



**The combination of a long acting GLP-1 analog (E-XTEN; VRS-859) and long acting glucagon (Gcg-XTEN; AMX-808) for superior weight loss and glycemic control in treatment of type 2 diabetes and obesity**

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Previous studies of a VRS-859, exenatide-XTEN (E-XTEN), demonstrated comparable weight loss and glycemic control to exenatide in mouse models. The long half-life of VRS-859 (60 hr in monkeys) provides a monthly dosage option in humans. Agonism of both the GLP1 and glucagon receptor may increase weight loss and glycemic control in type 2 diabetes and obesity. A novel glucagon-XTEN (Gcg-XTEN; AMX-808) construct was developed to allow weekly dosing of glucagon. The unique properties of XTEN, a hydrophilic tail of natural amino acids, allow these products to be combined and their doses and pharmacokinetic profiles to be adjusted to optimize the efficacy and safety. In diabetes induced obese (DIO) mice, VRS-859 was administered either every 2 days or 4 days along with AMX-808 administered BID or QD, respectively. Combination treated DIO mice had an approximate 25% weight loss and 40% decrease in fasting blood glucose after 28 days of treatment, and these changes were significant compared to the single agents or placebo. The combination treatment groups achieved glycemic control, increased insulin sensitivity, and significant reduction in cholesterol and triglycerides at the end of the study. The data suggest that the combination of the two products may represent a convenient and effective treatment for type 2 diabetes and obesity.

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