September 22, 2023

Company Name: GNI Group Ltd.
Representative: Director, Representative Executive Officer, President and CEO
Ying Luo, PhD
(Security Code: 2160, TSE Growth)
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F351 Presentation in An Academic Conference in the United States

GNI Group Ltd., (TSE Growth listed code: 2160; "GNI" or "the Company"; "we" or "the Group" including our subsidiaries and affiliates) today announced that Professor Lungen Lu, the principal investigator of Phase III clinical trial of F351 (Hydronidone) in China sponsored by one of our core subsidiaries Beijing Continent Pharmaceuticals Co., Ltd. ("BC"), will make a presentation at the poster session of The Liver Meeting of the American Association for the Study of Liver Diseases (AASLD) in Boston, Massachusetts, the United State on November 12, 2023.

The poster of the session is attached to the end of this disclosure. For more details of the conference, please refer to the AASLD's website below:

https://www.aasld.org/the-liver-meeting

China National Medical Products Administration (NMPA) designated F351 as a "Breakthrough Therapy" in 2021, and F351 forms a core of our future drug pipeline. The Group's core subsidiary BC is making steady progress in the Phase III clinical trial of F351 and is expecting to complete the subject enrollment well before the end of this year.

About F351 (generic name: Hydronidone):

F351 is a New Chemical Entity (NCE) derivation of ETUARY®, which inhibits hepatic stellate cell proliferation and TGF-β signaling pathway, both of which play major roles in the fibrosis of internal organs. BC holds the key patent rights for F351 in mainland China, while Catalyst Biosciences, Inc., an equity method affiliate of the Company, holds its rights in the other countries.

About GNI Group Ltd.:

The Company is a holding company of global healthcare company listed on the Growth Board of the Tokyo Stock Exchange and engaged in drug discovery, pharmaceutical development, biomaterial development, clinical studies, manufacturing, and

sales in both the United States and China. For more information, please visit our website below:
https://www.gnipharma.com/

About Beijing Continent Pharmaceuticals Co, Ltd:
Continent is a profitable fully integrated specialty biopharmaceutical company with a focus in the organ fibrosis market. With global research and development capabilities, commercial-scale manufacturing facilities, a deep distribution network across China, and a sales and marketing team of 300 people, Continent is a leading company in China of the idiopathic pulmonary fibrosis (IPF) treatment with its flagship medicine ETUARY® . The company has a rich pipeline of potential assets, including F351 for HBV associated liver fibrosis which is in Phase 3 study in China. For more information, please visit Continent's website below:
https://www.bjcontinent.com/en/

This material contains statements concerning the current plans, expectations and strategies of GNI Group Ltd. ("the Company"). Any statements contained herein that pertain to future operating performance and that are not historic facts are forward-looking statements. Forward-looking statements may include, but are not limited to, words such as "believe," "plan," "strategy," "expect," "forecast," "possibility" and similar words that describe future operating activities, business performance, events or conditions. Forward-looking statements, whether spoken or written, are based on judgments made by the management of the Company, based on information that is currently available to it. As such, these forward-looking statements are subject to various risks and uncertainties, and actual business results may vary substantially from the forecasts expressed or implied in forward-looking statements. Consequently, investors are cautioned not to place undue reliance on forward-looking statements.

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Hydronidone ameliorates liver fibrosis by inhibiting activation of hepatic stellate cells via Smad7-mediated degradation of TGFβRI

Xianjun Xu [1,2], Yuecheng Guo [1,2], Xin Luo [1,2], Zhenyang Shen [1,2], Zhongshang Sun [3], Bo Shen [1,2], Cui Zhou [1,2], Junjun Wang [1,2], Jingyi Lu [1,2], Qingqing Zhang [1,2], Yanping Ye [4], Ling Zhang[4], Ying Luo [4], Ying Qu [1,2], Xiaobo Cai [1,2], Hui Dong [1,2], Lungen Lu [1,2]

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4. Continent Pharmaceuticals Co., Ltd.

Abstract Number: 39904

Presentation Type: Poster

Objective

Liver fibrosis is a wound-healing reaction that eventually leads to cirrhosis. Hydronidone (HDD) is a new pyridine derivative with the potential to treat liver fibrosis. In this study, we explored the antifibrotic effects of HDD and its potential mode of action.

Methods

Histology, western blot, immunofluorescence staining, and RT-qPCR were used to detect the antifibrotic effect of HDD on 3, 5-diethoxycarbonyl-1, 4-dihydropyridine (DDC) and carbon tetrachloride (CCl_4) mouse hepatic fibrosis models. The effects of HDD on the activation of hepatic stellate cells were detected by western blot, immunofluorescence staining and RT-qPCR. Transcriptome sequencing analysis of HDD in hepatic stellate cells. Intervention of Smad7 in hepatic stellate cells with lentivirus and plasmid. The effect of HDD on transforming growth factor β receptor Ⅰ (TGFβR Ⅰ) was detected by western blot and immunoprecipitation. Construction of adeno-associated virus targeting Smad7 in hepatic stellate cells.

Results

In DDC and CCl_4 mouse hepatic fibrosis models, HDD alleviated liver damage, collagen accumulation, decreased the expression of fibrosis-related genes, and inhibited the activation of hepatic stellate cells. HDD decreased the expression of fibrosis gene in hepatic stellate cells. HDD significantly up-regulated Smad7 expression and inhibited TGFβ-Smad signaling pathway in hepatic stellate cells. HDD promoted Caveolin-1 (Cav-1) mediated TGFβR Ⅰ degradation via Smad7. Specific knockdown of Smad7 in vivo blocked the antifibrosis effect of HDD.

Conclusion

HDD ameliorates liver fibrosis by inhibiting hepatic stellate cells activation via Smad7-mediated TGFβR Ⅰ degradation. HDD is a potential drug candidate for the treatment of liver fibrosis.

Figure 1. HDD significantly improved liver fibrosis in CCl_4 and DDC mouse hepatic fibrosis models

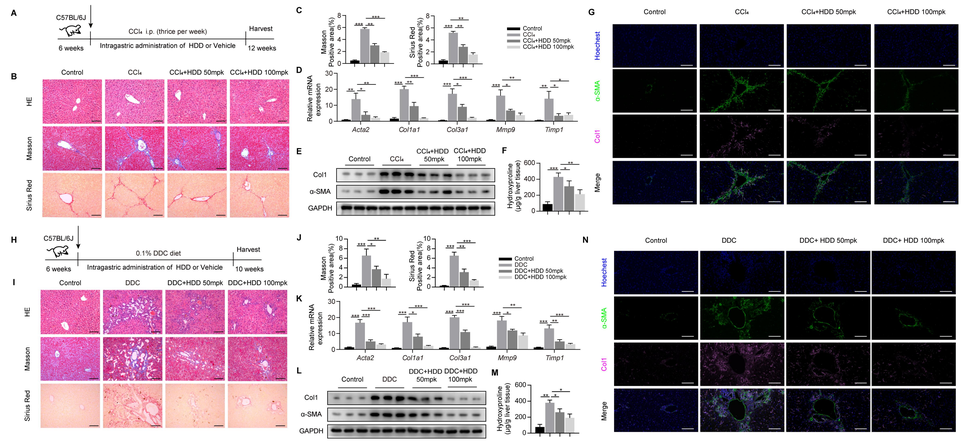


Figure 2. HDD inhibited the activation of hepatic stellate cells via Smad7

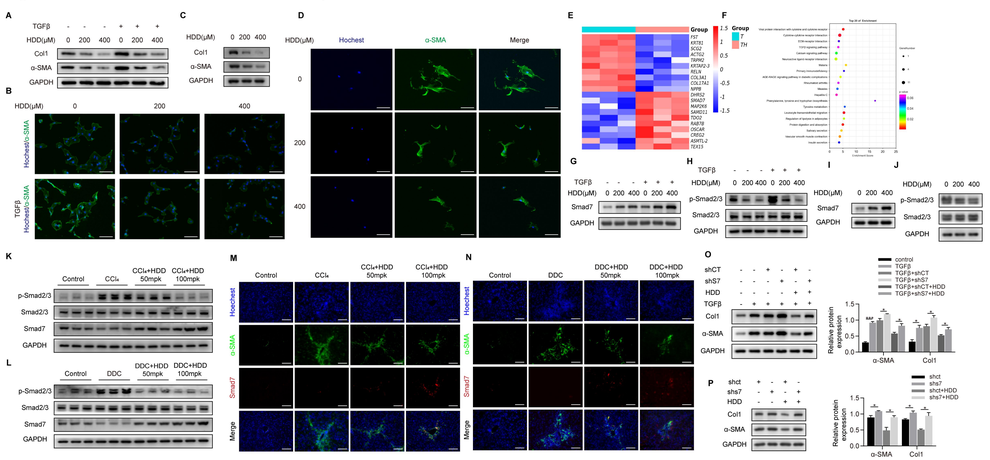


Figure 3. HDD promoted Cav-1-mediated degradation of TGFβR1 via Smad7 in a ubiquitin-proteasome dependent pathway

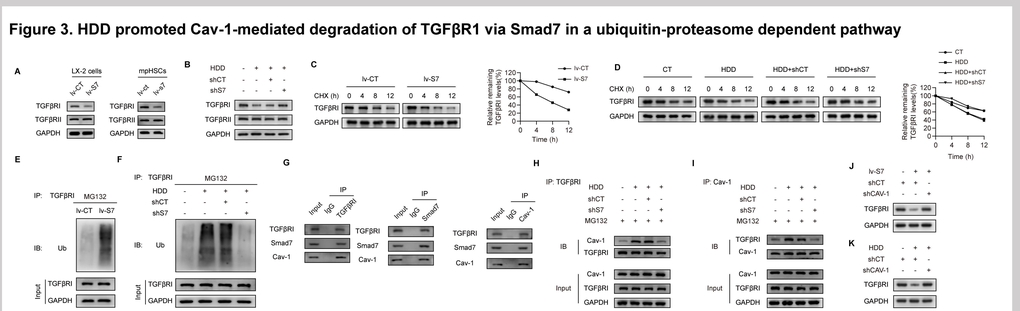
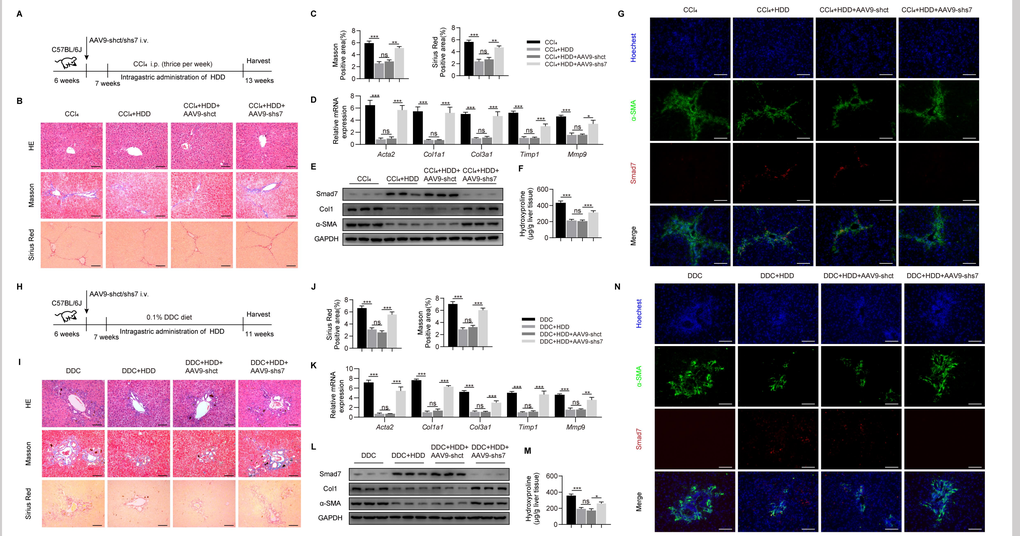


Figure 4. Knockdown of Smad7 diminished antifibrotic effect of HDD in mice



Financial disclosure: No relationships to disclose.