Gibela Therapeutics Announces Publication of Several Studies Confirming the Role of CNNM4 in Important Liver and Metabolic Diseases

Basel, Switzerland, 14 November 2025 - Gibela Therapeutics GmbH ("Gibela"), the Basel-based Biotech focusing on the treatment of liver diseases using siRNA technology to target the human gene CNNM4, announces the recent publication of several peer-reviewed scientific papers demonstrating that CNNM4 modulation addresses one of the core, shared mechanisms in many important liver diseases.

These diseases include MASLD (Metabolic dysfunction-Associated Steatotic Liver Disease), MASH (Metabolic dysfunction-Associated SteatoHepatitis) Cholangiocarcinoma and ALD (Alcohol-related Liver Disease). Over-expression of CNNM4 in the liver is a shared characteristic of these diseases, causing dysregulation of magnesium homeostasis. In turn, altered magnesium homeostasis in the liver results in both mitrochondrial dysfunction and endoplasmic reticulum stress.

Gibela is co-founded by Prof. Malu Martínez-Chantar and Dr. Naroa Goikoetxea together with serial biotech entrepreneur Nicholas Benedict. The company's research originates from the liver disease lab at CIC bioGUNE in Bilbao, Spain, where Gibela is actively investigating the potential of CNNM4 as a therapeutic target. These recent publications show encouraging results across a wide range of liver diseases.

One study, recently published in *Gut*[1] shows how the target CNNM4 is upregulated in cholangiocarcinoma patients, and how silencing CNNM4 through GalNAc-siRNA conjugates significantly reduces tumor growth, metastasis, chemoresistance, and cancer stem cell features.

In parallel, research published in *Science Advances*[2] shows that MASLD alone is sufficient to cause cognitive and sensorimotor deficits which can be reversed by the silencing of CNNM4 in the liver, providing strong experimental evidence for a targetable liver–brain axis in MASLD-associated neurobehavioral disorders.

In another recent publication in *Hepatology*[3], the group showed that CNNM4 therapy with siRNA restores magnesium homeostasis in ALD which promotes the repair of ethanol-damaged proteins.

These three studies reveal CNNM4 as a shared pathological driver in liver disease and liver-induced brain dysfunction. Further studies, published previously, also show

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[1] Gut, September 2025. Mercado-Gómez et al. *"Role of CNNM4 in the progression of cholangiocarcinoma: implications for ferroptosis and therapeutic potential"*

[2] Science Advances, October 2025. Cardoso-Delgado et al. *"Metabolic dysfunction–associated steatotic liver disease alters brain function and behavior: Insights from liver-targeted siRNA therapy"*

[3] Hepatology, August 2025. Gonzalez-Recio et al. *"Modulatory effects of CNNM4 on protein-L-isoaspartyl- O-methyltransferase repair function during alcohol-induced hepatic damage"*

highly promising results in MASH, drug induced liver, damage and cholestatic liver disease and several non-liver fibrotic conditions.

Prof. Malu Martinez-Chantar commented, “These recent publications add to the body of work highlighting the therapeutic potential of CNNM4 to restore magnesium homeostasis in diseased livers, thereby modulating metabolic, oncogenic, and neurocognitive pathways. These publications position Gibela Therapeutics at the forefront of research into CNNM4 based medicines to treat liver and metabolic diseases. I look forward to the company commencing IND-enabling studies during 2026.”.

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