## 10<sup>th</sup> Euro Global Summit and Expo on

## Vaccines & Vaccination

June 16-18, 2016 Rome, Italy

## Active immunization against proprotein convertase subtilisin/kexin type 9 (PCSK9): A new strategy to control hyperlipidemia

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Chronic, non-communicable diseases (NCDs), such as cardiovascular diseases represent a leading threat to human health in fooday's world. Passive immunotherapies using monoclonal antibodies (mAb) targeting endogenous proteins have fundamentally improved the treatment of NCDs. However, mAb face functional limitations in this chronic setting not only because of their relatively short *in vivo* half-lives necessitating frequent administration and thus increasing costs, but also because of their ability to induce the generation of neutralizing anti-antibodies. In recent years a novel approach to treat chronic diseases based on active rather than passive immunization was tested in preclinical as well as clinical settings. PCSK9 has been shown to be a key regulator of the low density lipoprotein receptor mediated cholesterol clearance pathway and to promote inflammation, thereby being involved in atherosclerosis development. We and others have developed vaccines targeting PCSK9. In preclinical studies we could demonstrate that active immunization approaches induce persistent, functional antibodies which reduce significantly plasma cholesterol levels for up to one year. Moreover, anti-PCSK9 immunization in an atherogenic mouse model resulted in a significant decrease in atherosclerotic lesions as compared to the control, which was accompanied by a significant reduction of plasma inflammatory markers. Compared to mAbs active immunotherapy offers the possibility to develop multivalent vaccines addressing multiple epitopes on a given target more easily. We could show that a bi-valent PCSK9 specific vaccine can evoke multi-functional antibodies that synergistically block PCSK9 activity. Summarizing, the advantages and limitations of active and passive immunotherapy approaches to treat NCDs will be discussed on the basis of PCSK9 specific immunotherapies.

## Biography

Gunther Staffler is the Head of Immunology Department at AFFiRiS AG, Austria. He is responsible for the development of an immunotherapy for the prevention or treatment of hypercholesterolemia and atherosclerosis. He has completed his degree in Biochemistry and Immunology at the University of Vienna. Apart from his research work at the Institute for Immunology he has been a Lecturer at the University of Vienna. After heading the Preclinical Department at Biovertis AG, he has joined AFFiRiS AG in 2007. During his research career he has authored many publications in international journals and was awarded different prizes.

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