**Background**

- MIL62 is a glycoengineered anti-CD20 antibody with a nearly completely afucosylated N-glycans in Fc region and enhanced ADCC function compared with wild type Fc anti-CD20 antibody (Figure 1). Single agent activity for MIL62 has demonstrated clinical activity in patients with r/r CD20-positive B-cell NHL which were heavily treated with prior therapies.
- Orelabrutinib (ICP-022) is a novel and highly selective irreversibly Bruton’s tyrosine kinase (BTK) inhibitor without inhibitory activity against IL2-associated tyrosine kinase (ITK). Orelabrutinib doesn’t interfere with the antibody-dependent cellular cytotoxicity (ADCC) of CD20 antibody in combined therapy and is therefore an attractive candidate for combo studies.
- This ongoing study is to evaluate the safety, tolerability and preliminary anti-tumor activity of orelabrutinib in combination with MIL62 in patients with refractory or relapsed CD20 positive B cell NHL.

**Study Design**

- This is a phase I/IIa dose escalation and dose expansion study (NCT 04304040). The study is divided into two parts, phase I is 3+3 Dose Escalation evaluating DLTs, phase IIa is dose expansion for NHLs.

**Patient Population**

As of June 30, 2021, 25 patients with DLBCL (18 pts) and other B cell NHLs (7 pts) have been treated with orelabrutinib and MIL62 combination therapy. Baseline characteristics and demographic data are shown in Table 1.

**Safety**

- **TRAEs, n (%)**
  - **Any grade**
    - All Patients (N=25): 13 (52.0)
    - ≥ 3 grade: 3 (12.0)
  - **Serious TRAEs**
    - 2 (8.0)
  - **Led to drug discontinuation**
    - 3 (12.0)
  - **Led to dose reduction**
    - 3 (12.0)
  - **Led to death**
    - 0

Note: Cutoff date: Jun. 30, 2021.

- **No dose-limiting toxicity (DLT) or unexpected adverse events**
- 12% (3/25) of patients reported grade ≥3 TRAEs.
- 12% (3/25) of patients TRAEs resulted in treatment discontinuation or dose reduction respectively.
- The most frequently (>10%) reported TRAEs were neutropenia (16%), leukopenia (12%), thrombocytopenia (28%), infusion related reaction (16%) and rash (12%).

**Efficacy**

- Twenty patients are evaluable for antitumor activity with at least one post-treatment assessment, overall response rate was 65.0% (95%CI: 40.8, 84.6) and CR rate was 35.0% across all dose groups in the combination therapy group.

**Conclusions**

- Orelabrutinib and MIL62 combination therapy was generally well tolerated. There is no reported DLT, unexpected toxicities or new safety signals. The safety profile of this study is consistent with previous results of orelabrutinib or MIL62.
- The combination therapy demonstrated encouraging antitumor activity, with ORR 65.0% and CR Rate 35.0% in R/R CD20-positive B-cell NHL.
- Phase IIa expansion groups of the study is ongoing.