

## Repurposing of the use of Doxorubicin



Madrid, 17 de noviembre de 2015



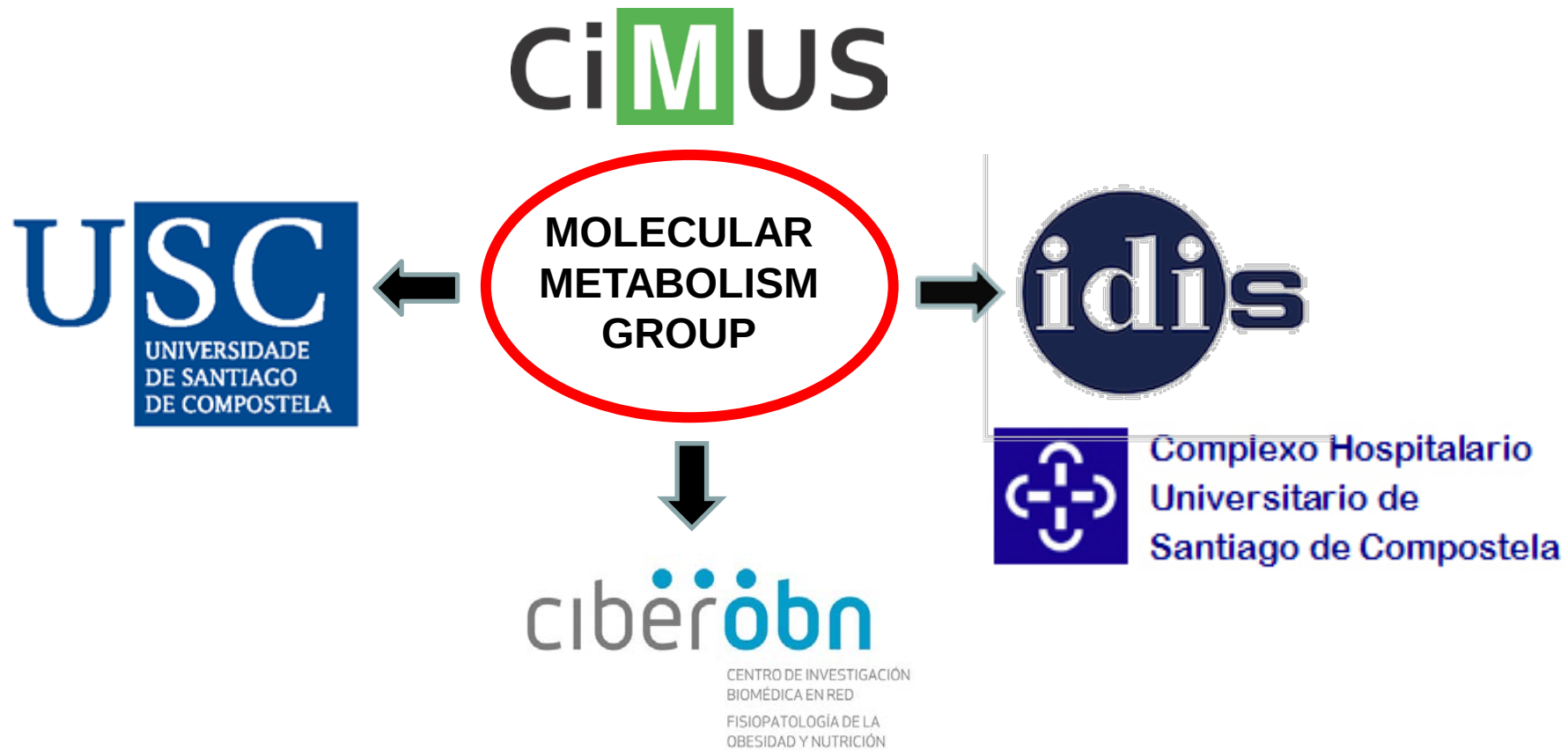
## Content

### 1. The Institution

### 2. The Product

- a) Target Indications
- b) Innovative mechanisms of action
- c) Differential features facing the market
- d) Current status of development
- e) IPR protection
- f) Pitfalls & Risks to be considered

### 3. Partnering Opportunities



## AREAS AND GROUPS

### CANCER

Anxo Vidal

Clara V. Álvarez

Román Pérez-  
Fernández

Jose Antonio  
Costoya

Celia M<sup>a</sup>  
Pombo

Carmen Rivas

Miguel González  
Blanco

### ENDOCRINOLOG Y AND NUTRITION

Carlos Diéguez

Miguel López

Rubén  
Nogueiras

Rosa Señarís

María García

Joaquín Lado

### NEUROSCIENCE

Francisco  
González

Antonio Canedo

José Luis  
Labandeira

Marián Castro

M<sup>a</sup> Josefa  
Guerra

Jannette  
Rodríguez

Jesús R.  
Requena

### CARDIOVASCUL AR

José Ramón  
González-  
Juanatey

Juan Zalvide

Dolores Viña

### DRUGS AND EXPERIMENTAL THERAPIES

Mabel Loza

M<sup>a</sup> José Alonso

### GENETICS AND FUNCTIONAL GENOMIC

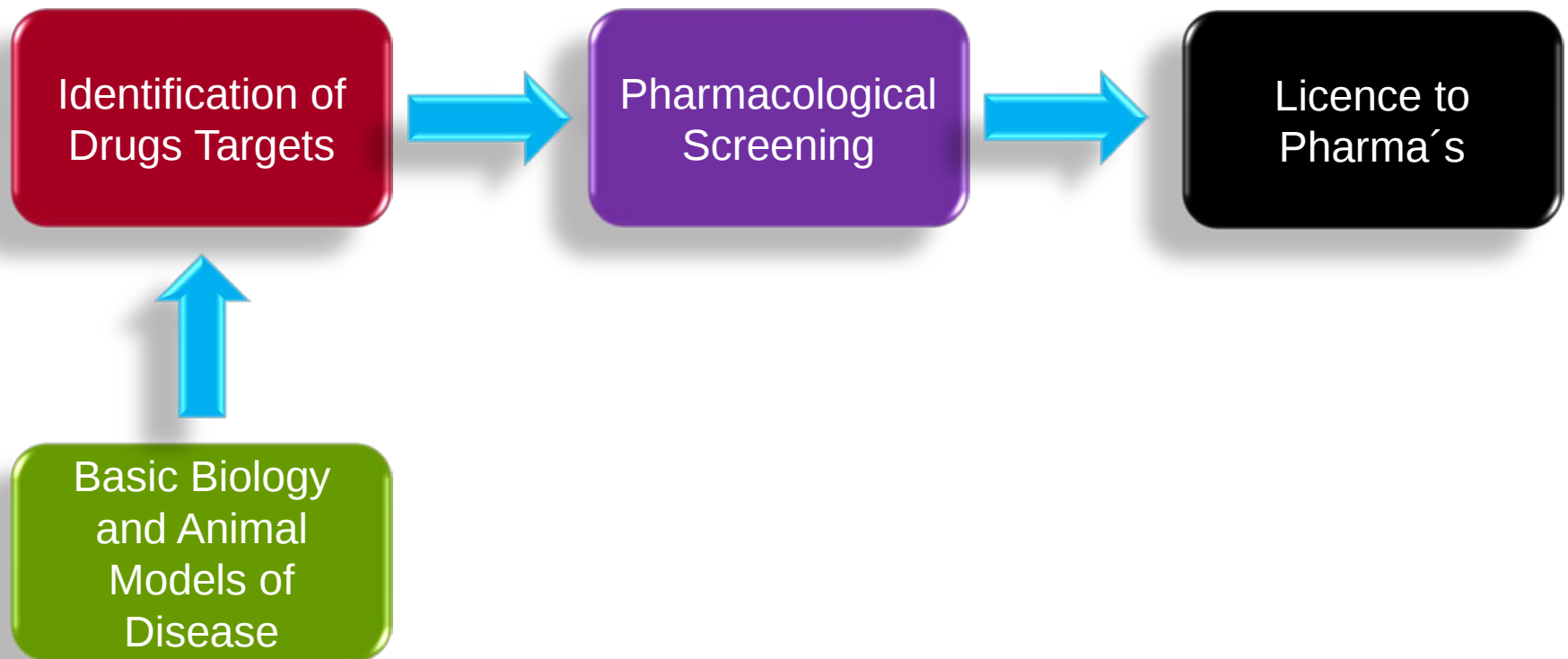
Ángel  
Carracedo

Fernando  
Domínguez

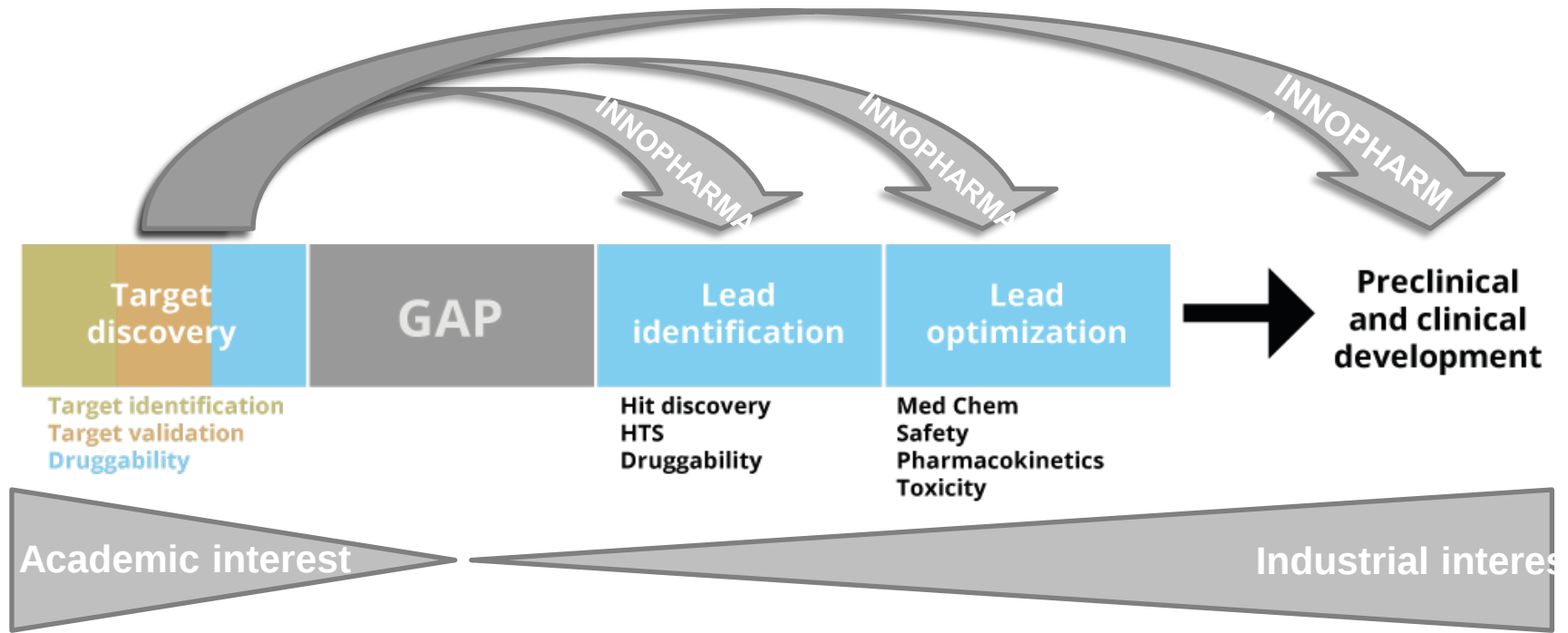
### BIostatistics PLATAFORM

Carmen  
Cadarso

### CIMUS WORK FLOW



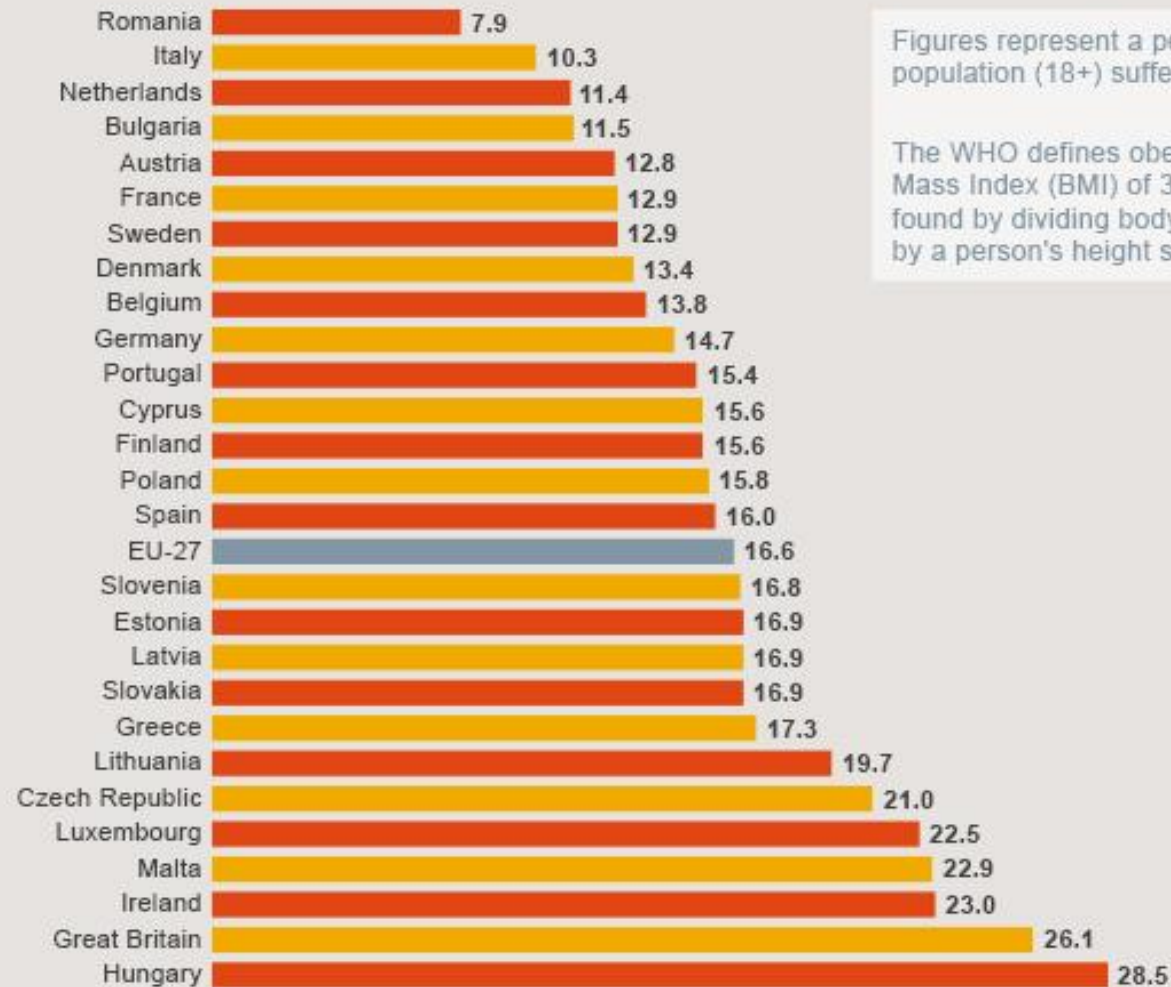
# INNOPHARMA: Building bridges in Drug Discovery



**Bridging the gap between basic research in new therapeutic mechanisms and industrial application.**

# The Product: Target Indications

## Obesity in the EU

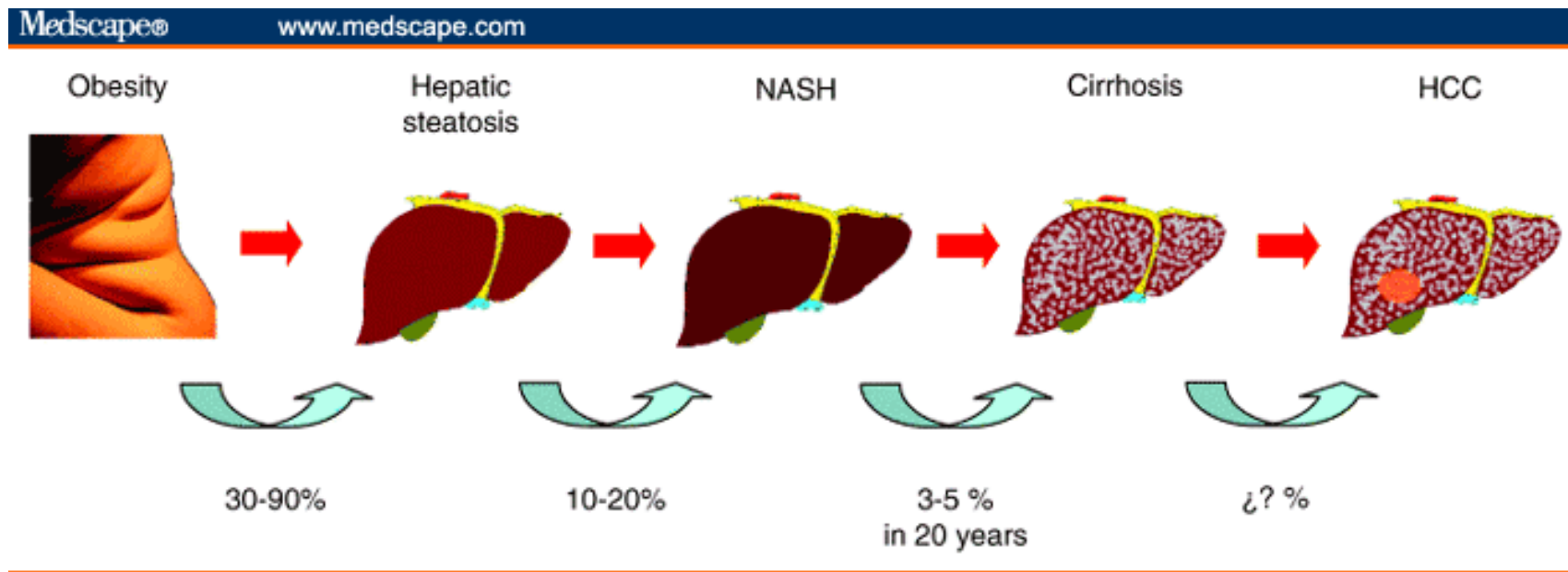


Figures represent a percentage of the adult population (18+) suffering from obesity.

The WHO defines obesity as having a Body Mass Index (BMI) of 30 or more. BMI is found by dividing body mass (in kilograms) by a person's height squared (in meters).

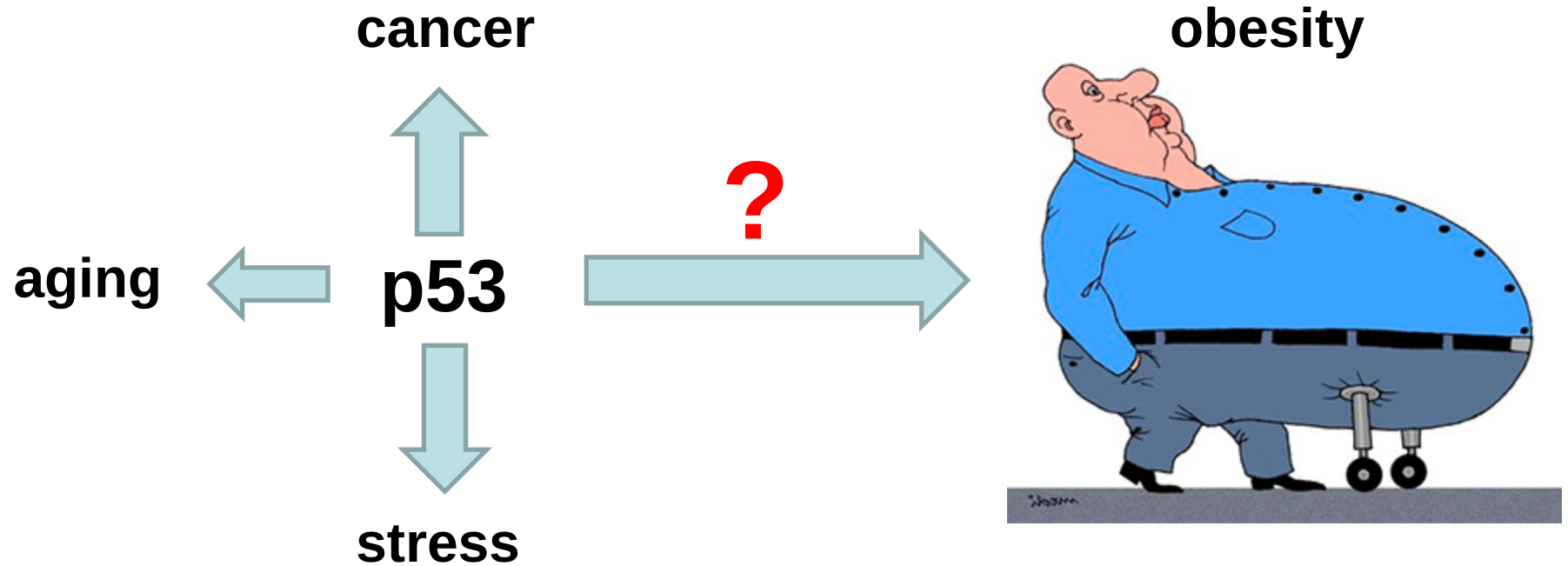
# The Product: Target Indications

## Natural history of nonalcoholic fatty liver disease (NAFLD)



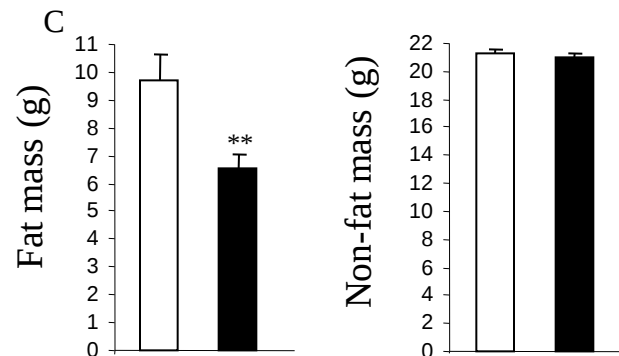
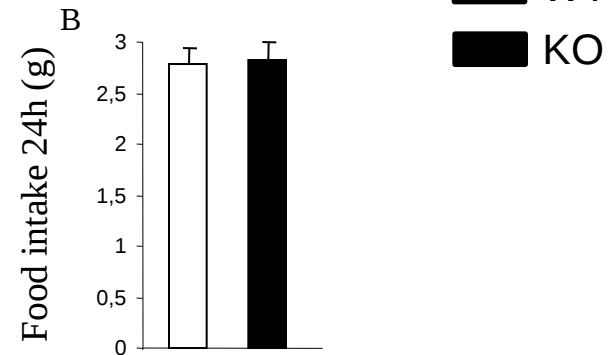
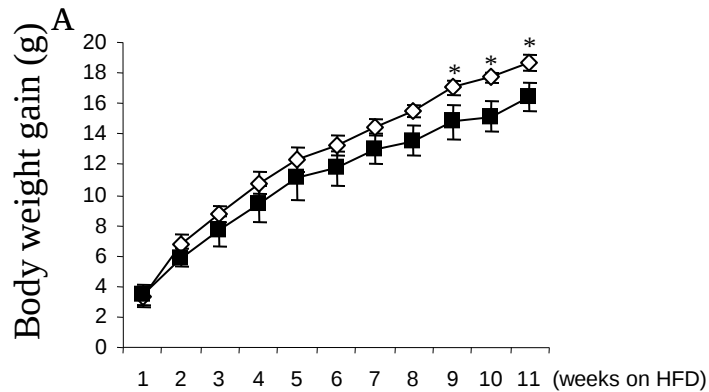
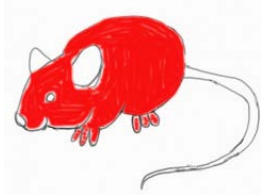
Obesity and insulin resistance are the major risk factors for nonalcoholic hepatic steatosis

## The Product: Innovative mechanisms of action



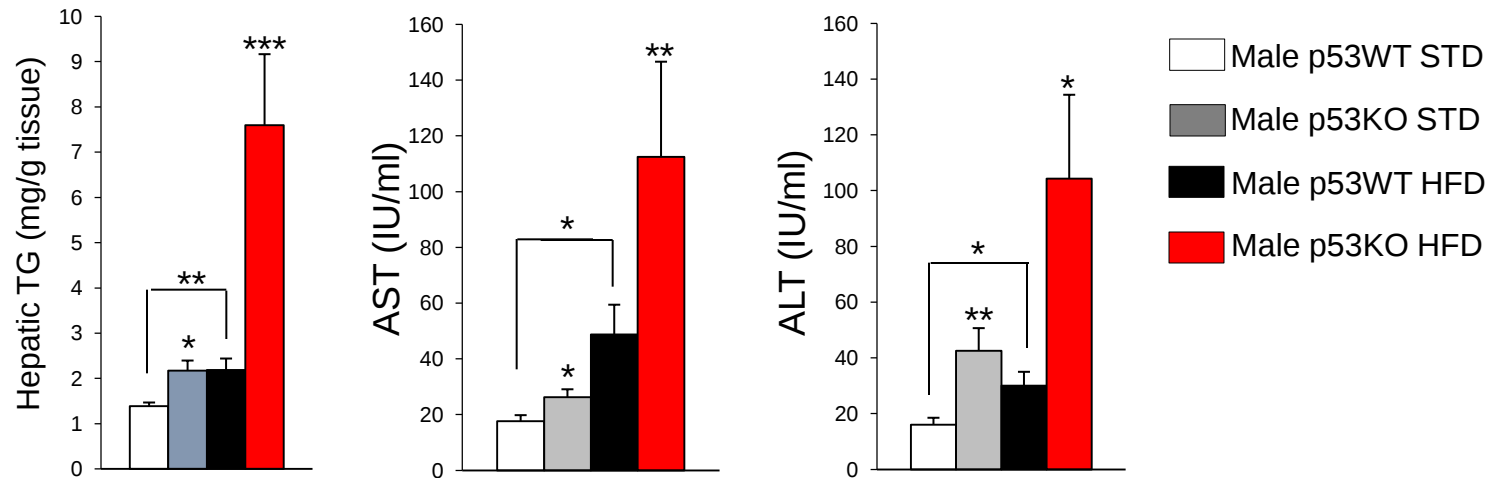
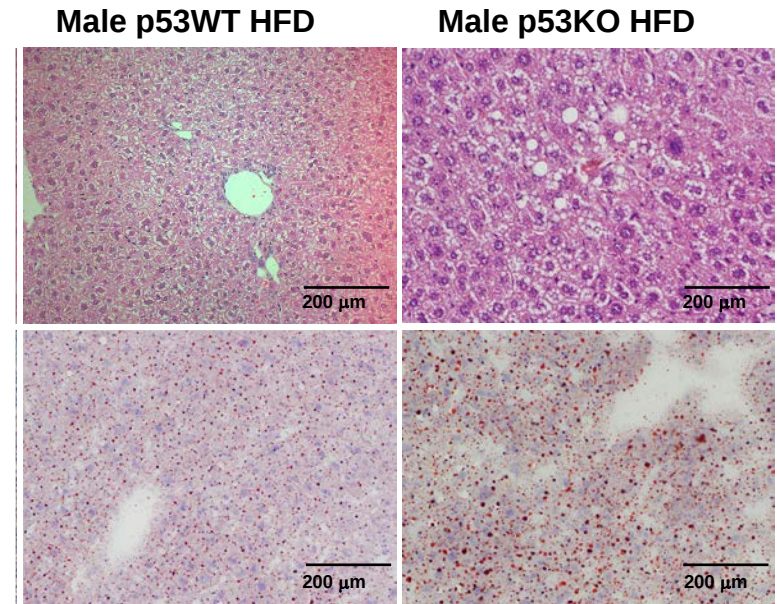
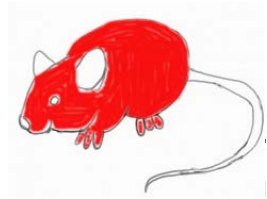
# The Product: Innovative mechanisms of action

## p53 KO mice are resistant to diet-induced obesity



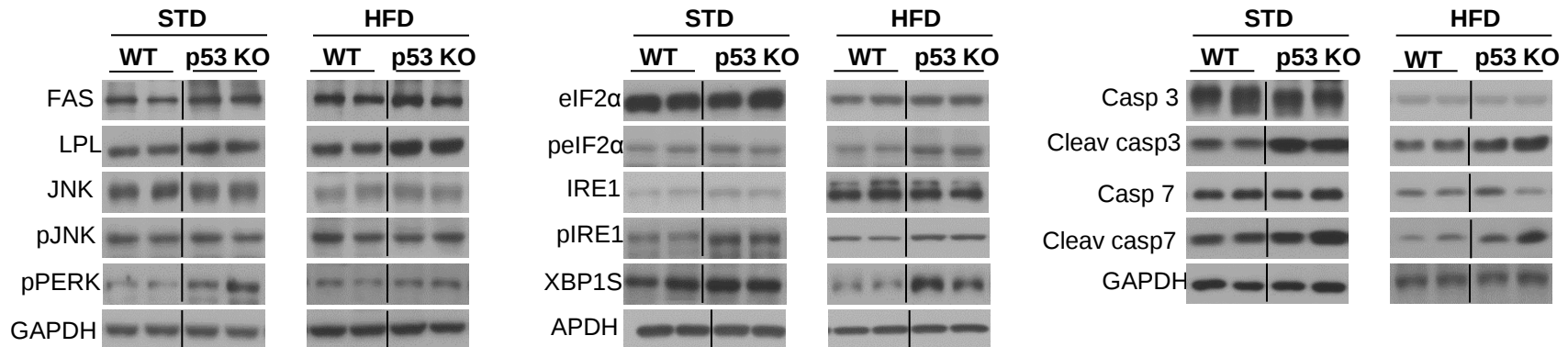
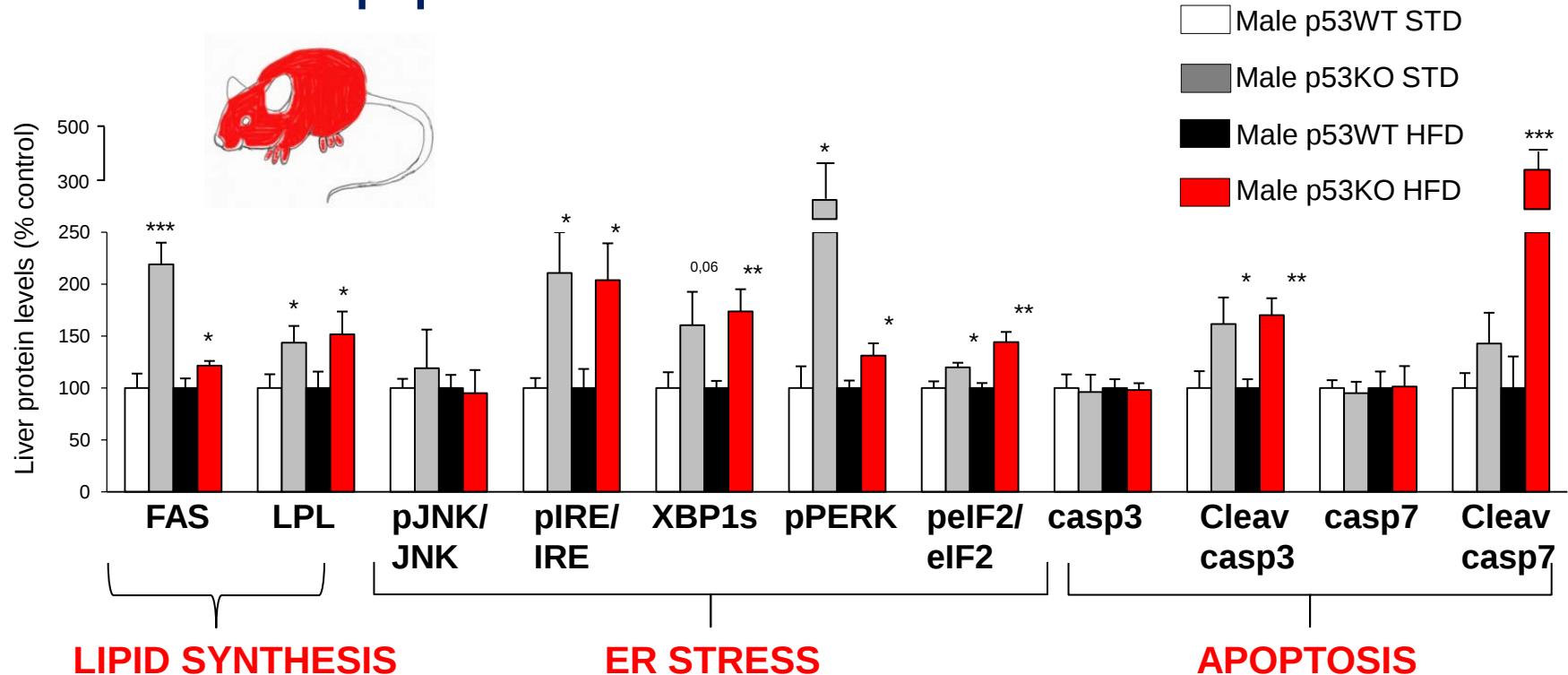
# The Product: Innovative mechanisms of action

## p53 KO mice fed a chow diet or HFD show exacerbated liver steatosis



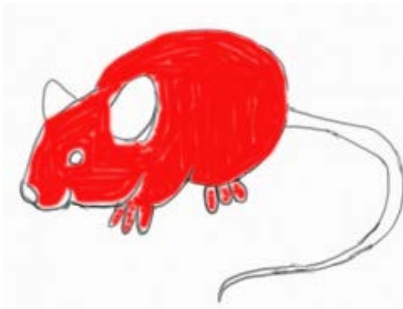
# The Product: Innovative mechanisms of action

## p53 KO mice fed a chow diet or HFD show increased lipid storage, ER stress and apoptosis

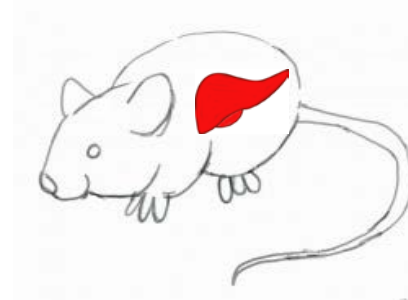


**What happens if we target specifically the liver?**

**p53 global KO**

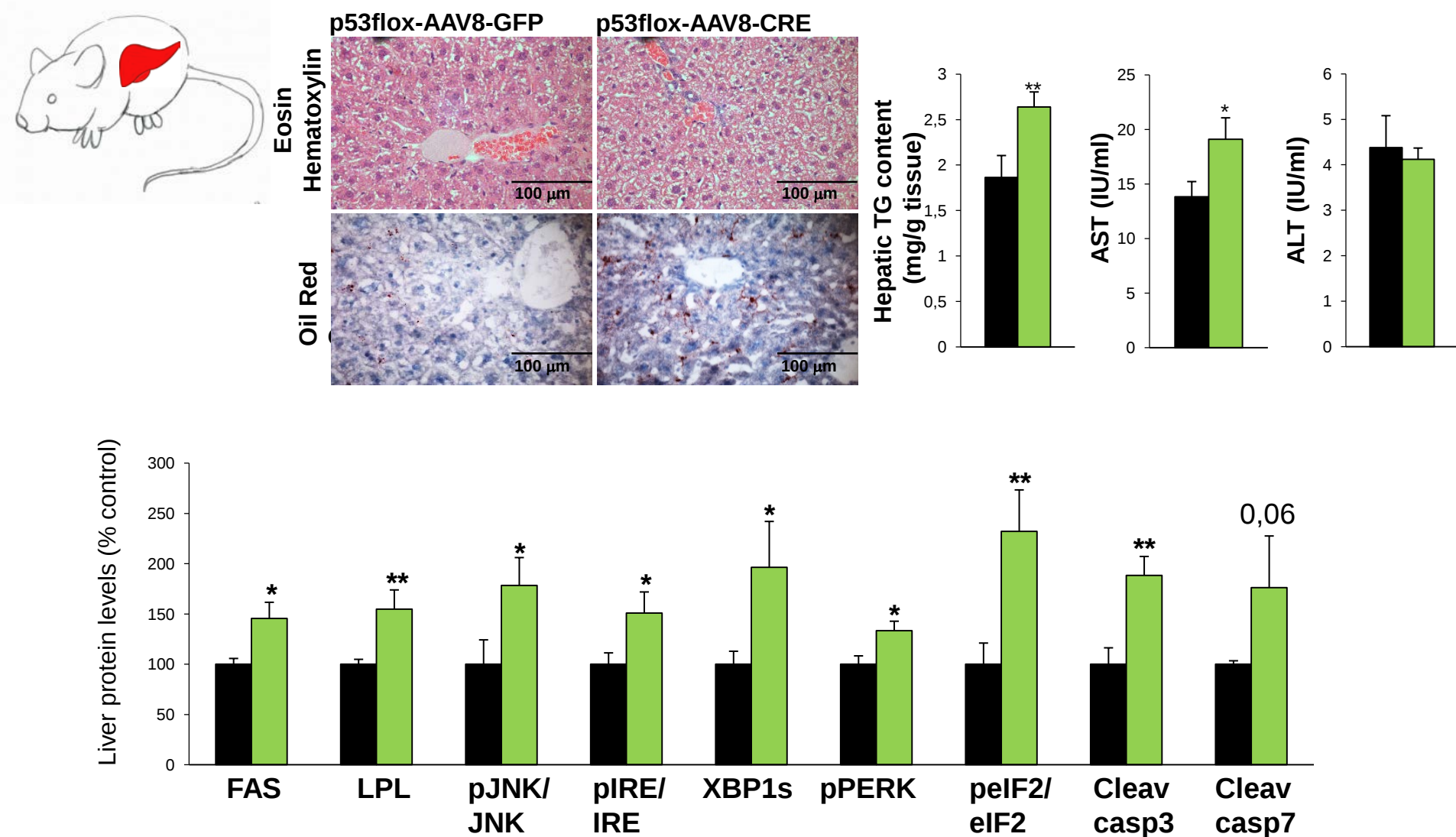


**p53 liver KO**



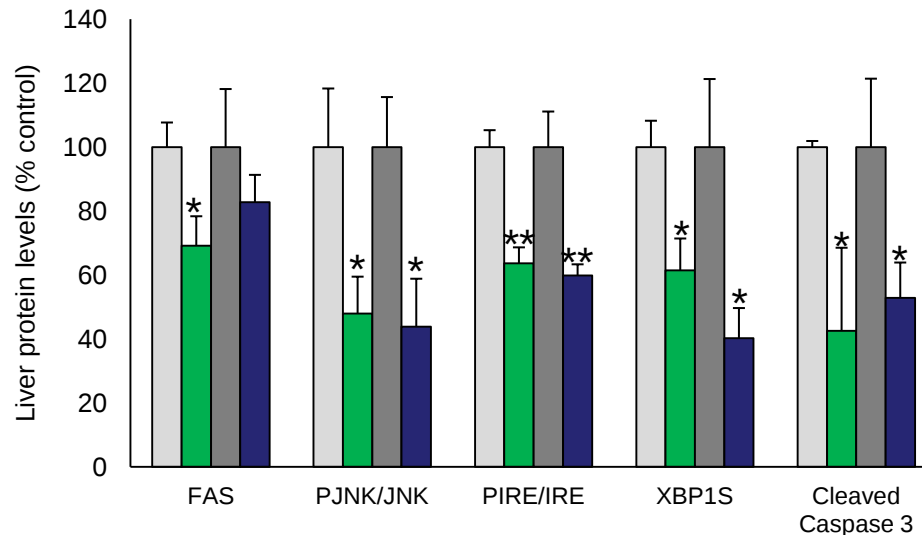
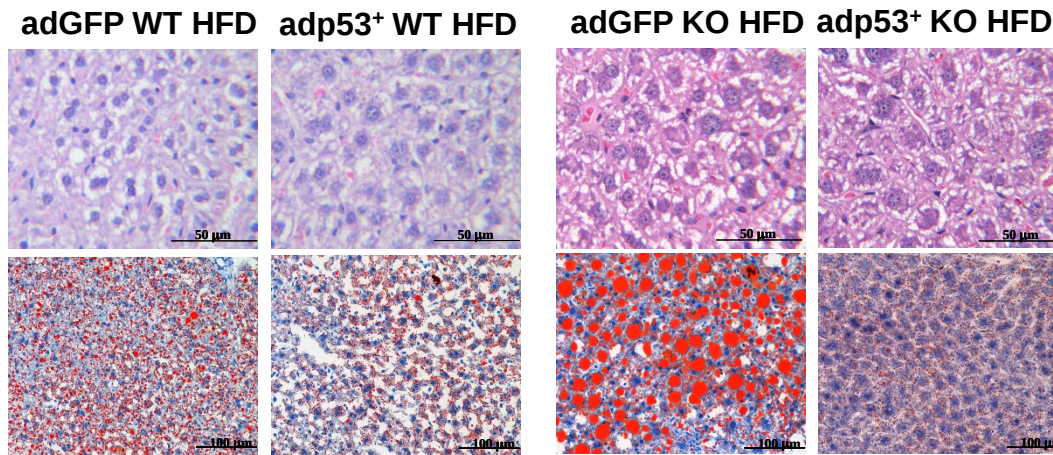
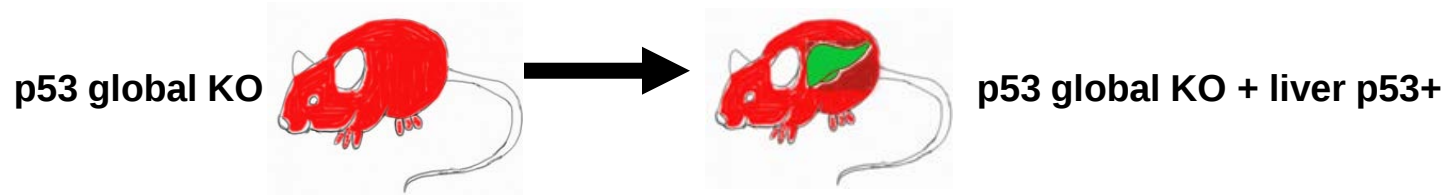
# The Product: Innovative mechanisms of action

## Down-regulation of p53 in the liver induces hepatic steatosis

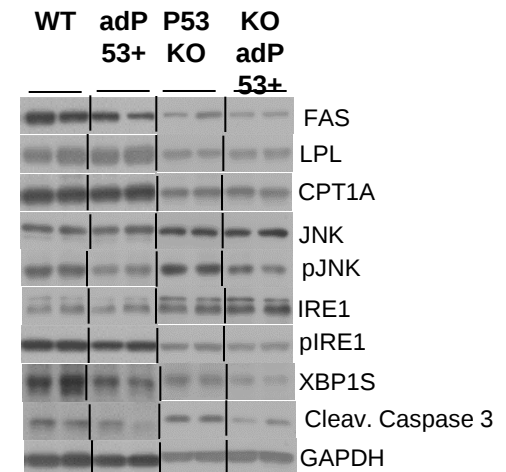


# The Product: Innovative mechanisms of action

## Recovery of p53 expression in the liver of mice attenuates hepatic steatosis



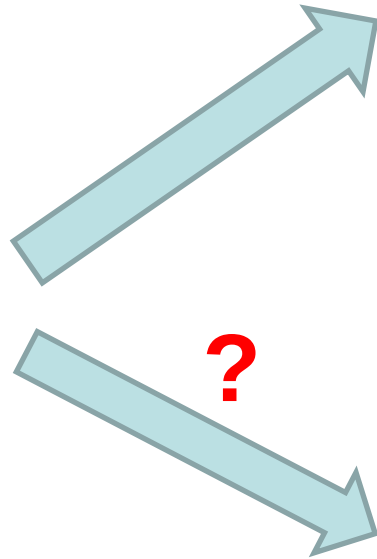
adGFP WT HFD  
adp53<sup>+</sup> WT HFD  
adGFP KO HFD  
adp53<sup>+</sup> KO HFD



# The Product: Innovative mechanisms of action



Activator of p53 in clinical  
use



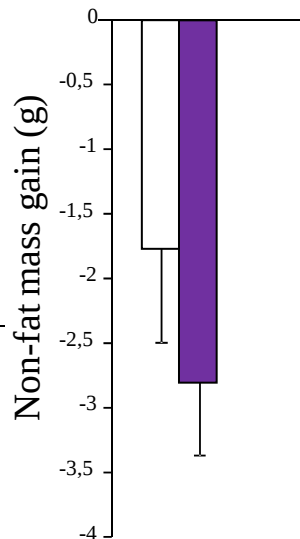
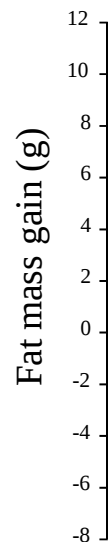
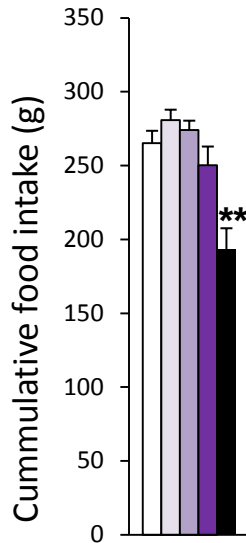
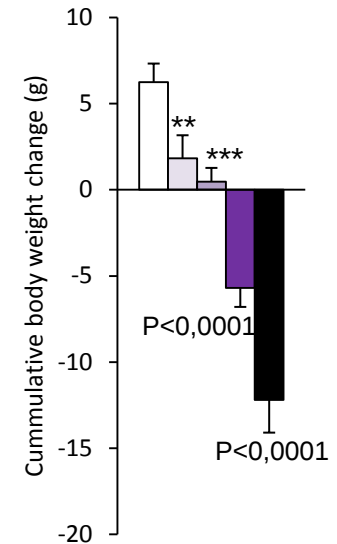
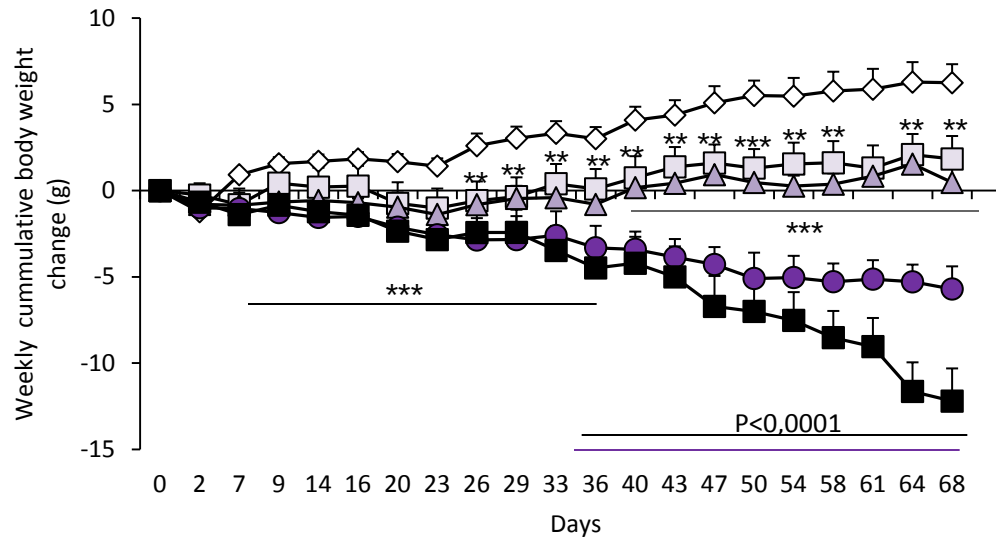
Clinical use  
(chemotherapy)



NAFLD

# The Product: Innovative mechanisms of action

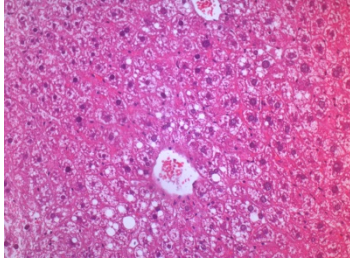
## INTRAPERITONEALLY 2 DAYS/WEEK DURING 68 DAYS SWISS MICE HFD (45% FAT)



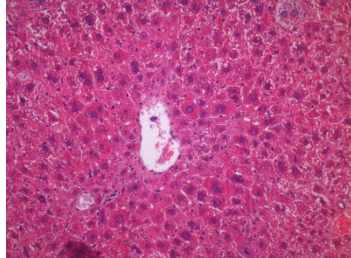
- SAL
- Doxo 0,15 mg/Kg
- Doxo 0,3 mg/Kg
- Doxo 0,6 mg/Kg
- Doxo 1,25 mg/Kg

# The Product: Innovative mechanisms of action

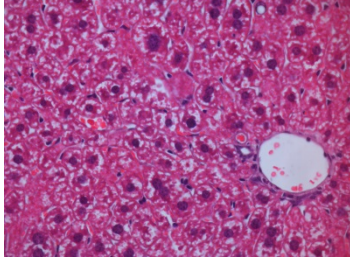
Salino 20x



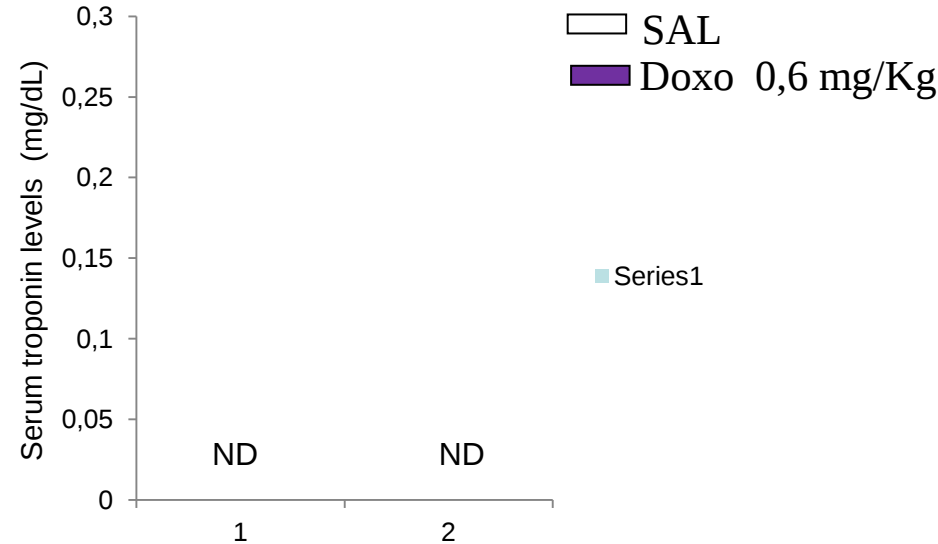
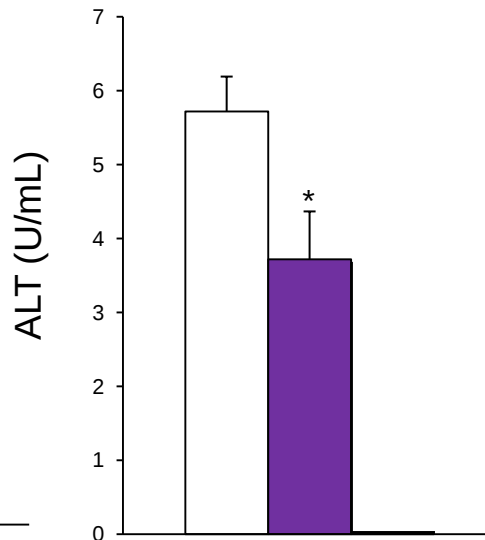
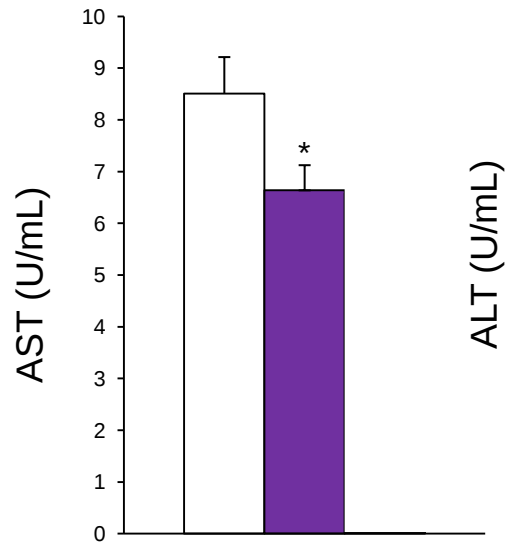
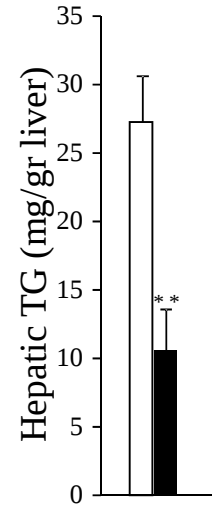
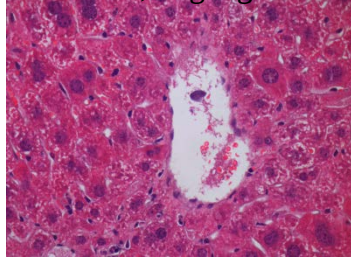
CIM 0,6mg/Kg 20x



Salino 40x

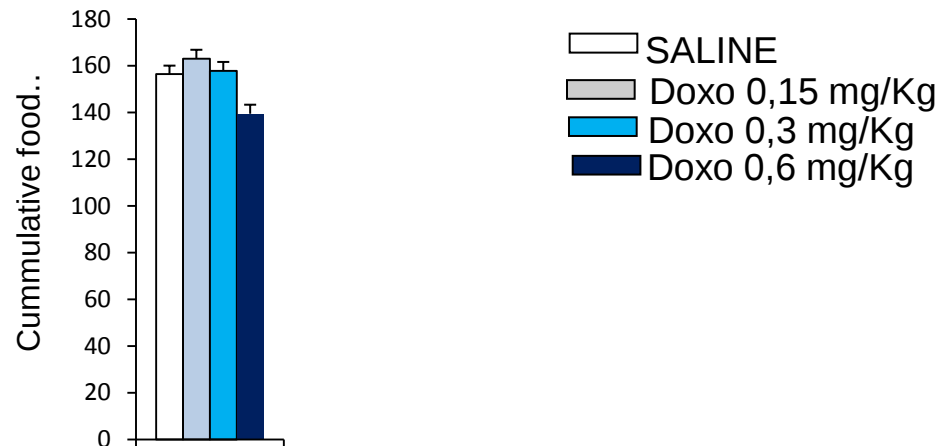
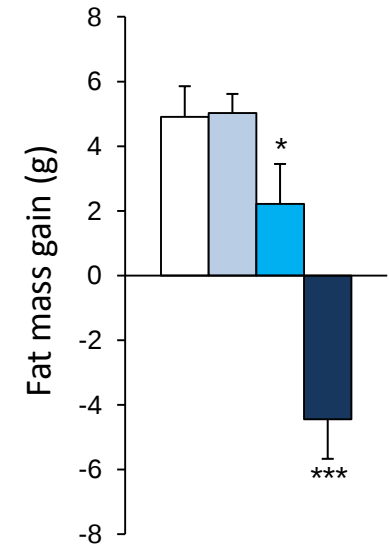
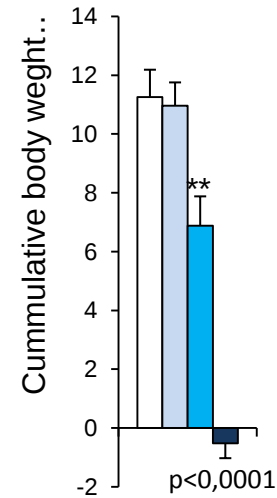
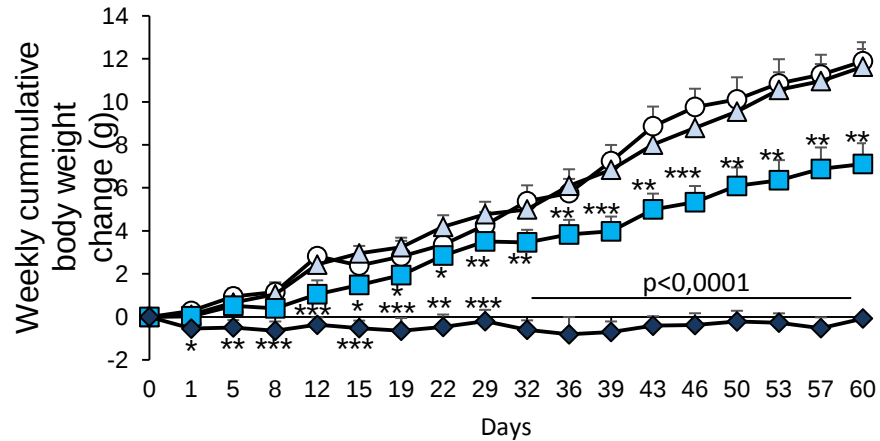


CIM 0,6mg/Kg 40x



# The Product: Innovative mechanisms of action

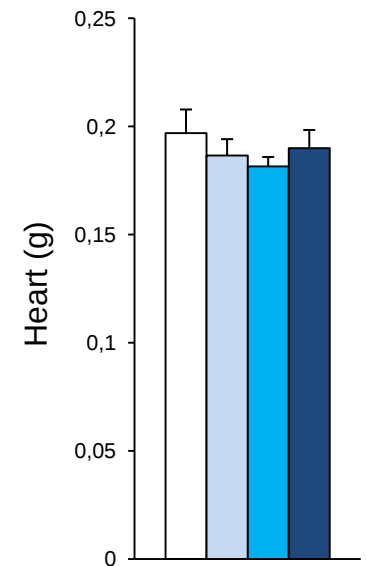
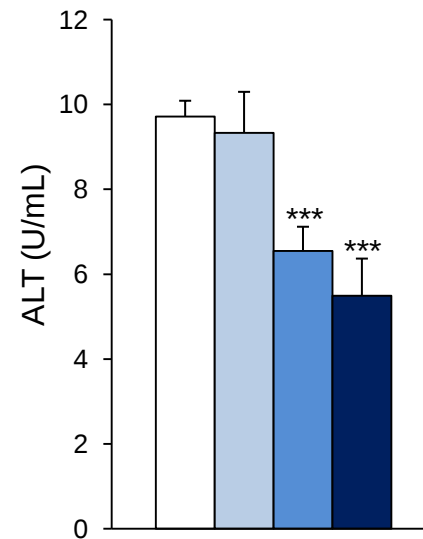
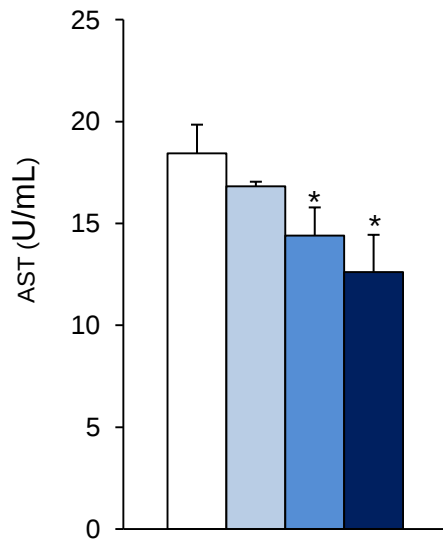
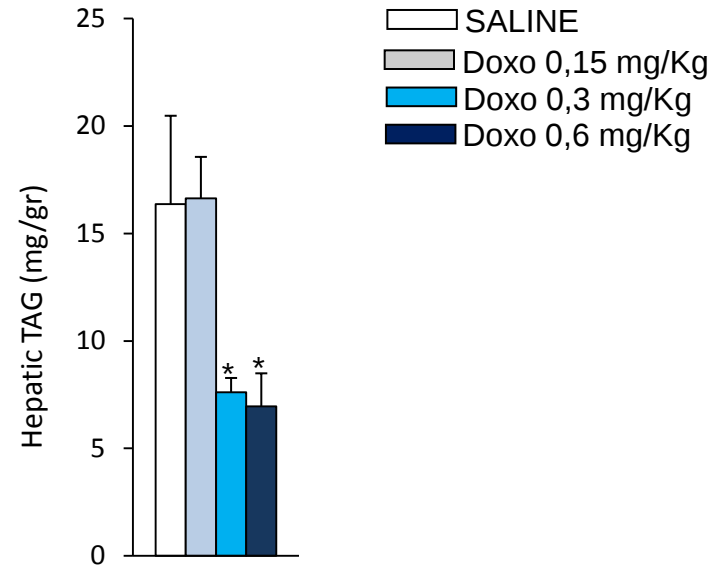
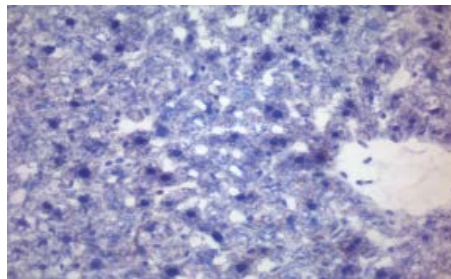
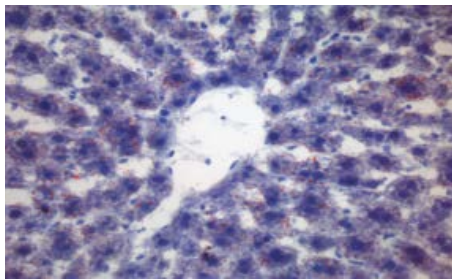
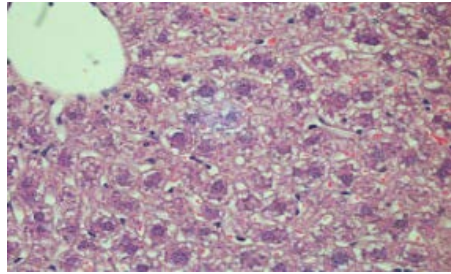
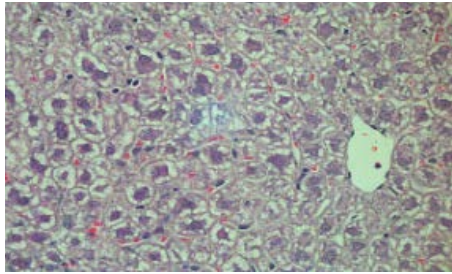
## INTRAPERITONEALLY 2 DAYS/WEEK DURING 60 DAYS C57/B6 MICE HFD (60% FAT)



# The Product: Innovative mechanisms of action

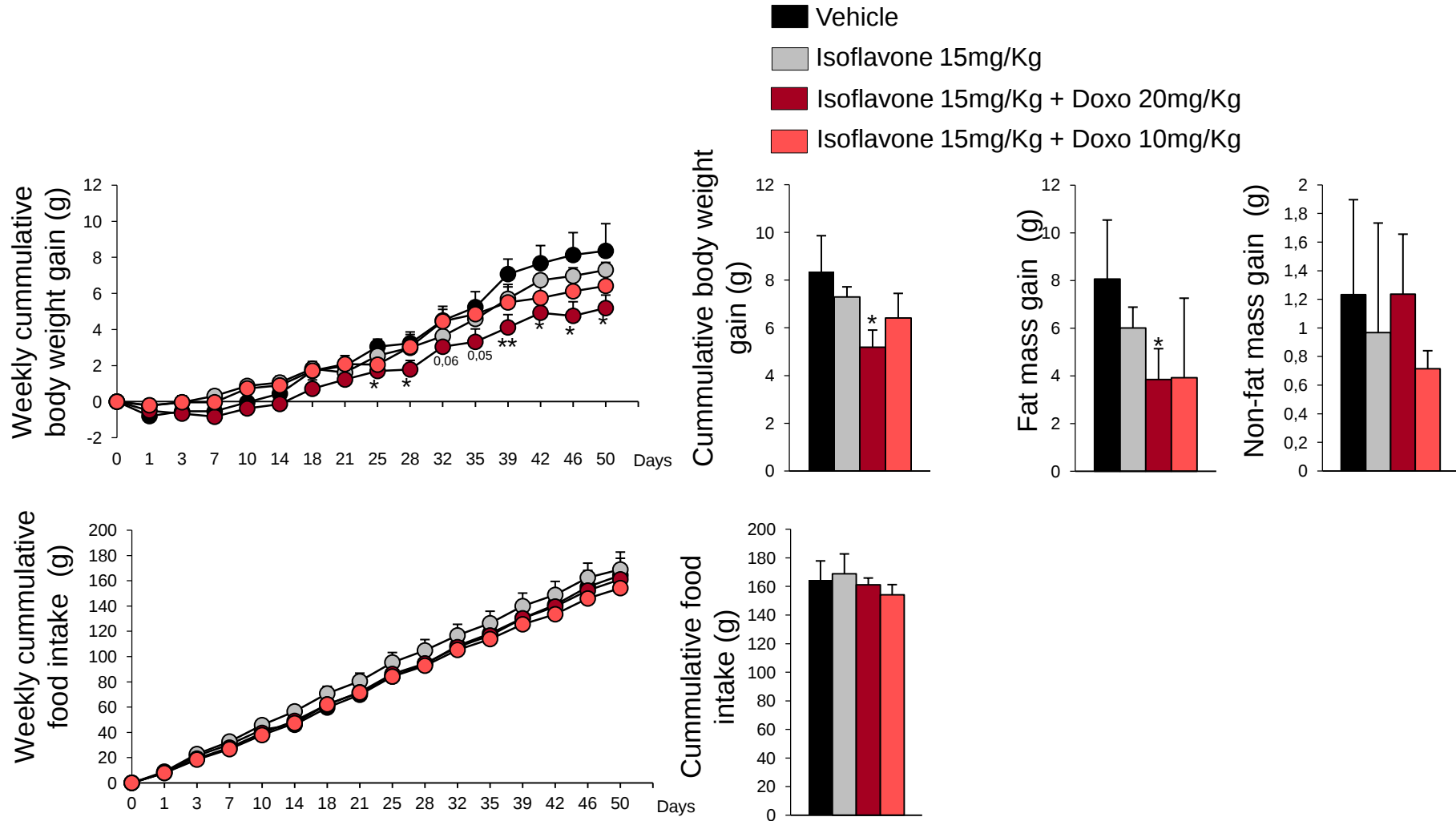
saline

Doxo (0.6 mg/kg)



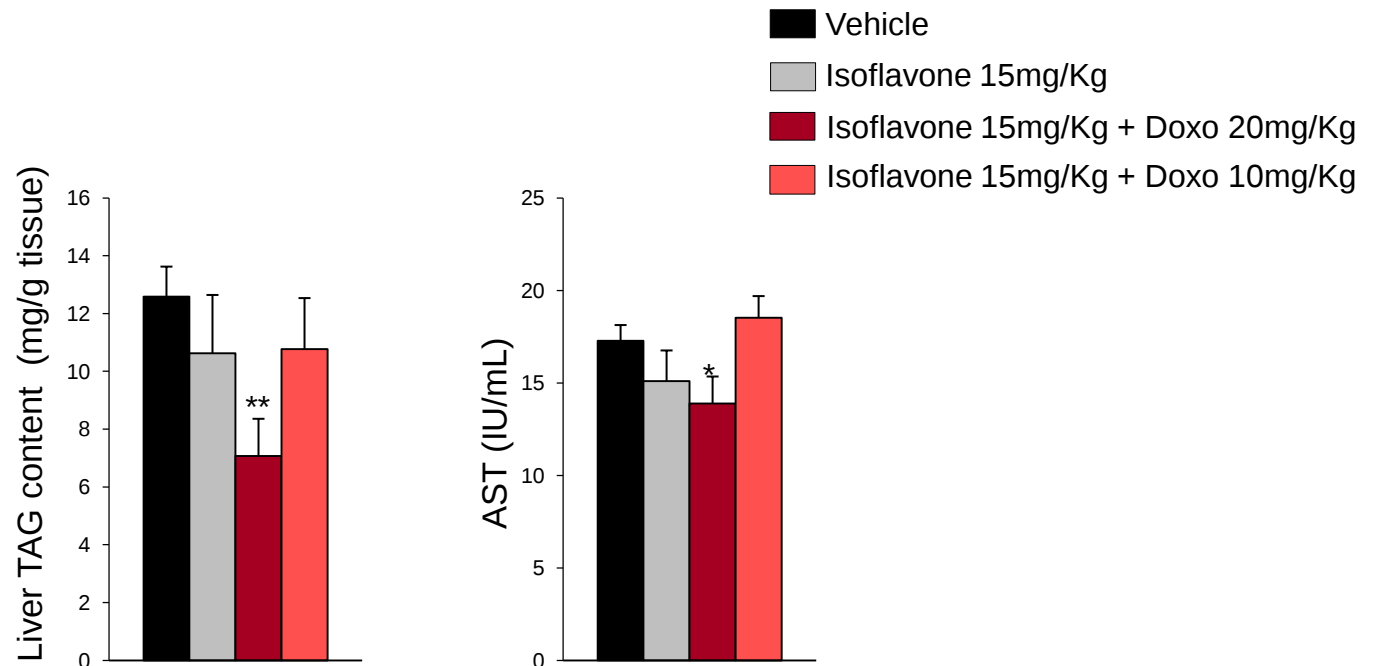
# The Product: Innovative mechanisms of action

## CIM ORAL GAVAGE 2 DAYS/WEEK DURING 50 DAYS C57/B6 MICE HFD (60% FAT)



# The Product: Innovative mechanisms of action

**CIM ORAL GAVAGE 2 DAYS/WEEK DURING 50 DAYS C57/B6 MICE HFD (60% FAT)**



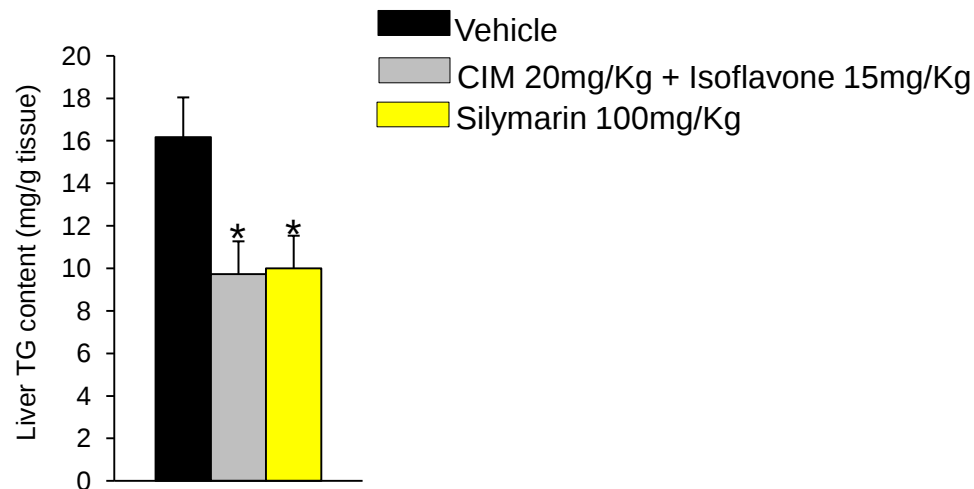
# The Product: Differential features facing the market

**NAFLD is an orphan disease.**

**No current treatment available (just change of lifestyle and diet)**

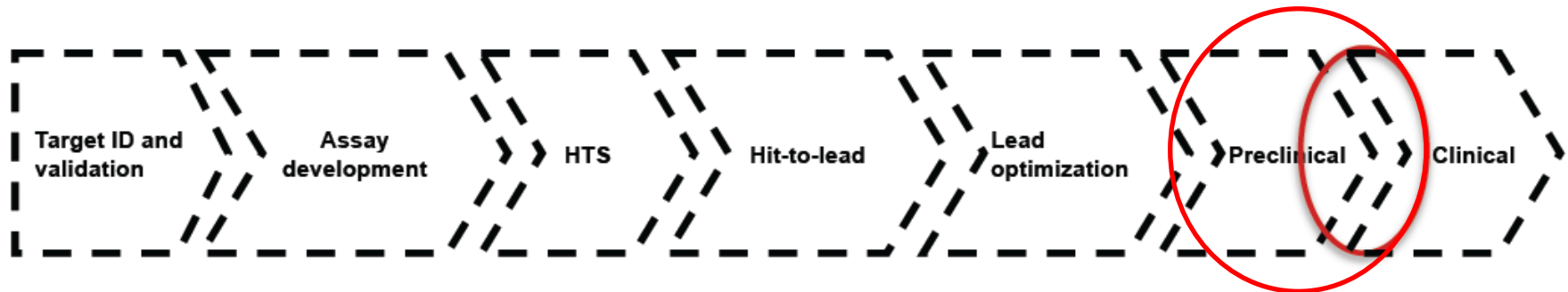
**Comparison of our compound vs an ongoing clinical phase-2 drug**

## LIVER TG CONTENT



## The Product: Current status of development

Preclinical regulatory application through:  
**European Research Council Proof of Concept call**



# The Product: IPR protection



## Acknowledgement of receipt

We hereby acknowledge receipt of your request for grant of a European patent as follows:

|                                               |                                                                                                                                                                                                                                   |
|-----------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Submission number                             | 300173808                                                                                                                                                                                                                         |
| Application number                            | EP15382519.5                                                                                                                                                                                                                      |
| File No. to be used for priority declarations | EP15382519                                                                                                                                                                                                                        |
| Date of receipt                               | 22 October 2015                                                                                                                                                                                                                   |
| Your reference                                | 900 564                                                                                                                                                                                                                           |
| Applicant                                     | Universidade de Santiago de Compostela                                                                                                                                                                                            |
| Country                                       | ES                                                                                                                                                                                                                                |
| Title                                         | Methods of using up-regulators of the expression of p53 and/or down-regulators or inhibitors of the expression of p63 for the treatment of NAFLD (Non-alcoholic fatty liver disease) and/or NASH (non-alcoholic steatohepatitis). |

## **The Product: Pitfalls & Risks to be considered**

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- 1. Doxorubicin is already commercialized**
- 2. High doses of doxorubicin are hepatotoxic and cardiotoxic**

## The Product: Partnering Opportunities

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**We are open and willing to have any kind of collaboration, from scientific advise to go on with the right assays in the project to a co-development.**