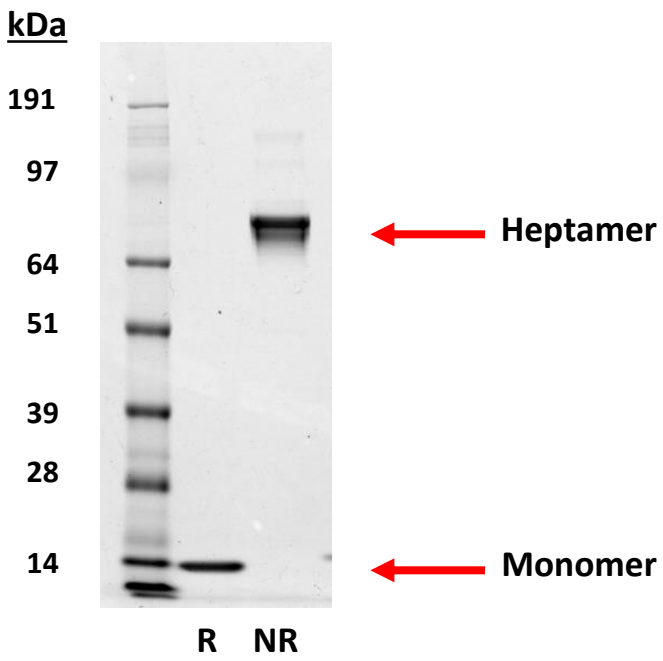




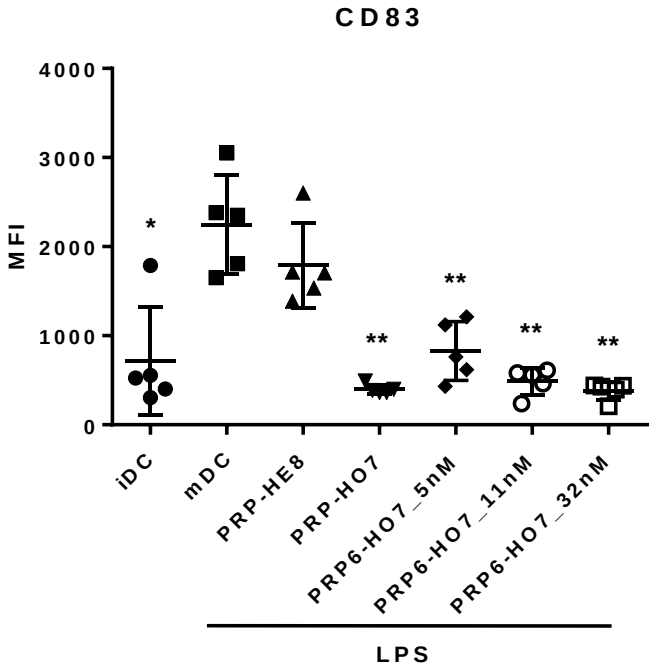
- **Symmetry**
- **Flexibility**
- **α-helix vs. β-sheet**

3. The Product (Current Status of Development)

PRP6-HO7 production (*E. coli*)



Dose-response relationship in human MoDCs

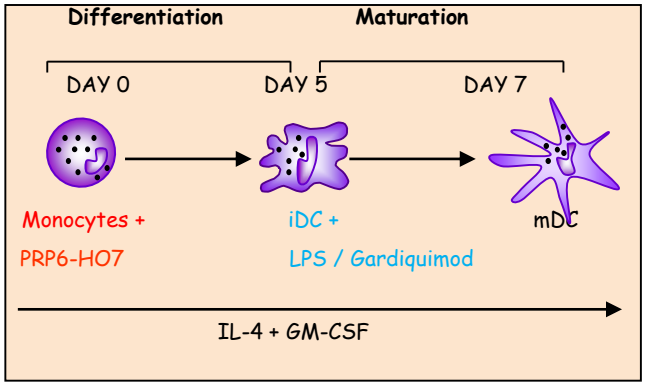


3. The Product (Current Status of Development)

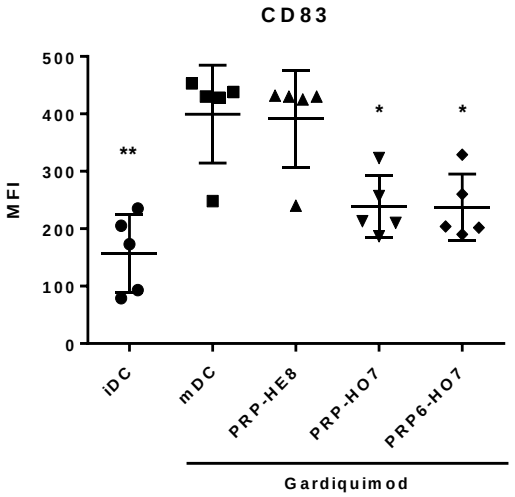
Towards "*personalized*" medicine:

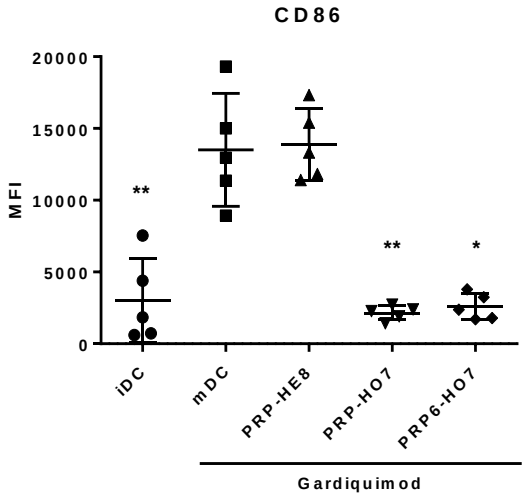
Predictive efficacy end-point functional assay for clinical trials

***In vitro* assay:**



SLE patient blood samples:





3. The Product (IPR Protection)

PATENTS:

1- "***Compositions and methods for immunomodulation***"
INVENTORS: (by order of signature): **Aran, J.M.**, Olivar, R.
REQUEST No.: **EP11382240**
PRIORITY COUNTRY: European Union
PRIORITY DATE: **15/07/11**
PCT APPLICATION: PCT/EP2012/063932 (16/07/12)
ENTITY: IDIBELL

2- "***C4BP-based compounds for treating immunological diseases***"
INVENTORS: (by order of signature): **Aran, J.M.**, Ruiz L.A., Ortiz, J., Lluch, N.
REQUEST No.: **EP17382187**
PRIORITY COUNTRY: European Union
PRIORITY DATE: **06/04/17**
PCT APPLICATION: PCT/EP2018/058773 (06/07/18)
ENTITY: IDIBELL

3- "***Compounds for immunomodulation***"
INVENTORS: (by order of signature): **Aran, J.M.**, Luque, A., Serrano, I.
REQUEST No.: **EP19382910**
PRIORITY COUNTRY: European Union
PRIORITY DATE: **17/10/19**
PCT APPLICATION:
ENTITY: IDIBELL

3. The Product (Pitfalls & Risks to be Considered)

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 PRP6-HO7 administration), or cell therapy using ex vivo PRP6-HO7-conditioned DCs.**

GMP Scaling up.-

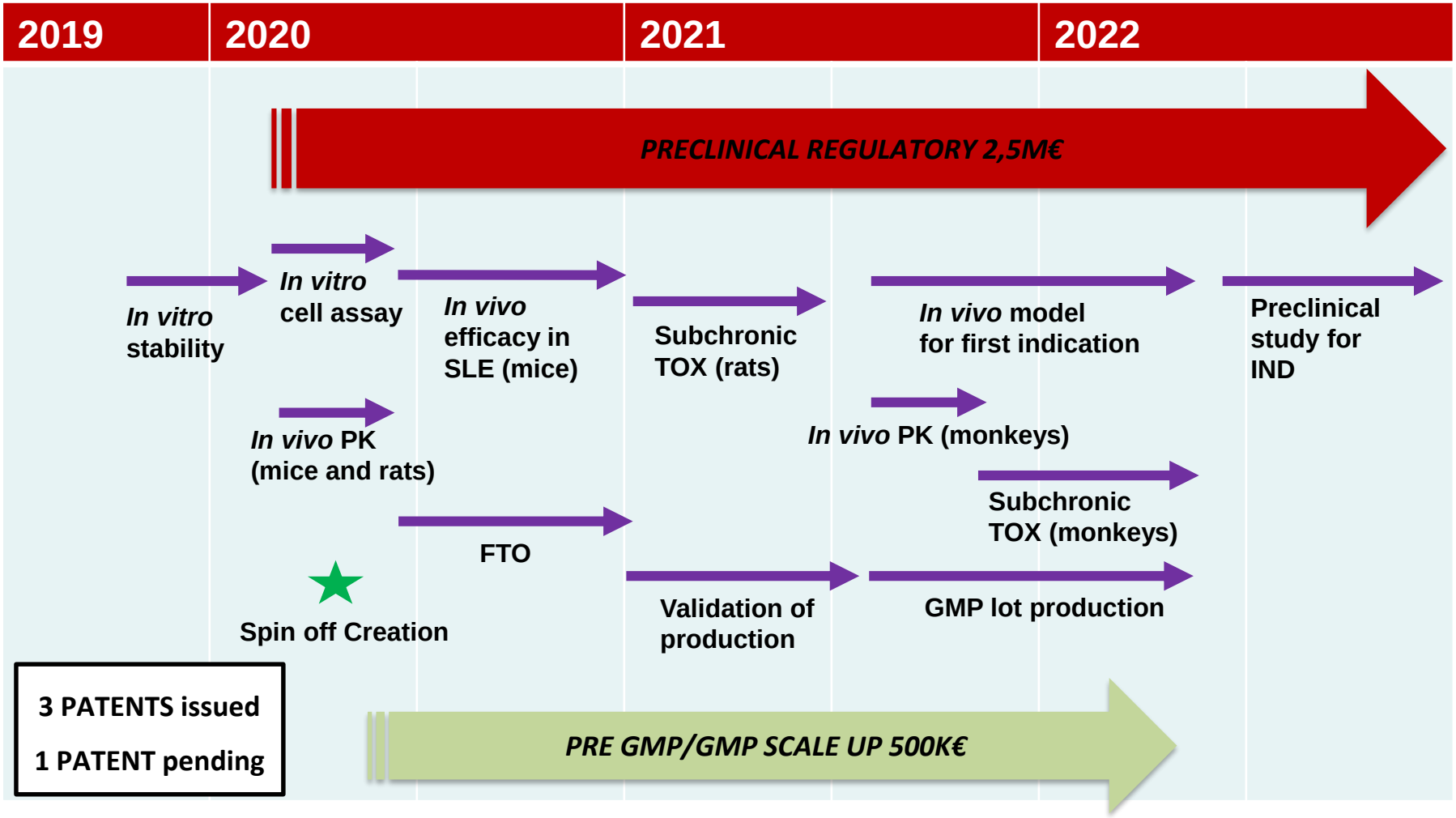
We have already designed a candidate to be produced in E. coli bioreactors, being fully scalable.

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 (licensing) to consolidate its market share.

4. Partnering Oportunities

***Precision medicine*: *First-in-class* immunomodulatory biologic for autoimmune diseases**



4. Partnering Oportunities

From the opportunity to the market: PRP-HO family - optimal cost/benefit)

- **Market application: Biotechnology / Pharmaceuticals.**

- **Cooperation type:** **-License agreement.**

- Joint further development (adaptation to specific needs):

Pre-clinical and clinical co-development

Regulatory compliance

Future scaling up

- Testing new applications.

- Joint venture agreement.

- Pre-seed and seed funding opportunities.

Thank you

PurPose Biotherapeutics

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ACCELERATOR MEETING POINT

Idibell.cat

Immunomodulation for autoimmunity