OVERVIEW


1. ND-654 Targets Allosteric Site in Biotin Carboxylase Domain

2. ND-654 is Well-Tolerated in the DEN Rat Model

3. ND-654 Results in Marked Reduction of Tumor Nodules

4. ND-654 Decreases Tumor Proliferation and Increases Tumor Necrosis

5. ND-654 Significantly Improves Survival in the Aggressive DEN Model

6. ND-654 Decreases Markers of Fibrosis and Inflammation

7. ND-654 Decreases Markers of Fibrosis and Inflammation in Primary Human Stellate Cells in vitro

CONCLUSION

• ND-654 preferentially distributes to the liver where it inhibits ACC activity without generating liver toxicity

• ND-654 inhibits HCC development by decreasing tumor proliferation and causing tumor necrosis

• ND-654 reduces markers of fibrosis and inflammation in the liver of DEN rat in vivo by Racyc model and in primary human stellate cells in vitro

• ND-654 improves overall survival and the efficacy of sorafenib in the DEN rat model

• Our results therefore provide further evidence that de novo fatty acid synthesis is an important mediator of hepatic carcinogenesis

• Selective inhibition of hepatic ACC is a potential therapeutic strategy for hepatocellular carcinoma

Trichrome
DEN + Sorafenib
TIMP1
8*

Sorafenib Improves Efficacy in the Treatment of Cirrhotic Rats with Hepatocellular Carcinoma

Highly aggressive rat DEN model of HCC

ND-654 demonstrates the ability modifying cirrhotic and HCC rele
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ND-654 is a potent allosteric inhibitor of the lipid master regulator Acetyl CoA Car

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ND-654 demonstrates excellent PK/ PD relationships in the target tissue, the liver (see text vs Malonyl CoA reduction), and is effective at modulating cirrhotic and HCC rele

ND-654 demonstrates the utility for tissue targeted ACC inhibition to decrease tumor burden, liver fibrosis and prolong survival in the highly aggressive rat DEN model of HCC.

ND-654 Improves the Efficacy of Sorafenib

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