TIME: A Phase 2b/3 Evaluation of TG4010 in Combination with First-Line Therapy in Advanced Non-Small Cell Lung Cancer (NSCLC). Phase 2b results

**Summary**

Background: TG4010 is an immunotherapy product based on a proviral (MoMLV) coding for the MUC1 tumor-associated antigen and imidazo-2,1-phenazine. A previous study showed that, in a normal baseline level of Triple Positive Adenocarcinomas (TPA+), TG4010 (10E+6 MUC1 – C3H/10B6DH2) might be a predictive biomarker for TG4010 efficacy in NSCLC rescued Cervical 2013-12:1325-33. The Phase 2b part aims at prospectively validating the baseline MUC1 concept.

Methods: This is an uncontrolled double-blind phase 2/3 study (NCT00123414) comparing the combination of first-line therapy with TG4010 in a randomized design. Primary endpoint is PFS in the Phase 2b part of the study to see any progression-free survival (PFS) according to RECIST 1.1. between TG4010 and placebo arms using a Bayesian design. Secondary objectives were response rate, safety, survival and subgroup analyses according to stratification factors.

Results: Updated results are presented in this paper as a cut-off date of 22 August 2014. 221 patients were enrolled out of which 170 patients were with a normal TPA level level (pre-determined threshold) and an analysis of PFS was conducted in this cohort after 144 events of progression were reached. The observed hazard ratio (HR) for PFS at 12 months (95% CI) was 0.66 (0.53; 0.83). This corresponds to a 34% reduction in the treatment arm, with a significant improvement in overall survival (OS) of 12.6 months in patients receiving TG4010 compared to placebo. The results from this Phase 2b study are consistent with the observed results in the Phase 3 study. An updated analysis of key factors that contributed to the improved efficacy and safety profile in stage IIIB NSCLC patients treated with TG4010 is ongoing.

Conclusions: These data support the concept that baseline TPA level is a potential biomarker to identify patients more likely to benefit from TG4010 treatment. They also confirm the TG4010 efficacy and safety profile in stage IIIB NSCLC patients treated with TG4010 and demonstrate the prolongation of overall survival with the combination of TG4010 and docetaxel.

**Study Design & Objectives**

**Efficacy in Normal TpPal patients**

- **Population**: Triple positive (TPA+) NSCLC patients treated with TG4010 (10E+6 MUC1).
- **Endpoints**: TPA level and imaging.
- **Subgroup Analyses**: TPA level and imaging.

**Subgroup Analyses**

- **Primary endpoint**: TPA level and imaging.
- **Secondary endpoints**: TPA level and imaging.

**Forefront of PFS by Subgroup**

- **Primary endpoint**: TPA level and imaging.
- **Secondary endpoints**: TPA level and imaging.

**Conclusions**

- **Main result**: TPA level and imaging.
- **Secondary result**: TPA level and imaging.

**Safety**

- **Main result**: TPA level and imaging.
- **Secondary result**: TPA level and imaging.

**Supporting information**

- **Abstracts**: 5152
- **Supporting tables and figures**: TG4010-131
- **Supporting tables and figures**: TG4010-132
- **Supporting tables and figures**: TG4010-133

**Acknowledgments**

- **Patients and their families, investigators and their staff**
- **Sponsors providers**