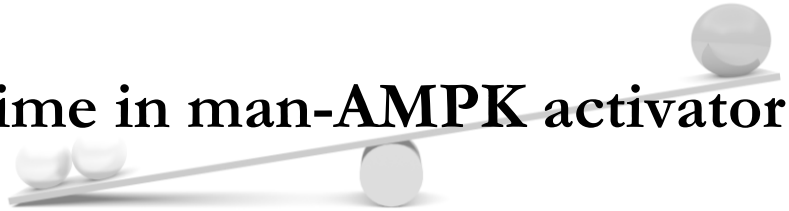
First time in man-AMPK activator O304



Betagenon AB/Baltic Bio AB announces the initiation of Phase I clinical studies with O304, an orally available AMPK activator.

The epidemic increase in obesity has generated a concomitant increase in fatty liver, non-alcoholic steato-hepatitis (NASH) and type 2 diabetes (T2D). Physical inactivity and T2D in elderly are in turn strongly associated with peripheral arterial disease (PAD), caused by reduced blood flow to the legs. Several 100 millions of patients globally live with NASH, T2D or PAD. There are very limited therapeutic options for NASH and PAD, and few new innovative drugs to treat T2D and associated complications. Thus, these diseases represent a serious threat to health care systems globally.

One desirable, albeit elusive, research goal is to identify orally active drugs that can mimic the positive effects of exercise and caloric restriction on general health, especially in elderly, and in obese and metabolically challenged individuals. Drugs that activate the master metabolic regulator **AMP Activated Protein Kinase** (**AMPK**) are predicted to correct energy imbalances and to increase physical performance, and thus to have beneficial effects on metabolic and cardiovascular diseases, in large populations of obese and elderly individuals.

AMPK regulates fat metabolism and insulin sensitivity in liver, glucose disposal in muscle and glucose sensing in β-cells. In a humanized animal model of T2D, **AMPK activator O304** reduces fatty liver and peripheral insulin resistance and improves impaired β-cell function, hallmarks of T2D. O304 also increases glucose-stimulated insulin secretion in human islets. Thus, O304 is expected to reduce fatty liver and to improve glucose homeostasis in T2D.

O304 also enhances endurance both in aged sedentary normal mice and in obese diabetic mice by improving vascular function. O304 increases peripheral blood flow and the formation of arterioles in muscle. O304 also reduces blood pressure and platelet activation. Thus, by improving vascular function, O304 is predicted to show efficacy in PAD and to reduce vascular complications associated with T2D.

Diet-induced increase in plasma levels of IGF-1 are correlated to increased T2D mortality, and to increased incidence of certain cancers. AMPK activation inhibits proliferation of tumour cells by both direct and indirect mechanisms. O304 reduces plasma levels of both IGF-1 and insulin, and inhibits lipid synthesis and mTOR signalling, which in combination inhibit tumour cell proliferation.

As an AMPK activator, O304 is expected to have beneficial effects in large populations of individuals with various manifestations of metabolic and cardiovascular diseases.

O304 exhibits favorable pre-clinical pharmacology and toxicology profiles.
Phase I clinical studies of O304 approved by the Swedish Medical Products Agency (MPA) have been initiated .

Betagenon AB is a privately owned Swedish Biotechnology company focused on the development of small molecule AMPK activators for multiple indications. **Baltic Bio AB** is a subsidiary of the investment company Fort Knox Förvaring AB, Umea, Sweden. **Contact:** thomas.edlund@betagenon.com