**Background**

Growth Differentiation Factor 15 (GDF15) has been shown to have both immune suppressive and pro-cachectic effects. NGM120 is a novel, 1st-class, humanized monoclonal antibody that inhibits GFRAL (the receptor for GDF15) resulting in both anti-tumor and anti-cachexia effects in preclinical animal models. In a phase 1 voluntary study, NGM120 (10-400 mg) was well tolerated with a favorable safety profile. We present the data from Ph1a/1b dose finding study (NCT04068896) of NGM120 and NGM120 + gemcitabine (Gem/Nab-paclitaxel) in advanced cancer patients.

A mAb targeting GDF15/GFRAL engagement of autocrine immune system for its pleiotropic effects in addition to its central emergency circuit (black arrow).

**Phase 1a – Monotherapy in Advanced Solid Tumors**

**NGM120 Safety Profile**

- No dose-limiting toxicities observed and maximal tolerated dose not reached.
- Most AEs were Grade 1-2 and not attributed to NGM120, with fatigue (20%), nausea (13%), GIT increase (20%), and nausea (20%) being most frequent.
- Seven subjects experienced 11 SAE events, none of which were attributed to NGM120, but to the underlying diseases.

**Anti-cachexia and Anti-Tumor Assessments**

- Four patients showed >3.5% increased lean body mass at Week 8 among the evaluable patients (see below).
- Three subjects (30%) in the 30 mg cohort and two subjects (20%) in the 100 mg cohort had stable disease based on their best response according to RECIST 1.1 criteria, although no objective response was observed.

**Pharmacokinetics**

- Beta-trend of dose-dependent reduction in beta-hydroxybutyrate.
- Beta-hydroxybutyrate is a form of ketone bodies, which are proportional to the extent of lipolysis induced by GDF15, therefore, a PD biomarker for pathway inhibition.

**Phase 1b – Chemotherapy Combination in Pancreatic Cancer**

**Safety Profile Consistent with Gem + Nab-P Treatment**

- No dose-limiting toxicities observed and maximal tolerated dose not reached.
- Most AEs were not attributed to NGM120, with Grades 1-3 diarrhea (50%), nausea (50%), and fatigue (50%) being most frequent, which are commonly seen in the context of Gem+Nab-P therapy.
- Five subjects experienced 10 SAE events; however, none of them were related to NGM120, but to the chemotherapy and/or underlying disease.

**Six CT-evaluable Patients Exhibit a 4% Average Maximal Increase in Lean Body Mass**

- 4/6 CT-evaluable Patients Exhibit >5% Substantial Reduction in Tumor Biomarker

**CONCLUSION**

- Treatment with NGM120 is well tolerated, exhibiting no dose-limiting toxicities as monotherapy or in combination with Gem/Nab-P.
- PK exposure increased with dose.
- Increases in lean body mass and body weight were observed in a subset of the patients in both the monotherapy and combination settings.
- Five SIDs (LOD; 20%) were observed in the monotherapy cohorts in advanced solid tumors, but no objective responses were observed.
- All 4 CT-evaluable pancreatic cancer patients treated with NGM120 in combination with Gem/Nab-P demonstrated disease control at 16 weeks, with three PIs and three SDs, five of whom extending to at least 32 weeks.

A randomized, placebo-controlled, single-blind Phase 2a study is ongoing to further evaluate NGM120 in the 1st-line setting of pancreatic cancer in combination with Gem/Nab-P.

**References**

2. Chaus SS et al. Immunity, 2017
3. Dan G et al. Front Immunology, 2018

**Acknowledgements**

We thank our clinical investigators, all clinical investigators, clinical teams and NGM120 project team for their contributions to this study.

**Clinical trials**

1. NCT04068896
2. NCT03392116
3. NCT03505960
4. NCT03932116
5. NCT03932116

**Disclosure**

Dr. Rishi Jain has received clinical research institution funding from Belagene, NGM Biopharmaceuticals and Zymeworks Inc for the role as site principal investigator.

**This study was funded by NGM Biopharmaceuticals, Inc.**