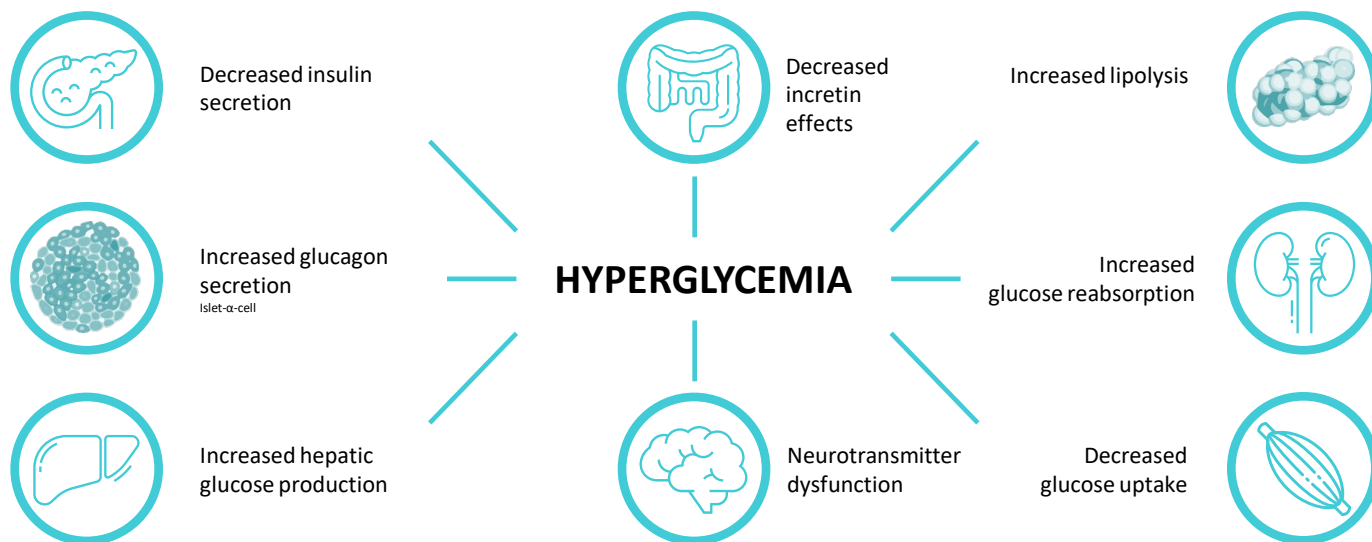
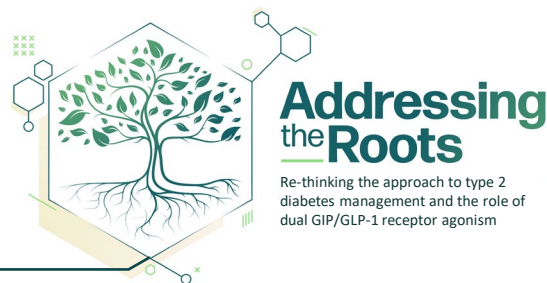


# Key Historic Focus of Diabetes Management:

## Glycemic Control and The Ominous Octet<sup>1</sup>



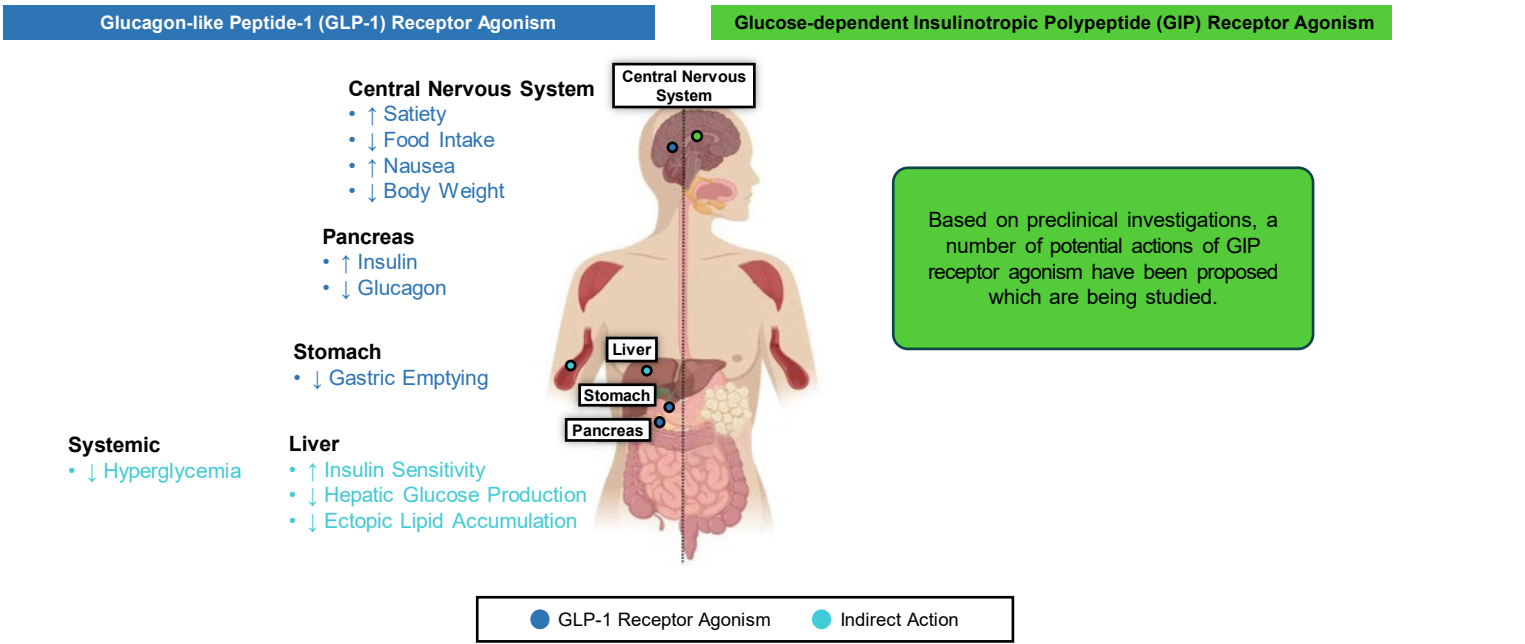
- While glycemic control remains a cornerstone of diabetes management, overall treatment goals are more comprehensive, including cardiorenal protection.
- Adiposopathy, or “sick fat” is an underlying mechanism for many disease states, including T2D

- Therapies for T2D address different components of the pathophysiology – an ideal therapy would address multiple components, including glycemic control, cardiorenal risk reduction and adiposopathy
- Dual GIP/GLP-1 receptor agonism has demonstrated A1C and body weight reductions superior to placebo, to GLP-1 receptor agonism and to basal insulin in clinical trials.

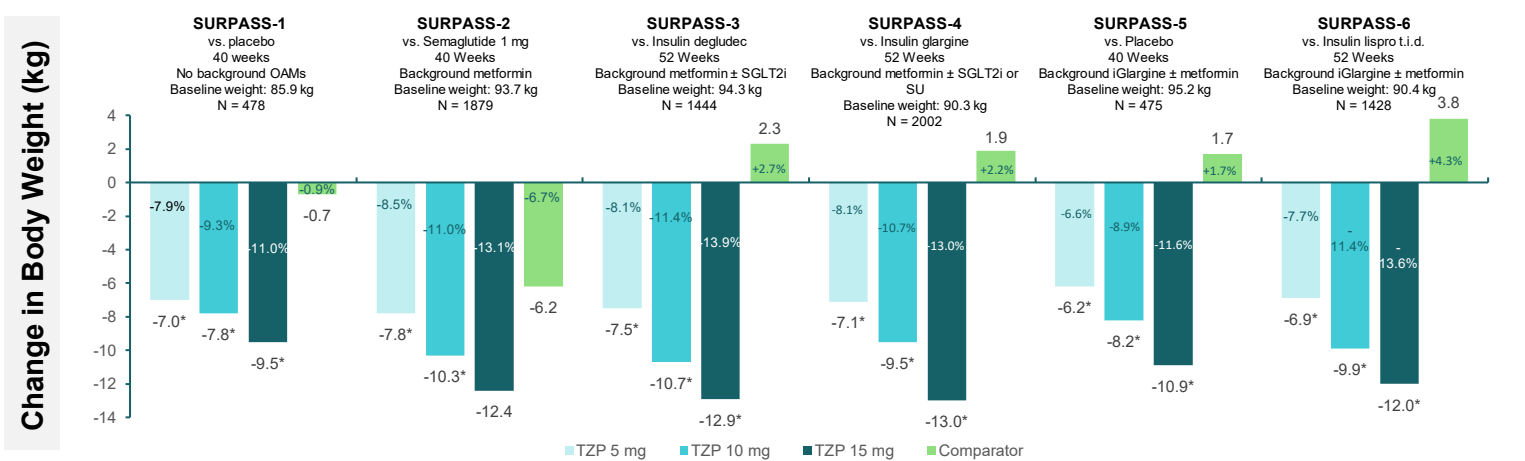
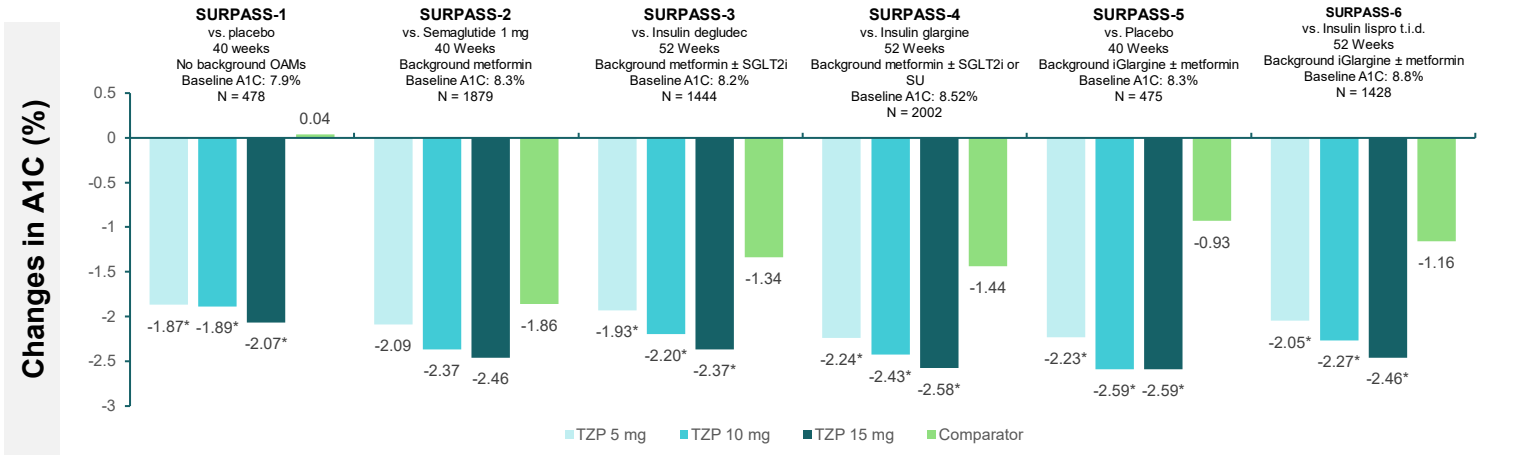
## Evolving View of Antihyperglycemic Therapies, Including Cardiorenal Protection and Decreased Body Weight<sup>1-3</sup>

Mechanism	Metformin	SU / glinide	TZD	DPP4i	GLP1-RA	SGLT2i	GIP/GLP-1RA
↑ insulin secretion		✓	✓	✓	✓		✓
↓ glucagon secretion				✓	✓		✓
↓ hepatic glucose production	✓		✓	✓	✓		✓
Incretin pathways				✓	✓		✓
↓ lipolysis			✓				?
↓ glucose reabsorption						✓	
↑ glucose uptake	✓		✓	✓	✓		✓
↓ neurotransmitter dysfunction					?		?
↓ cardiorenal risk					✓	✓	?
Decrease Body Weight					✓	✓	✓

# Effects of GIP/GLP-1 Dual Agonism Extend Beyond Glycemic Control<sup>4</sup>



## SURPASS Trials with the GIP/GLP-1 Receptor Agonist Tirzepatide: Summary of Effects on A1C and Body Weight<sup>5-10</sup>



References:  
 1. DeFronzo RA. Diabetes. 2009; 58(4):773-95; 2. Abdul-Ghani M, et al. Diabetes Care 2017; 40:1121-7; 3. Lipscombe L, et al. Can J Diabetes. 2020; 44(7):575-91; 4. Adapted from Samms RJ, et al. Trends Endocrinol Metab. 2020; 31(6):410-21; 5. Rosenstock J, et al. Lancet. 2021; 398(10295):143-55; 6. Frias JP, et al. N Engl J Med. 2021; 385(6):503-15; 7. Ludvik B, et al. Lancet. 2021; 398(10300):583-98; 8. Del Prato S, et al. Lancet. 2021; 398(10313):1811-24; 9. Dahl D, et al. JAMA. 2022; 327(6):534-45; 10. Rosenstock J et al. Presented at American Diabetes Association – 83rd Annual Scientific Sessions; 2023. Poster 750-P.