

# Research & development

*Anne Kristin Holmeide, PhD ,director research and development*



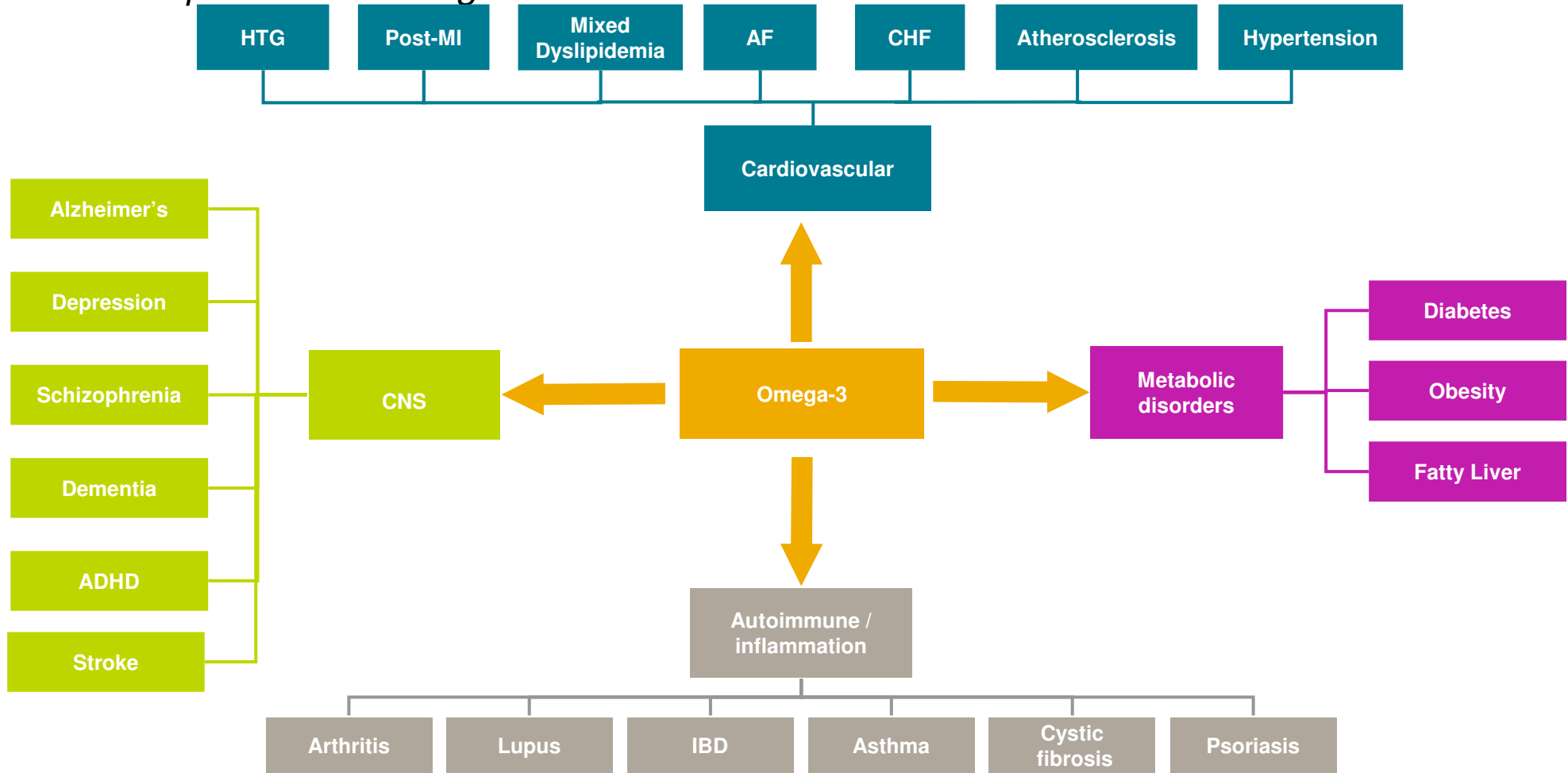
---

**Disclaimer:**

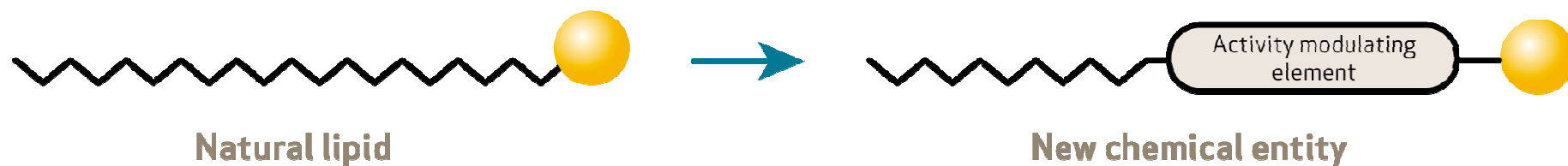
THIS PRESENTATION HAS BEEN PREPARED BY PRONOVA BIOPHARMA ASA (THE "COMPANY") EXCLUSIVELY FOR INFORMATION PURPOSES. THIS PRESENTATION HAS NOT BEEN REVIEWED OR REGISTERED WITH ANY PUBLIC AUTHORITY OR STOCK EXCHANGE. THE DISTRIBUTION OF THIS PRESENTATION AND ANY OFFERING, SUBSCRIPTION, PURCHASE OR SALE OF SECURITIES ISSUED BY THE COMPANY IN CERTAIN JURISDICTIONS IS RESTRICTED BY LAW. POTENTIAL INVESTORS ARE REQUIRED BY THE COMPANY TO INFORM THEMSELVES ABOUT AND TO COMPLY WITH ALL APPLICABLE LAWS AND REGULATIONS IN FORCE IN ANY JURISDICTION IN WHICH IT INVESTS AND MUST OBTAIN ANY CONSENT, APPROVAL OR PERMISSION REQUIRED UNDER THE LAWS AND REGULATIONS IN FORCE IN SUCH JURISDICTION. THE COMPANY SHALL NOT HAVE ANY RESPONSIBILITY OR LIABILITY FOR THESE OBLIGATIONS. THIS PRESENTATION DOES NOT CONSTITUTE AN OFFER TO SELL OR A SOLICITATION OF AN OFFER TO BUY ANY SECURITIES IN ANY JURISDICTION TO ANY PERSON TO WHOM IT IS UNLAWFUL TO MAKE SUCH AN OFFER OR SOLICITATION IN SUCH JURISDICTION.

# Omega-3 PUFAs have wide ranging effects

*A substantial amount of pharmacological and clinical data the last 15-20 years show a wide spectrum of biological effects for  $\omega$ -3 PUFAs*

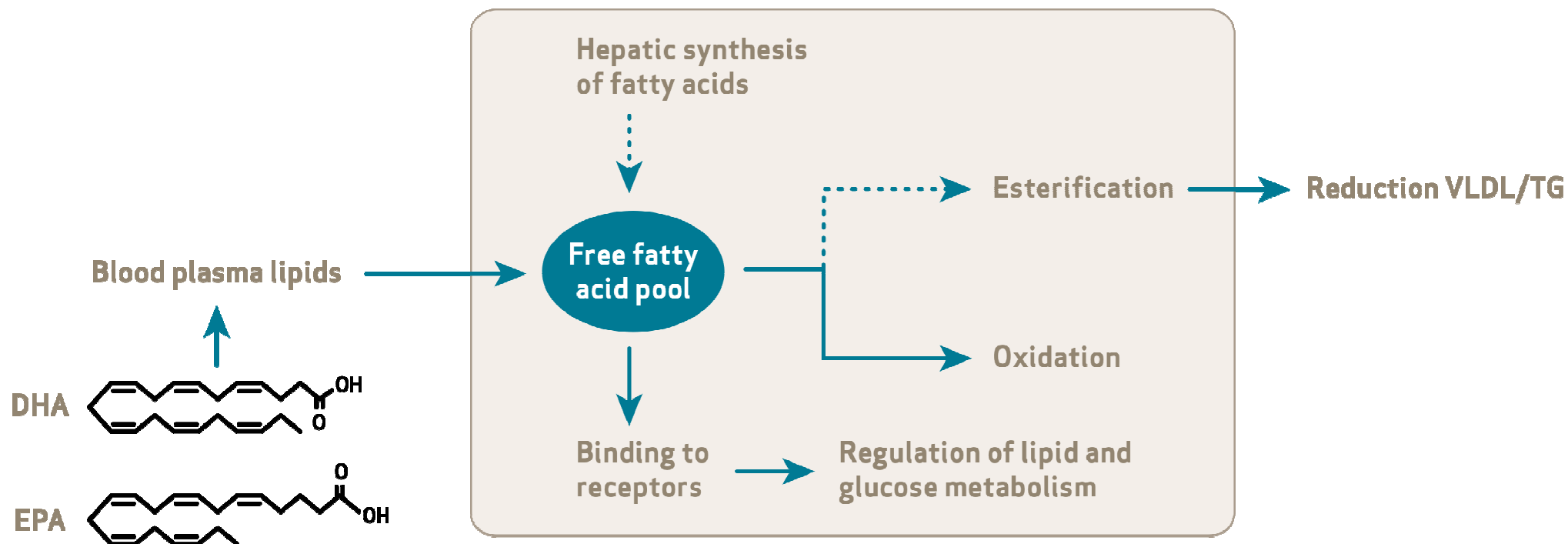


# Lipid derived pharmaceuticals



- New drug concept with novel structural features
- Based on unique experience within the lipid area
- Biological targets selected from targets proven to be affected by natural omega-3 polyunsaturated acids
- Huge potential within major disease areas
- Covered by a broad patent portfolio

# Omacor/Lovaza, mechanisms of action



***Omacor/Lovaza increases the oxidation of other fatty acids and reduces the hepatic synthesis of fatty acids → reduced synthesis of TG***

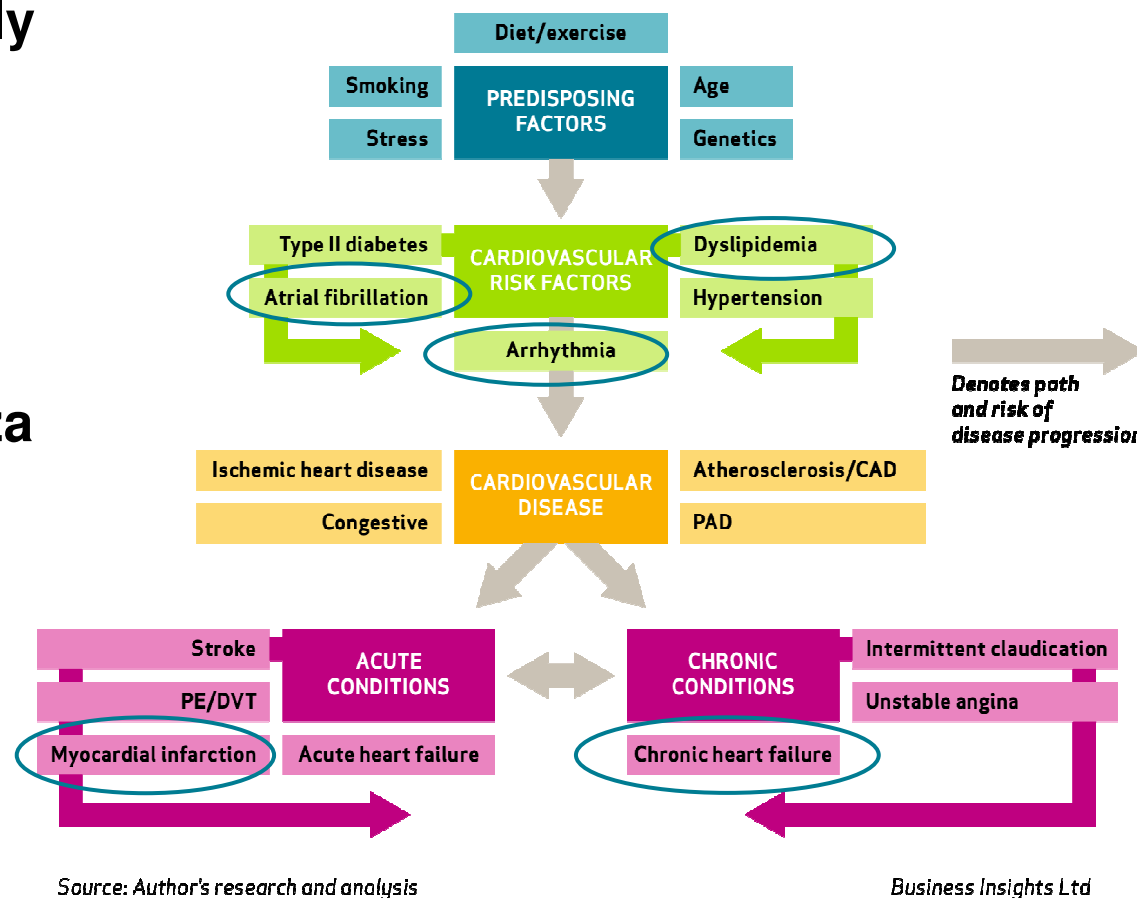
# Benefits with lipid derived pharmaceutical

---

- **Potentially improved therapeutic index compared to existing pharmaceuticals**
  - *Safety profile similar to Omacor/Lovaza*
  - *Higher affinity towards target receptors than natural polyunsaturated fatty acids*
- **Improved pharmacokinetics compared to Omacor/Lovaza**
  - *Remains active longer*
- **More specific bio-distribution than Omacor/Lovaza**
  - *Tissue targeting*
- **Application in new indications outside of Omacor/Lovaza areas**

# Cardiovascular diseases (CVD)

- CVD cause >1/3 of all deaths globally
- Many therapies available
  - for treatment of both cardiovascular risk factors and cardiovascular diseases
- Death reduction with Omacor/Lovaza
  - Sudden cardiac death reduction (45% GISSI-P)
  - Cardiovascular death reduction (30% GISSI-P)
- Unmet need in CVD population



# Hyperlipidemia study – ApoE\*3L mice

## Objective :

- Study the effect of pipeline products on lipid metabolism in a hyperlipidemic animal model

## Measured parameters:

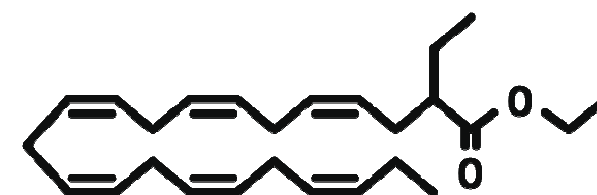
- TG and cholesterol

## PRB-2 tested in 3 different doses:

- 0.1, 0.3, 1.0 mmol/kg bw/day

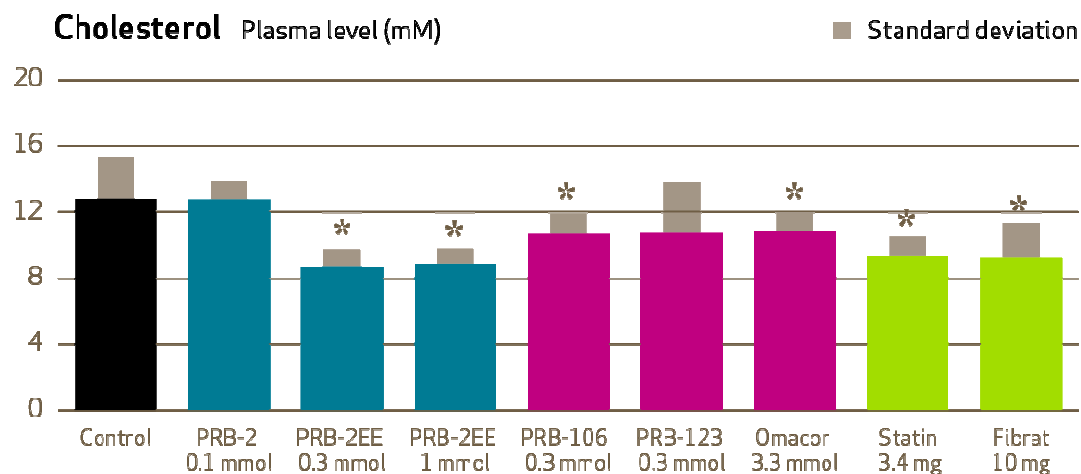
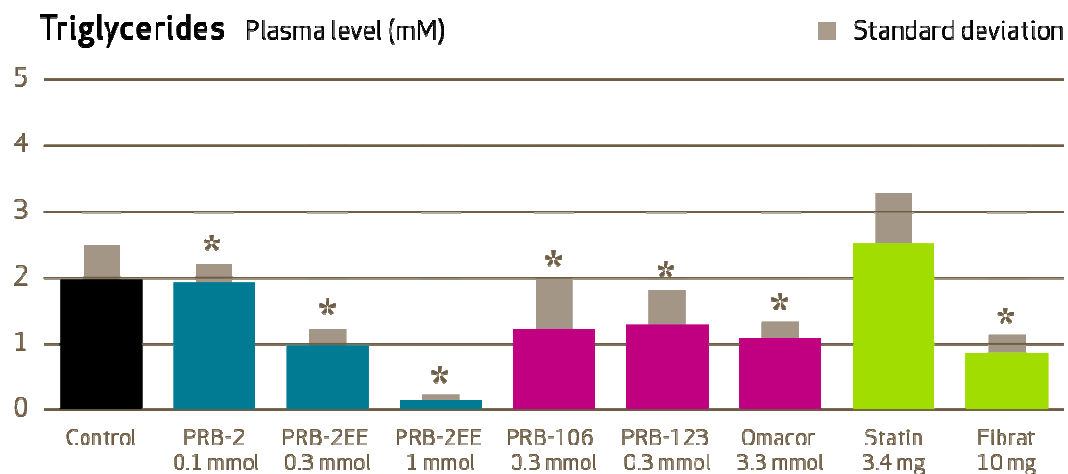
## PRB-106 and PRB-123 tested in one single dose:

- 0.3 mmol/kg bw/day
- Control treatments:
  - Lovaza/Omacor (3.3 mmol/kg bw/day)
  - Lipitor (statin 3.4 mg/kg bw/day)
  - Tricor (fibrate 10 mg/kg bw/day)



PRB-2

# Triglycerides and Cholesterol – ApoE\*3L mice



# Diabetes type II

---

- **Dramatic increase**
  - *in the prevalence of diabetes in the major markets*
- **Diabetes is an important risk factor for CVD**
- **Type 2 diabetes or non-insulin dependent diabetes mellitus accounts for 90-95% of the diagnosed diabetic population**
- **Focus of therapy**
  - *Glucose control and lipid lowering, diet control*

*There is a strong, unmet need for development of new classes of anti-diabetic drugs, with fewer side effects and better tolerability*

# Type II diabetes study – ob/ob mice

---

## **Objective:**

- Study the effect of PRB-2 on glucose metabolism in a diabetic animal model

## **Measured parameters:**

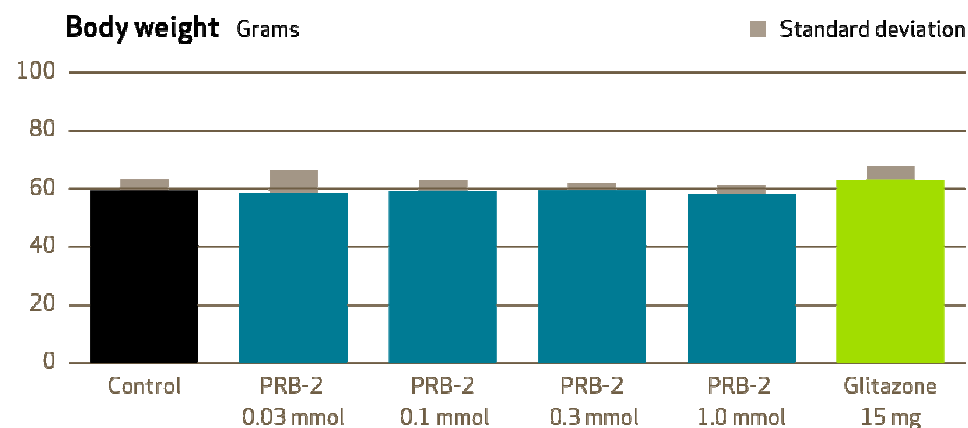
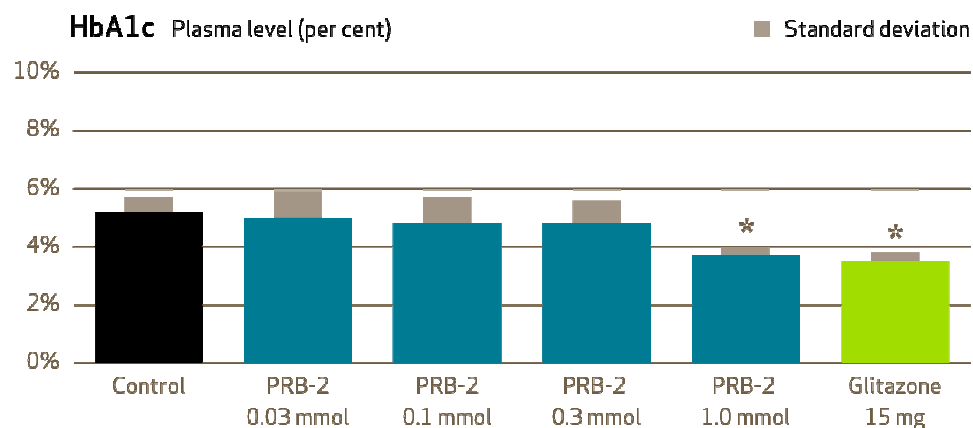
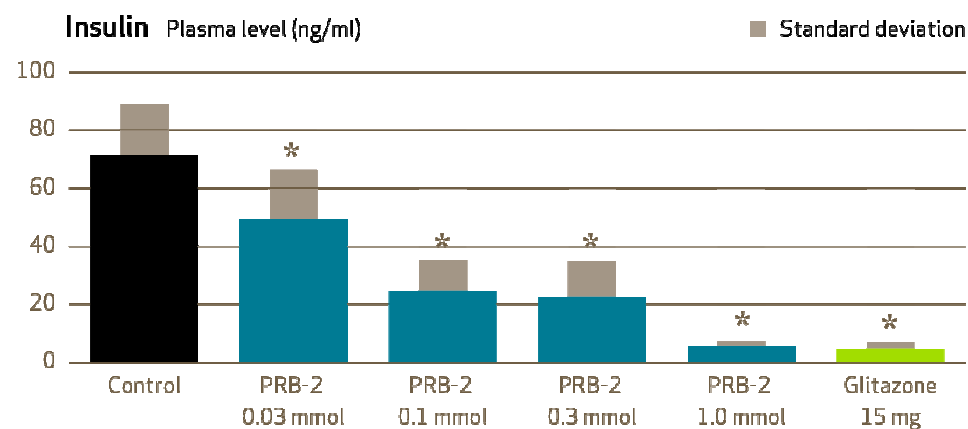
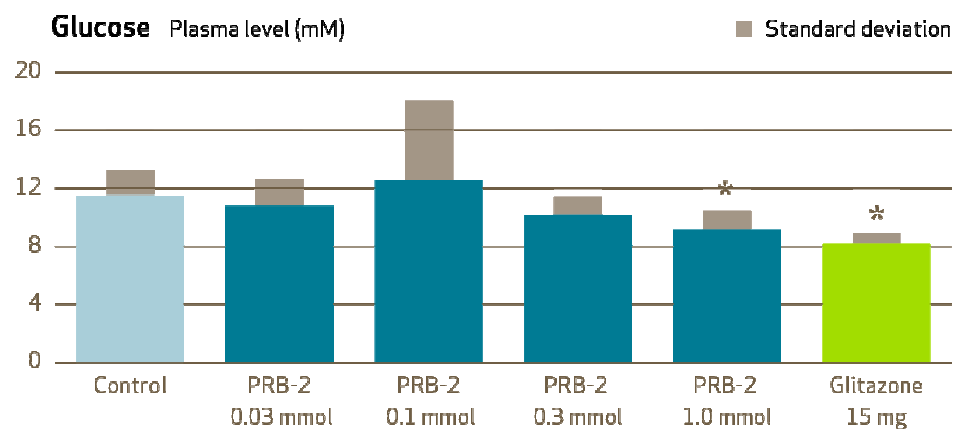
- Glucose, HbA1c, Insulin, BW

## **PRB-2 tested in 4 different doses:**

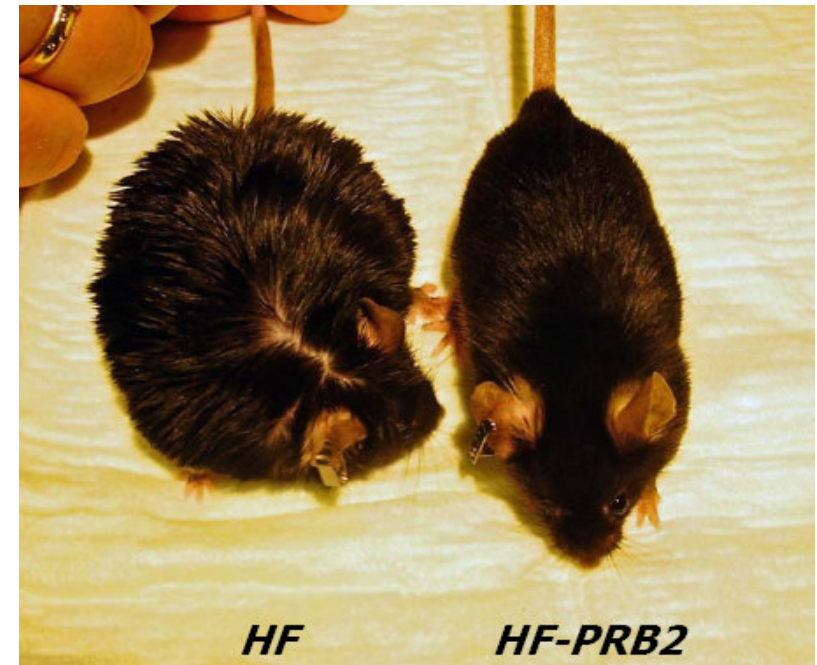
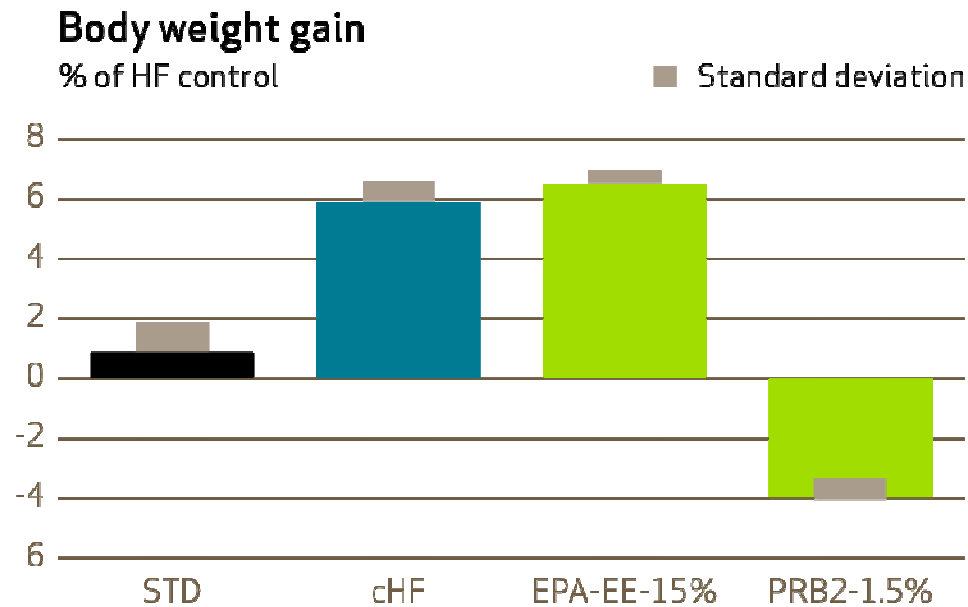
- 0.03, 0.1, 0.3 and 1 mmol/kg bw/day

**Actos (glitazone) used as a positive control (15 mg/kg bw/day)**

# Type II diabetes study – ob/ob mice



# Obesity study – high fat fed mice



# Summary: R&D in Pronova BioPharma

---

- **Has identified lipid compounds with enhanced biological activity compared to natural PUFAs in relation to lipid lowering effects, insulin sensitivity and weight reduction**
- **Has synthesized numerous new lipid substances**
- **Is in actively screening these substances (in vitro and in vivo)**
- **Has identified a new drug candidate: PRB-2**
- **PRB-2 has been tested in a toxicology program, analysis phase ongoing according to plan**
- **Also working with identification of backup candidates**