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TITLE: NGM282, A Novel Variant of FGF-19, Demonstrates Biologic Activity in Primary Biliary Cirrhosis Patients with an Incomplete Response to Ursodeoxycholic Acid: Results of a Phase 2 Multicenter, Randomized, Double Blinded, Placebo Controlled Trial

ABSTRACT BODY: Sponsorship - This study was sponsored by:(If this abstract was not sponsored please indicate) (Oral or Poster Submission): NGM Biopharmaceuticals, Inc.

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ABSTRACT BODY:

Abstract Body: Background: PBC patients with an incomplete biochemical response to ursodeoxycholic acid (UDCA) are at increased risk for disease progression and with limited treatment options. NGM282 is a novel engineered variant of FGF-19 that inhibits the CYP7A1-mediated bile acid (BA) synthesis in animals and healthy volunteers. The biologic activity was therefore evaluated in PBC patients.

Methods: 45 subjects with a baseline (BL) alkaline phosphatase (ALP) >1.67xULN after 1yr of UDCA were randomized to NGM282 0.3 or 3mg vs placebo (PBO) as a daily SC injection for 28d. Change from BL ALP was the primary endpoint, with key secondary efficacy endpoints of liver chemistries and BA synthesis (7a-hydroxy-4-cholesten-3-one or C4). Pruritus was measured at all study visits with the 5D Itch and Visual Analogue Score (VAS). Post-hoc sub-analyses evaluated ALP response by BL ALP< or ≥3xULN.

Results: All study arms were balanced for typical PBC patient characteristics (female=91%, mean age=56y, mean BL ALP=297 IU/L, mean UDCA dose=15mg/kg/d). Pruritus at BL was 54%, 64% and 67% of PBO, 0.3mg and 3mg arms, respectively. NGM282-treated subjects had a significant, dose-dependent reduction in ALP vs PBO ($p<0.05$), with the greatest decrease in BL ALP>3xULN (Table 1). Significant reductions were also seen in liver chemistries ($p<0.05$). NGM282 3mg suppressed C4 by >90% supporting a potent biologic effect. NGM282 was safe and well tolerated with no observed safety signals. Adverse events occurring >10% of both NGM282 treatment arms were diarrhea (PBO=6.7%, 0.3mg=21.4%, 3mg=25%), headache (PBO=6.7%, 0.3mg=14.3%, 3mg=25%) and nausea (PBO=6.7%, 0.3mg=14.3%, 3 mg=12.5%), the majority of which were mild. There was no clinically significant evidence of drug-induced pruritus by either VAS or 5D itch.

Conclusions: These data demonstrate the biologic activity of NGM282 in PBC and support a therapeutic potential in other BA-mediated diseases. Studies are ongoing of longer duration, increased dose and BL predictors of response to identify optimal PBC patient populations for potential treatment with NGM282.

TABLE TITLE: Table 1 Mean change in liver and BA Parameters

Table 1 Mean change in liver and BA Parameters			
.	PBO (n=15)	0.3mg (n=14)	3mg (n=13)
ALP(IU/L)	4	-49	-69
ALP (BL>3xULN)	17	-71	-103
ALP (ALP<3xULN)	-7	-27	-40
ALP %	-1.2%	-15.8%	-19.2%
ALP % (BL>3xULN)	1.2%	-19%	-22.4%
ALP % (BL<3xULN)	-3.2%	-12.7%	-16.4%
ALT (IU/L)	1	-18	-27
AST (IU/L)	2	-11	-16
GGT (IU/L)	-6	-29	-51
C4 (ng/mL)	0.9	-1.8	-15.3