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The Lx linker technology for development and production of antibody-drug conjugates with distinguished features

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Abstract

Antibody-drug conjugates (ADCs) are a cutting-edge modalities in the pharmaceutical field because they allow targeted delivery of drugs, which are otherwise too potent/toxic to be applied systemically, selectively to cancer cells. However, a greater control is desirable in the stochastic conjugation technology used to synthesize ADCs. We have recently introduced a metalorganic platinum(II) linker, an ethylenediamineplatinum(II) moiety called Lx, that allows to provide ADCs with some unique features, such as targeting the histidine residues of native unmodified antibodies and an improved hydrophilicity of synthetic intermediates and presumably metabolites. The general concept of this novel linker technology (shown in the scheme below) for the preparation of stable and efficacious ADCs will be presented. The milestones of the Lx platform development as well as the key features of thus produced Lx-based ADCs such as serum stability, biodistribution, in-vitro cytotoxicity, and in-vivo efficacy data, along with some recent highlights such as dual radiolabeling of Lx ADCs with 195mPt and 89Zr radioisotopes, will be presented. Finally, first results will be shown regarding the manufacturing of our lead ADC, with the corresponding “semi-final” product being successfully produced at a multi-gram scale and the original Lx ADC conjugation method successfully technology-transferred to a CMO for a near-future upscaling and manufacturing.

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Biography

Eugen Merkul has completed his PhD with Summa Cum Laude from the University of Düsseldorf/Germany, and Post-doctoral studies from the University of Antwerp/Belgium, followed by industrial experience at German and Dutch Companies. He is the Head of Chemistry of LinXis B.V., an innovative Dutch Biotech Company developing a proprietary ADC (antibody-drug conjugates) platform technology. He is an author/coauthor of 23 papers in reputed peer-reviewed journals and inventor/coinventor of 10 patent applications. merkul@linxispharmaceuticals.com.

