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ADVANCING DRUG DEVELOPMENT IN ALZHEIMER'S DISEASE

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Converging evidence suggests that the pathophysiology of neurodegenerative diseases (NDDs) begin years, if not decades, prior to the onset of clinical symptoms, including memory impairment, motor disturbances and non-motor related abnormalities. Therefore, individuals at very early stages are the most likely to benefit from disease-modifying therapies should they become available. Currently, NDDs are viewed as multi-etiological disorders with a concomitant occurrence of several pathogenic mechanisms and thus, the challenge is to find the meaningful biological targets for a rapid translation of knowledge into clinical drug development. In addition, significant efforts are put in the development of novel drugs to address symptomatology with compounds directed towards biochemical systems that not necessarily constitute the underlying pathology of the disease in question but might contribute to a significant relief in patient's quality of life. In my talk, I will elaborate on strategic pre-clinical steps and major considerations in drug design intended to accelerate the drug candidate development process. Also, which pre-requisites a candidate must fulfil in the path to IND-enabling studies to reduce the time and risk of Alzheimer's disease drug development. I will provide examples of molecules which do or do not meet industry criteria such as compounds with insufficient PK characterization, small molecules that generates a toxicchemically reactive metabolite in vivo, insufficient potency, selectivity or efficacy, poor target engagement, model predictability etc. and a priori comprehension of these essentials will help the translation into clinic more efficient and reliable.

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