PRESS RELEASE **June 26, 2023**

Caelus Health announces the first clinical data on its' second lead microbiome-based product *Intestinimonas* to be presented at an International Endocrinology Congress in Rome.

Amsterdam – An extensive program of clinical investigations in cardio-metabolic diseases, including Type 2 diabetes and pre-diabetes is running at the University Hospital of the University of Piemonte Orientale in Novara, Italy. This academic research group is led by Prof. Flavia Prodam, MD. One of the main research topics at the group of Prof. Prodam is the development and early prevention of Type 2 Diabetes in individuals who are overweight and who have a loss of insulin sensitivity. Caelus is closely working with the team in Piemonte Orientale in Novara to study the potential impact of a microbiome-based intervention on the delay of onset or even prevention of Type 2 diabetes in people at risk of developing diabetes.

Following the discovery *of Intestinimonas butyriciproducens* and its capacity of producing butyrate from sugars, lysine and fructoselysine by Dr. Nam Bui and Prof. Willem M. de Vos (1), this next-generation microbe was further studied and patented by the Laboratory of Microbiology at Wageningen University in the Netherlands. Based on promising preclinical results, a European project was initiated to further scale up production and to start clinical development of a selected strain in a group of prediabetic subjects who have an impaired tolerance of glucose and are at risk of developing Type 2 diabetes. The Proof-of-Concept clinical trial has 2 phases: first a randomised placebo-controlled phase comparing a low oral dose of *I. butyriciproducens* (in a capsule) with placebo. The second phase is an open-label comparison of a high dose of the microbe with the low dose as used in the first phase.

The first results of this Proof-of-Concept trial have just been analysed by the team in Novara and have been accepted for presentation at the International Congress of Endocrinology which will be held in the period of 28 June – 1 July in Rome, Italy.
This first part of the clinical trial demonstrates that the product based on *I. butyriciproducens* improves insulin sensitivity and enhances glycemic control in this group of pre-diabetic individuals. Based on a reduction of specific markers in the circulation, the product also demonstrates the potential to reduce the risk of cardiometabolic damage in the body. Finally, the second part of the trial showed an excellent safety profile of the product in both low and high dosages with highest efficacy levels in the latter. These promising results call for further follow-on studies to explore the potential of *I. butyriciproducens*.

The Principal Investigator of the Proof-of Concept study, Prof. Flavia Prodam, MD (UNI UPO) stated: *"This clinical trial clearly demonstrates the potential of I. butyriciproducens in the delay of developing type 2 diabetes and provides an excellent basis for further development. In addition, it underpins the tentative value of the microbiome to enhance health in early phases of disease."*

Prof Willem M de Vos who together with Prof Max Nieuwdorp co-founded Caelus Health added: *"the results of this trial showcase the importance of butyrate-producing anaerobes in the human gut and demonstrates the potential of Intestinimonas butyriciproducens to reduce undesired or toxic components due to its highly versatile metabolism"*

In addition, Luc Sterkman, MD, CEO of Caelus commented: "*These promising results on the safety and efficacy of our second lead Intestinimonas provides an excellent follow-up to the outstanding results on our most advanced lead Anaerobutyricum soehngenii, which has recently been endorsed by the FDA as GRAS and which we intend to launch shortly in the US via a strategic partner. In this way we are gradually building an attractive portfolio of next generation microbes which are the basis of meaningful products in the area of cardio-metabolic diseases."*

***Caelus Health** is an Amsterdam-based biotech company. Caelus is dedicated to the commercialisation of functional food and pharmaceutical products for the prevention and early treatment of cardio-metabolic diseases. Based on the strong correlation between the intestinal microbiome and health, the company is developing an entirely new class of microbiota-based therapeutics for the reduction of insulin resistance and prevention of Type 2 Diabetes Mellitus (T2DM) in people with metabolic syndrome (MetS). In addition, the company has built an extensive range of patents based on the gut microbiome and fecal Microbiota Transplant (FMT) -studies In Type 1 Diabetes, cancer cachexia and liver disorders.*

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(1) Bui N, J Ritari, S Boeren, P de Waard, CM Plugge & WM de Vos (2015) Production of butyrate from lysine and the Amadori product fructoselysine by a human gut commensal. Nature Comm 6:10062 https://www.nature.com/articles/ncomms10062