The impact of greater than 8% weight loss on overall survival in subjects with non-small cell lung cancer (NSCLC) treated in a phase IIb trial of GTx-024

Background
Cancer cachexia causes muscle wasting and decline in physical function. Studies show that NSCLC patients with weight loss at diagnosis have worse treatment outcomes and shorter overall survival. This muscle wasting and decline in function may have detrimental consequences early in the course of a patient’s malignancy, underscoring the importance of diagnosing and treating this condition at an early stage. We conducted a Phase IIb, randomized, double blind, placebo controlled multi center study to evaluate the effect of GTx-024 on muscle wasting and physical function in patients with cancer cachexia.

Methods
Subjects (n=159) were randomized to oral GTx-024 (1 or 3 mg) or placebo (pbo) daily for 16 weeks. Subjects were males >45 y and postmenopausal females, had experienced ≥2% weight loss in the 6 mths prior to randomization, had a BMI <35 and either NSCLC, colorectal cancer, non-Hodgkin’s lymphoma, chronic lymphocytic leukemia or breast cancer. The primary endpoint was change in total lean body mass (muscle). We report on overall survival in the entire study population and NSCLC cohort based on weight loss of > or ≤8% in the previous 6 months.

Results
In pbo subjects in the ITT population, overall survival was significantly (P=0.003, log rank) reduced in subjects with >8% weight loss compared to subjects with ≤8% weight loss. Among NSCLC subjects (n=61) pbo subjects with >8% weight loss demonstrated a similar survival disadvantage (P=0.04); 4 month Kaplan-Meier estimates 100% vs 49% ±14.8%. In GTx-024 treated subjects in both the ITT and NSCLC groups, increased weight loss did not negatively affect survival.

Conclusions
Preceding weight loss among NSCLC patients not treated with GTx-024 is predictive of decreased overall survival. In this 16 week Phase IIb trial, NSCLC subjects randomized to placebo with >8% weight loss at baseline were 2 times more likely to die than subjects with ≤8% weight loss. In the GTx-024 group weight loss was not predictive of overall survival. These data suggest that GTx-024 treatment may overcome the negative prognostic effect of >8% weight loss. Further research is needed to assess the effect of GTx-024 on overall survival.