

Preclinical development of KARS1-target drug candidate with broad and high efficacy for treatment of MASH (metabolic dysfunction-associated steatohepatitis)



METABOLIC	Preclinical
Product Type	Small molecules
Indication	MAS score 4, F2 fibrosis or more metabolic dysfunction-associated steatohepatitis (MASH)
Target	KARS1 (lysyl-tRNA synthetase 1)
MoA(Mechanism of Action)	<p>KARS1 is a fundamental enzyme involved in protein synthesis and generally present in the cytoplasm. KARS1 is secreted out of the hepatocytes in an inflammatory liver and binds to the surface of circulatory monocytes / macrophages in blood stream to infiltrate them into liver, resulting in hepatocyte steatosis by release inflammatory cytokines and liver fibrosis through the transition of hepatic stellate cell to myofibroblast.</p> <p>Our drug candidate, ZMC003 blocks the proinflammatory signaling activity of secreted KARS1, thereby suppressing inflammatory microenvironment, fibrosis and steatosis in liver.</p>
Competitiveness	<p>Lead compound ZMC001 shows the broad spectrum of efficacy on the pathologic systems of MASH such as inflammation, fibrosis and steatosis with novel mechanism of action targeting extracellular KARS1. We have developed a final candidate ZMC003 that maintains the characteristics of ZMC001 while improving <i>in vitro</i> activity, <i>in vivo</i> stability, and half-life.</p> <p>With the high and broad efficacy and unique mode of action, ZMC003 can be the world's first disease-modifying agent (DMA) that can be administered as a mono-therapy and in combination with resmetirom or other available drugs. In addition, some MASH patients have increased levels of KARS1 in their blood, and we plan to use this as a diagnostic marker to select patients who will respond to ZMC003 in clinical trial.</p>
Development Stage	Preclinical
Route of Administration	PO QD

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