



***Capitalizing On Expanded Opportunities  
Cardiovascular, Metabolic, and  
Endocrine Disease (CVMED)***

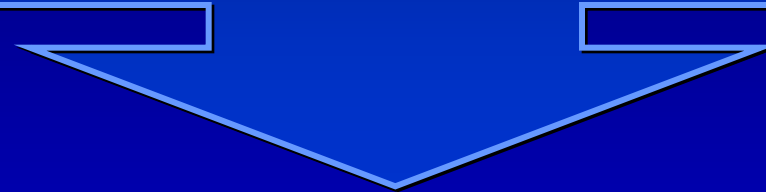
**Steven Ryder, M.D.  
Senior Vice President  
Therapeutic Area Development Head**



## ***Vision And Strategy***

### ***VISION***

**To Deliver Innovative Products and Solutions  
that Maintain Health and Reduce  
CVMED Disease Burden.**



### ***STRATEGY***

**To Achieve a CVMED Portfolio Mix and Create  
an Environment that Maximizes Value by Pursuing  
Long-term Growth Investments in Prevention  
and Disease Treatment.**



# ***In-Line Portfolio Focused on Risk-Factor Modification and Disease Intervention***

## **Risk-Factor Modification**





## **Disease Intervention**



***Healthy Aging Population***



# Development Portfolio Focused on Risk-Factor Modification and Disease Intervention

Health Maintenance	Risk-Factor Modification	Disease Intervention
<p><b>Healthy Aging Population</b></p>	<p>CP-945,593 Obesity </p>	<p> Phase 3/Registration</p>
	<p>MTPi* Obesity</p> <p>PPAR<math>\alpha</math> Lipid/IR</p> <p>DPPIV Diabetes</p>	<p>CP-533,536* Bone Healing</p> <p>PD-348,592* Thrombosis</p> <p>Esperion CV</p> <p>Peg GH GH Deficiency</p>
	<p><math>\mu</math> opioid Obesity</p> <p>11<math>\beta</math> HSD Diabetes</p> <p>Torcetrapib HDL</p> <p>Combos Obes &amp; DM</p> <p>CCKa Obes &amp; DM</p> <p>PPAR<math>\alpha</math> Lipid/IR</p> <p>CETPi HDL</p>	<p>PDE5i CV</p> <p>Phase 1</p> <p>* = new disclosure</p>



## **An Evolving Strategy**

### **Intervention**

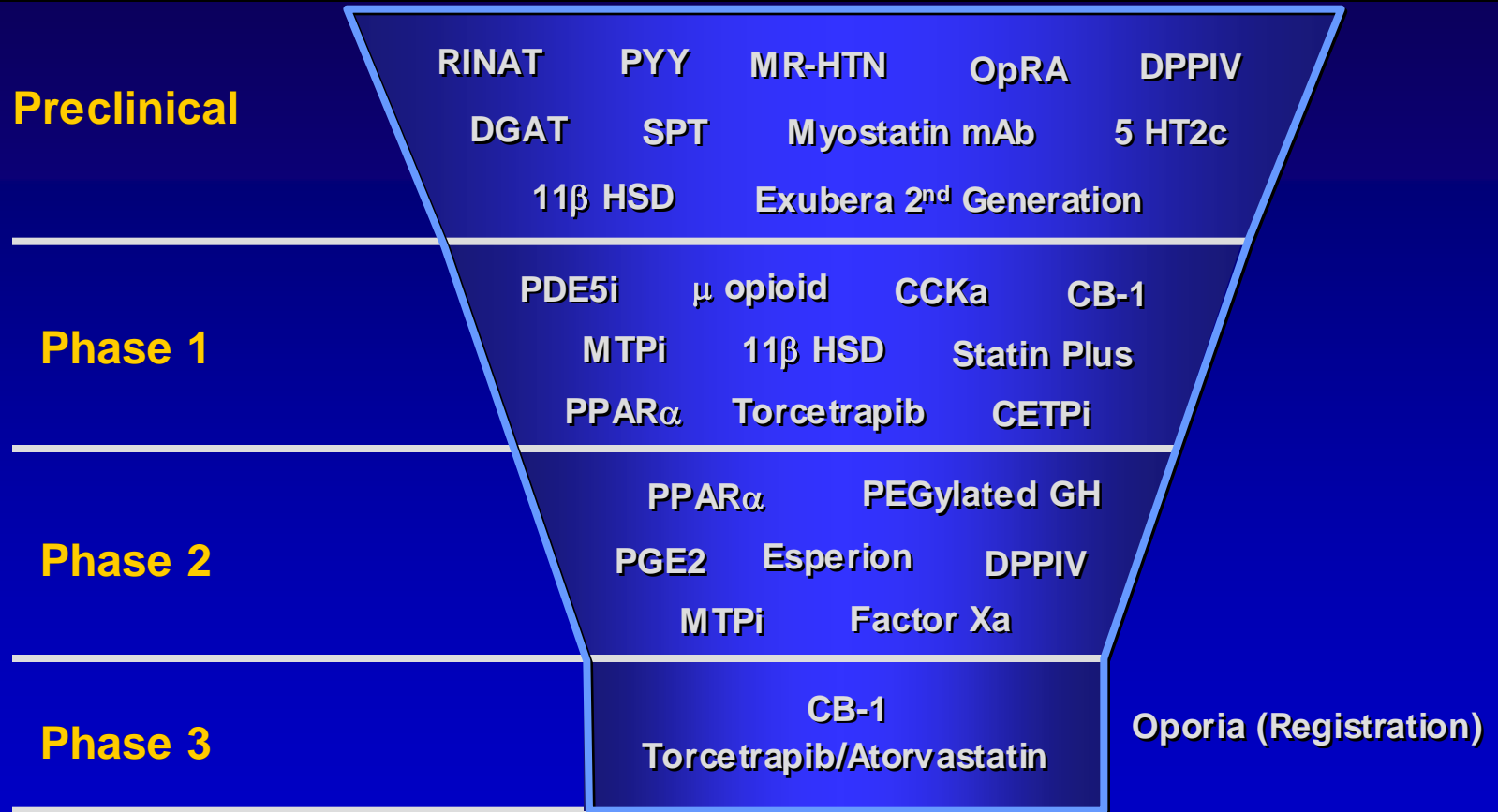
**Thrombosis**  
**Coronary Heart Disease**  
**Diabetes (e.g. Insulin)**  
**Growth Hormone Deficiency**  
**Bone Healing**

### **To Prevention**

**Obesity**  
**Diabetes**  
**Insulin Resistance**  
**Hyperlipidemia**  
**Muscle Loss**  
**Bone Metabolism**



# Expanding Scope Of CVMED R&D



## In-Line Portfolio





## **CVMED R&D**

### **Current WW Market Size/ Opportunity (\$U.S. Billion)**

◆ <b>Atherosclerosis</b>	<b>\$34.0</b>
◆ <b>Obesity</b>	<b>\$35.0</b>
◆ <b>Diabetes</b>	<b>\$19.5</b>
◆ <b>Bone and Muscle Health</b>	<b>\$10.6</b>
◆ <b>Thrombosis</b>	<b>\$5.6</b>

*Obesity*

- ◆ Major Health Problem
- ◆ Risk Multiplier for Many Diseases
- ◆ Unmet Medical Need

*Managing the Entire Patient*



# Multiple Approaches In Obesity

## Central & Peripheral Anorectics

(Inhibit Desire to Eat)

5HT<sub>2c</sub>, CB-1, NPY<sub>5</sub>, MCR<sub>4</sub>, Ghrelin, AGRP, NT-1, MCH, 5-HT<sub>6</sub>, PYY, MTPi, CCK-A, NT-1, PP, DGAT, SCD-1

## Thermogenic & Metabolic Stimulators

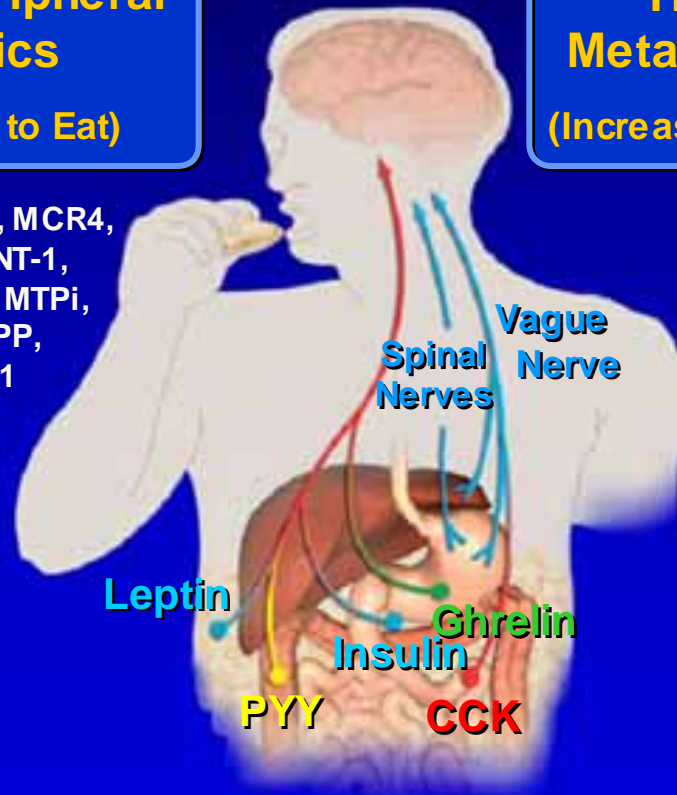
(Increase Calorie Expenditure)

MCR<sub>4</sub>, AGRP, CB-1, 11 $\beta$ HSD, PPAR, DGAT, GPRs, SCD-1, ACC, Ghrelin, SGLT1

## Absorption Inhibitors

(Limit Fat Absorption)

MTPi

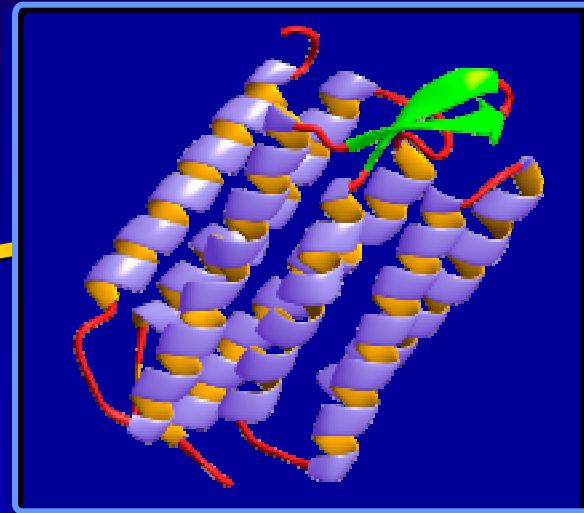


*Maximal Efficacy will Likely Require Co-Administration of Agents with Multiple Mechanistic Targets*



# Cannabinoid Receptor-1 Antagonism

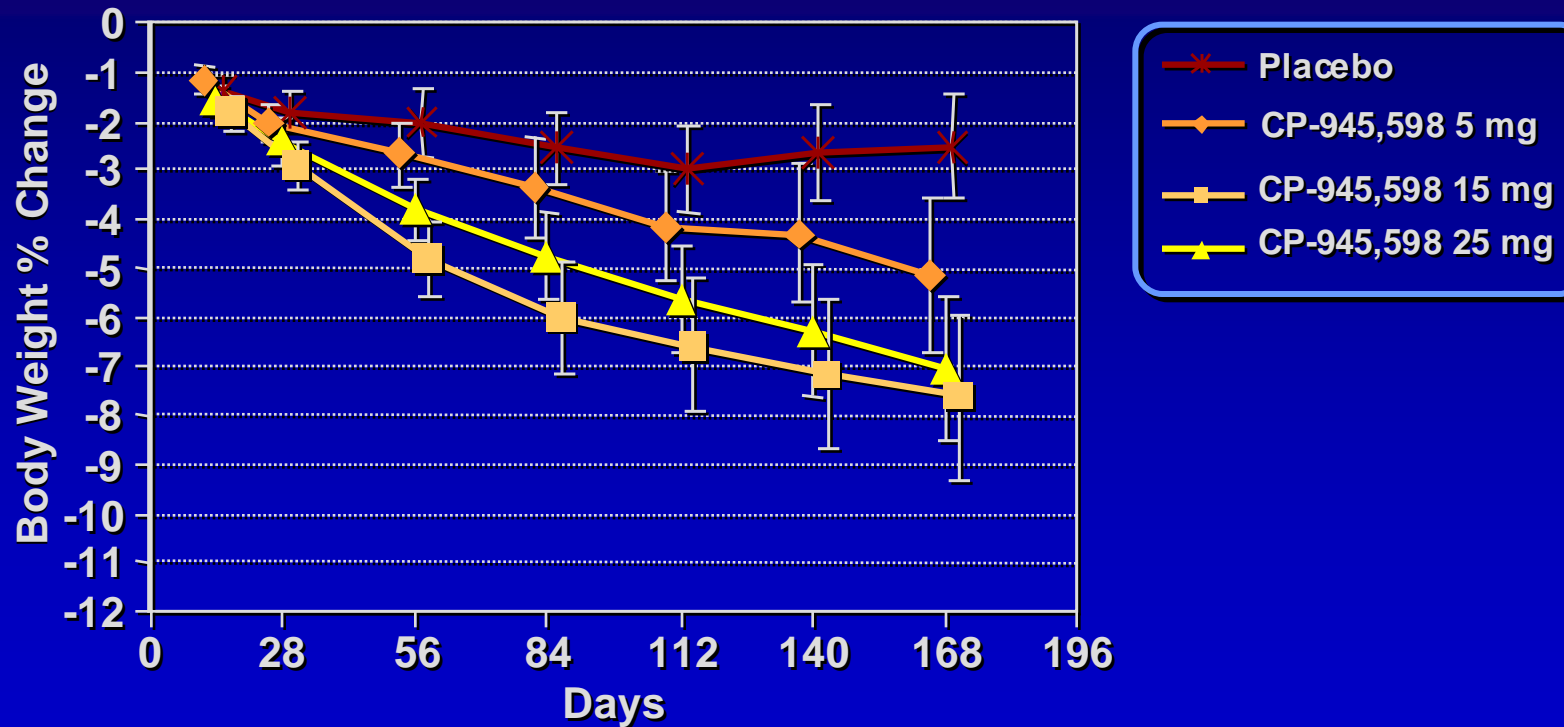
CP-945,598 – Phase 3



*G-Coupled Protein CNS-Mediated Effect*



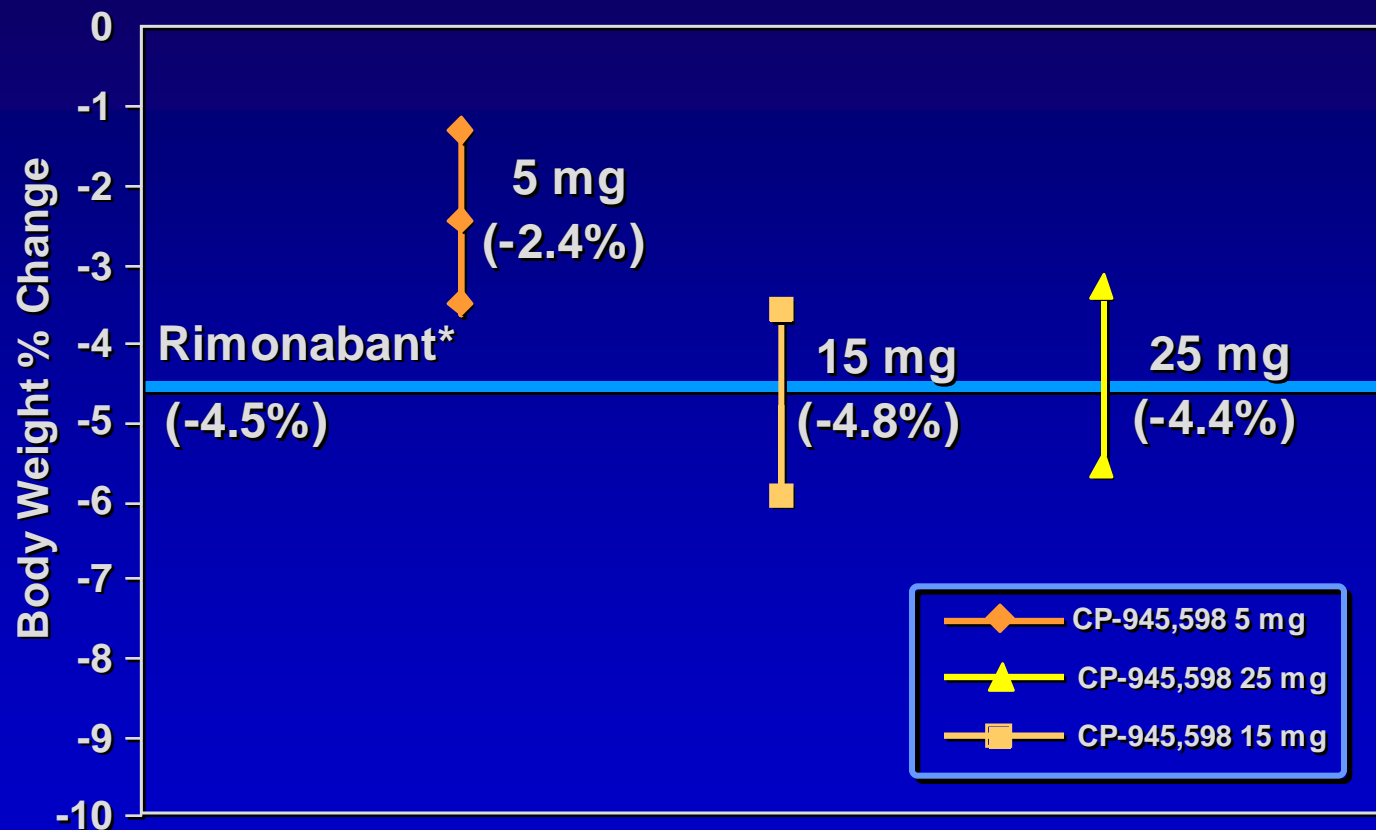
# CP-945,598 (CB-1 Antagonist) Phase 2 Study: % Change in Body Weight





# CP-945,598

## Placebo-Adjusted Percent Change In Weight At 6 Months



\* Extrapolation Full ITT RIO EU; PBO-Adjusted



## **CP-945,598** **CB-1 Antagonist**

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- ◆ **Well Tolerated in Phase 1 and 2**
- ◆ **Phase 3 Started**
- ◆ **Additional Cb-1-Antagonist Candidates in Phase 1 Development**



## **Obesity**

### *The Opportunity With MTP Inhibitors*

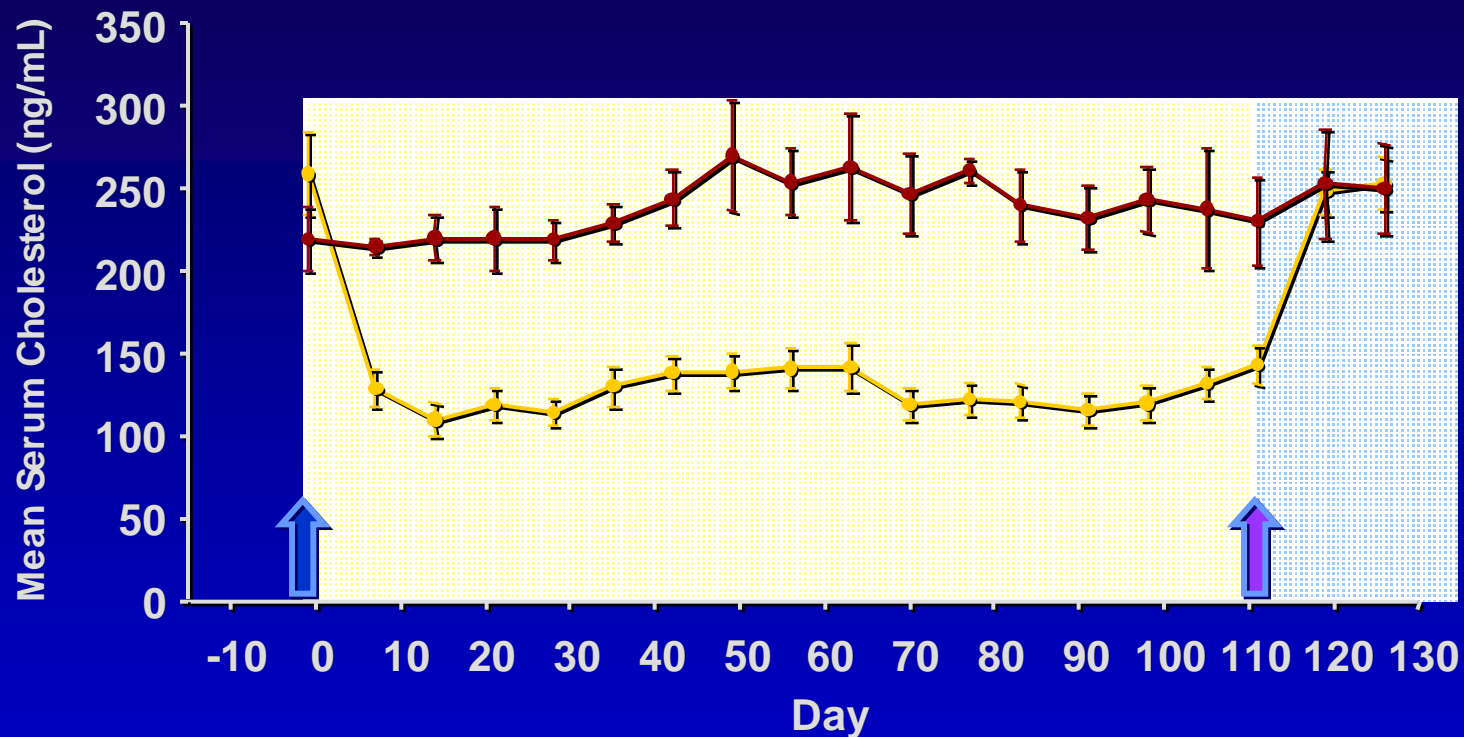
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- ◆ **MTP (Microsomal Triglyceride Transfer Protein) Continues to Emerge as One of the Most Compelling Targets in the CVMED Portfolio**
  - **LDL/VLDL Cholesterol Reductions**
  - **Clinical Weight Loss Better Than Current Therapy**
  - **Potential Best-In-Class Therapy for Obesity**



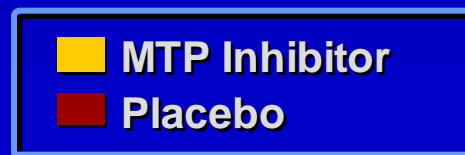
# MTP Inhibitor in Dogs

## Significant Cholesterol Reduction



↑ Begin Study Drug Administration

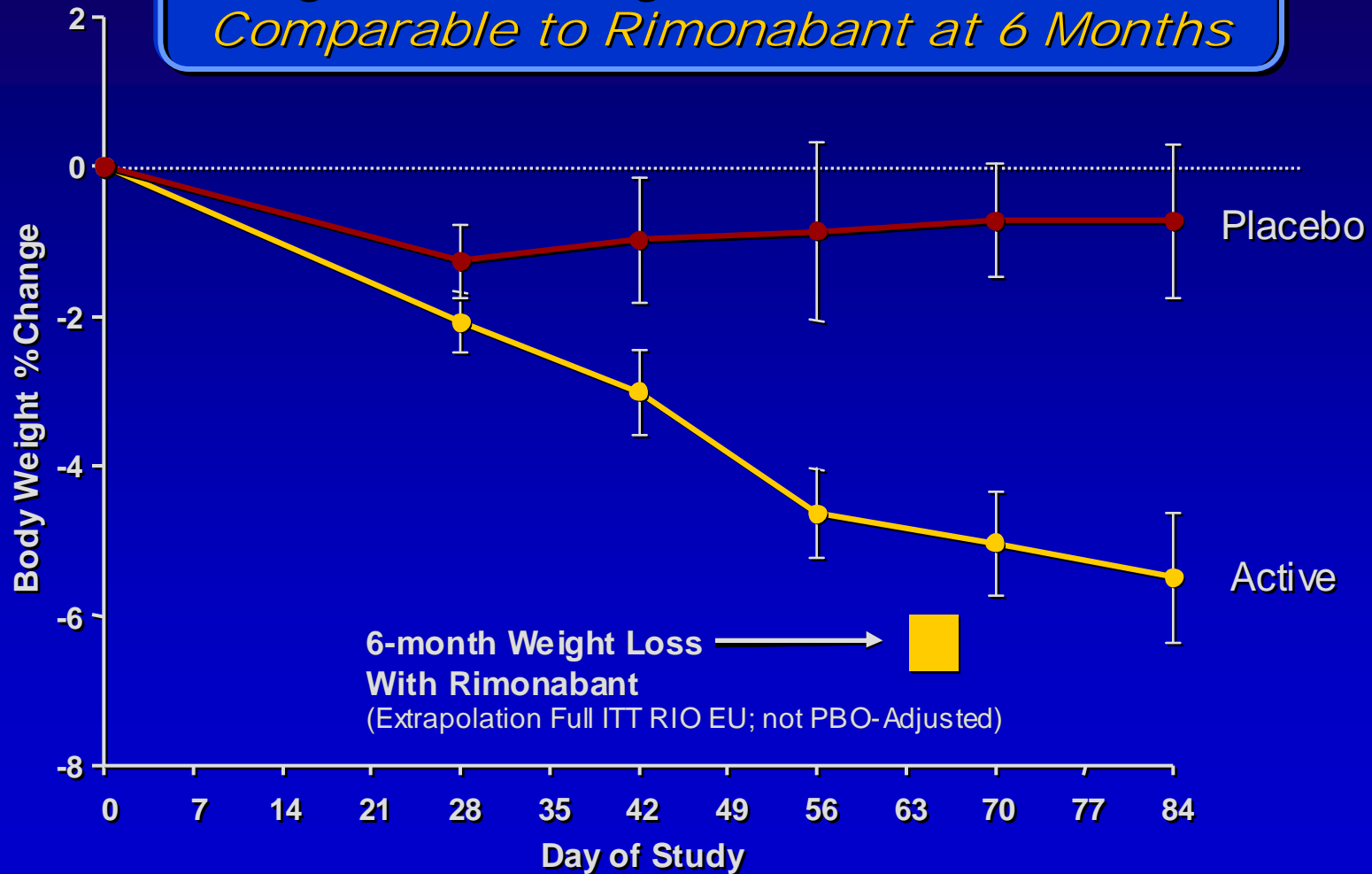
↑ End Study Drug Administration





# MTP Inhibitor

*Significant Weight Loss at 3 Months  
Comparable to Rimonabant at 6 Months*



- ◆ Atherosclerosis
- ◆ Obesity
- ◆ **Diabetes**
- ◆ Bone and Muscle Health
- ◆ Thrombosis