NA-931, a novel quadruple IGF-1, GLP-1, GIP and Glucagon receptor agonist attenuates alcohol mediated behaviors

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Abstract

Statement NA-931 is a quadruple agonist of the insulin-like growth hormone- (IGF-1), glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) and glucagon receptors has been shown a proof of safety and efficacy for the potential treatment of metabolic disorders such as obesity. Preclinical studies showed that NA-931 reduce alcohol mediated behaviors.

Body Weight Reductions

In the 28-day randomized doble blind placebo control Phase 1 study, subjects receiving NA-931 (n=74) demonstrated dose-dependent reductions in mean body weight from baseline, ranging up to 6.4%, ranging up to 5.3% relative to placebo.

Safety and Tolerability

NA-931 demonstrated encouraging safety and tolerability following 28 days of once-daily dosing. Mild nausea and vomiting were not reported among any NA-931-treated subjects. Diarrhea was reported in one subject (2.3%) receiving NA-931 compared with two subjects (10%) receiving placebo. No muscle loss was observed. Overall, no clinically meaningful differences were reported for GI-related adverse events among subjects treated with NA-931 compared with placebo. In addition, no serious adverse events (SAEs) have been reported to date.

Potential Treatment of Alcohol Drug Use

NA-931 has been shown to target central brain areas involved in reward and motivation, including the ventral tegmental area and nucleus accumbens. Herein we investigated the effects of the NA-931 on various measures of alcohol-induced reward as well as on alcohol intake and alcohol seeking behavior in rodents. Treatment with NA-931 at a dose with no effect per se, attenuated alcohol-induced locomotor stimulation and accumbal dopamine release in mice. Furthermore, conditioned place preference for alcohol was abolished by both acute and chronic treatment with NA-931 in mice.

We found that NA-931 treatment decreased alcohol intake, using the intermittent access 20% alcohol two-bottle-choice model, as well as alcohol seeking behavior, using the progressive ratio test in the operant self-administration model, in rats. These novel findings indicate that GLP-1 signaling attenuates the reinforcing properties of alcohol implying that the physiological role of NA-931 extends beyond glucose homeostasis and food intake regulation. Collectively these findings implicate that the quadruple agonist may be a potential target for the development of novel treatment strategies for alcohol use disorders.



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Lloyd is a scientist with 25-year experience in drug development and clinical trials management. He is an inventor with a number of patents in drug therapeutics in the treatment of neurological and metabolic disorders.
Lloyd serves as the chairman and CEO of Biomed Industries, Inc.
In his early career, he was employed as a research scientist at G.D. Searle, (a subsidiary of Pfizer), and was the director of R&D at Biomed Pharmaceuticals.
Lloyd graduated with a BSc(Honours) and completed a PhD in medicinal chemistry at University of Otago and Wellington University of New Zealand.