GM-60106 is a Novel Drug Candidate for Non-alcoholic Steatohepatitis (NASH)

JD BIOSCIENCE

GM-60106 Highlights

- **GM-60106 is a first-in-class drug candidate for NASH.**
- **GM-60106 blocks the novel target 5-hydroxytryptamine receptor 2A (HTR2A) that is directly connected to fibrosis and correlated steatosis.**
- **Preclinical and toxicology studies were completed and showed that the compound can improve both hepatosteatosis and liver fibrosis and is not permeable to blood-brain barrier (BBB); thus, it does not induce any central nervous system (CNS) mediated side effects.**
- **GM-60106 will enter clinical phase in Q3 of 2022 in Australia to assess the safety, tolerability, and pharmacokinetics of GM-60106.**

Overview of GM-60106

JD Bioscience (JDB) is a South Korean-based venture company currently developing GM-60106, a novel therapeutic compound for NASH with potent efficacy in liver fat accumulation and fibrosis by blocking of HTR2A in serotonin pathway.

Experts estimated that about 2~5% of US population has NASH and 20~30% of these patients progress to liver fibrosis in 7 years. However, there are no drugs commercially approved for NASH and off-target drugs are currently used for treatment. There are drug candidates for NASH treatment in phase 2 or 3 clinical trials, but majority of them only can improve fatty liver and lipotoxicity but cannot improve liver fibrosis.

Preclinical studies have shown that GM-60106 improved NASH-related fibrosis and steatosis effectively by directly suppressing HTR2A in translatable preclinical animal models. According to the preclinical data, GM-60106 showed superior pharmacokinetics (PK) profiles and minimized blood-brain barrier permeability, thus it can directly inhibit the target only in the peripheral tissues but not in the brain.

Conclusively, the novel mechanism for liver fibrosis and superior pharmacokinetics can differentiate GM-60106 from the current clinical drug candidates for NASH.

Differentiated Profile of GM-60106

Direct mechanism for NASH-related fibrosis

- Suppressing HTR2A with GM-60106 can directly deactivate hepatic stellate cells (HSCs), which is critical for liver fibrosis.

Superior efficacy, kinetics, and safety

- GM-60106 has stronger efficacy for liver fibrosis and inflammation compared to other drug designs in vivo.
- The compound shows optimal PK profiles for an oral administrative drugs.
- Safe from CNS-mediated safety issues.

IP protection

JDB filed patents for a composition of matter in US/Europe/Asia/South America in 2019 and also filed patents for back scaffolds in 2022.

Partnering interest

JDB is seeking an exclusive (including geographical right) out-licensing opportunity of GM-60106 after its phase 1 clinical study.

Summary of a Preclinical Study

Pharmacokinetics, safety, and efficacy of GM-60106 Analysis

- PK values of GM-60106 are optimal for oral medication development.
- GM-60106 appears to be a safe compound, judged by the toxicity and safety pharmacology data in preclinical animal studies. It is not expected to have CNS-related adverse effects since it is not permeable to blood brain barrier (BBB).
- It showed stronger effect on liver fibrosis and inflammation compared to prevailing drug candidates for NASH.

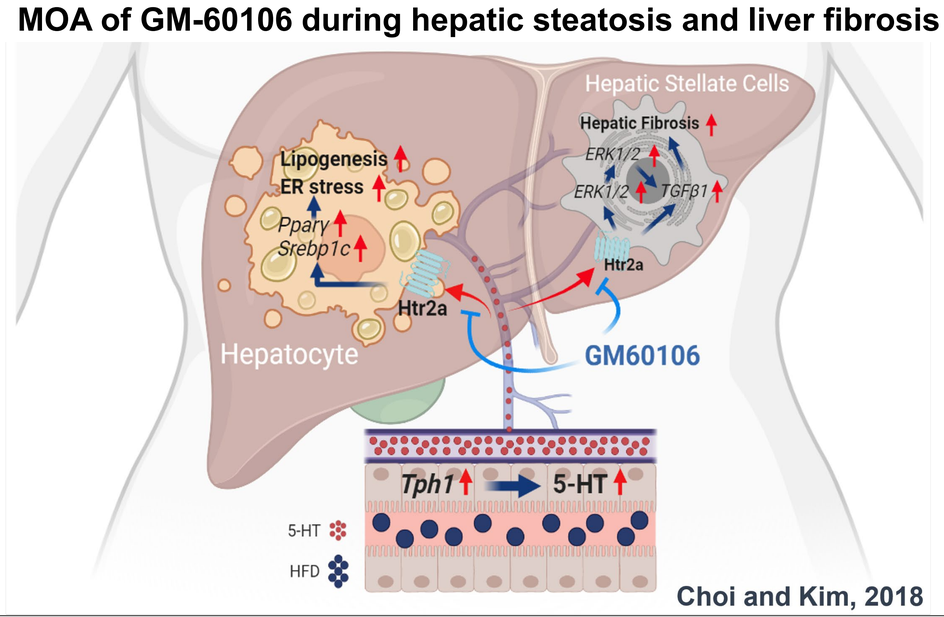
Summary of chemical profiles and pharmacology of GM-60106

Assays	Results
Physicochemical Property studies	✓
In vitro assays	✓
Pharmacokinetic assays	✓
In vivo efficacy assays	✓
Metabolic stability assays	✓
CMC studies	✓
Preclinical toxicity studies	✓

Novel Mechanism of Action (MOA)

- High fat diet increases both serotonin levels and HTR2A expressions in the liver that induces signaling important for lipogenesis, inflammation, and fibrosis.
- The expression of HTR2A is increased during hepatic stellate cells (HSC) activation that is directly connected to the progression of liver fibrosis. The inhibition of HTR2A deactivates the HSCs.
- Blocking of HTR2A with GM-60106 can improve steatosis, inflammation, and liver fibrosis in the liver.

MOA of GM-60106 during hepatic steatosis and liver fibrosis



Choi and Kim, 2018

Thoughts from medical hepatology KOLs in the US

"There has not been a specific serotonin antagonists trial done in U.S. for NASH."

"Antifibrotic compound along with anti-inflammatory effects could be a game changer."

"The FDA will most likely approve a drug within the next 3-5 years. By the time combination therapies may be on the table. So, drug candidates with novel MOA like GM-60106 is a favorable partner for a combination therapy."

For more information, please contact:

Sungmin Song, Ph.D. (+82-62-974-9380, seaflow@jdbiosci.com)

Peter Goughnour, Ph.D. (+82-2-406-9380, petergoughnour@jdbiosci.com)