A randomized, placebo-controlled trial to evaluate the efficacy and safety of BIO101 on Sarcopenic Obesity.

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Introduction

Sarcopenia (SO), an emerging condition defined by the loss of muscle mass and function and a concomitant increase of fat mass, is mainly affecting older obese individuals. Establishing a consensus definition of SO has represented the first challenge, since most of previous studies specifically focused on body composition (gain of fat mass and loss of muscle mass) and not on physical function. SO definition also reveals the problem of its wide range prevalence (4-84% in men and 4-94% in women depending on definitions and body composition methods used; Batsis et al., 2013) and consequently of its recognition as a geriatric condition. Thus, despite SO high relevance, appropriate clinical studies associating body composition and physical function measurements are needed to better define its prevalence in the ageing population.

We developed the drug candidate Active Pharmaceutical Ingredient (API) BIO101, by purifying 20-hydroxyecdysone (>97%) from Stenammaanthus carthamoides. Sarconeos is the investigational pharmaceutical product formulated with BIO101 for the treatment of sarcopenia including sarcopenic obesity. 20-hydroxyecdysone (20E), a polyhydroxylated sterol found in plants and pharmacologically active in mammals, has been reported in vitro to inhibit myostatin gene expression and to enlarge muscle fibers. These effects involve the activation of MAS receptor, a GPCR, whose endogenous ligand is Angiotensin 1-7. In vivo, 20E oral treatment prevents adipose tissue development, decreases myostatin gene expression in muscles, while enhancing expression of several markers of myogenesis. In the few clinical trials reported up to now, 20E induced fat mass reduction in obese subjects, and reduced lean mass loss in athletes submitted to intense physical training.

We aim to perform a Phase 2 trial on sarcopenic including sarcopenic obese elders. Given the unknown prevalence of sarcopenic obesity in the pre-identified clinical investigation centers, we will first perform pilot studies in Europe and USA to better characterize the target population and to facilitate subsequent enrollment in the main clinical trial (CT). We are also performing safety and pharmacokinetic studies in order to confirm previous results obtained with 20E. The design of both preparatory studies are presented here and will clearly pave the way towards the Phase 2 clinical trial with BIO101.

Conclusions

Sarconeos Efficacy and Safety CT in Sarcopenic Obesity of older Patients (SARA-int) will be implemented both in the EU and USA. Prior to the main study, a pilot observational CT (SARA-obs) will allow to characterize sarcopenic obesity subpopulation in the framework of sarcopenia, based on the wide range of reported prevalence of this condition. Additionally, a PK/PD CT (SARA-pk) will be conducted in older adults. These preparatory studies will pave the way for a smoother implementation of SARA-int, the planned interventional Phase 2 CT.