Preliminary Results of a First-in-Human, Phase 1 Study of GLB-002, a Novel Molecular Glue Degrader of IKZF1/3, in Patients with Relapsed or Refractory Non-Hodgkin Lymphoma

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INTRODUCTION

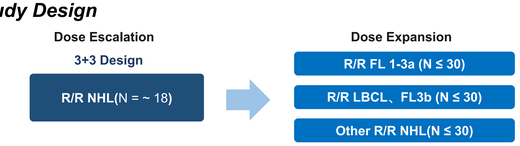
- GLB-002 is a novel cereblon E3 ubiquitin ligase modulator selectively targeting Ikaros (IKZF1) and Aiolos (IKZF3) for degradation.
- GLB-002 is currently being evaluated as a potential therapy for relapsed or refractory (R/R) NHL in an ongoing first-in-human phase 1 study.

OBJECTIVES

- To assess the safety, tolerability, preliminary efficacy and recommended phase 2 dose (RP2D) of GLB-002 monotherapy in patients with R/R NHL, and to characterize its pharmacokinetic profile.

METHOD

Study Design



GLB-002 is dosed once daily with 2 intermittent dosing schedules:
- *14/28 = 14 Days on/14 Days off in each 28-day dosing cycle*
- *10/28 = 10 Days on/18 Days off in each 28-day dosing cycle*

Key Inclusion Criteria

- Patients with R/R B-NHL must have received ≥2 prior lines of therapy including an anti-CD20 antibody-containing regimen (exception for 1 line in transplant-unfit LBCL patients);
- Patients with R/R T-NHL must have received at least 1 prior line of therapy.

RESULTS

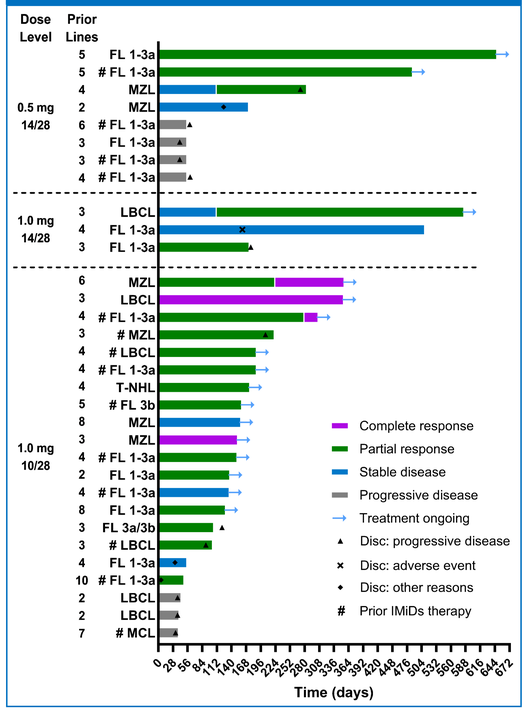
Patients

- As of June 13, 2025, 36 patients with R/R NHL were enrolled including 9 patients in 0.5 mg 14/28 (DL1), 3 patients in 1 mg 14/28 (DL2) , and 24 patients in 1 mg 10/28 (DL3) (**Table 1**).

Table 1. Baseline Characteristics

	DL1 (n=9)	DL2 (n=3)	DL3 (n=24)	Total (N=36)
Age (year), median (range)	58 (47-76)	55 (43-66)	63.5 (37-79)	60.5 (37-79)
Sex, n (%)				
male	6 (66.7)	3 (100)	20 (74.1)	26 (72.2)
Diagnosis, n (%)				
FL 1-3a	6 (66.7)	2 (66.7)	9 (37.5)	17 (47.2)
DLBCL	1 (11.1)	1 (33.3)	7 (29.2)	9 (25.0)
FL 3b	0	0	1 (4.2)	1 (2.8)
Other (MZL, MCL, etc)	2 (22.2)	0	7 (29.2)	9 (25.0)
Duration (month), median (range)	67.30 (20.7, 112.6)	10.60 (8.7, 30.9)	53.15 (11.8, 150.0)	40.45 (8.7, 150.0)
Stage IV during screening, n (%)	5 (55.6)	2 (66.7)	14 (58.3)	21 (58.3)
Prior lines, median (range)	4 (2-6)	3 (3-3)	3 (2-8)	3 (2-8)
IMiDs, n (%)	5 (55.6)	0	12 (50.0)	17 (47.2)

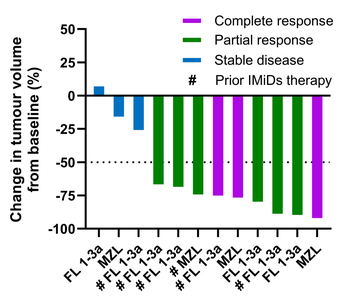
Figure 1. Treatment Duration and Response in R/R NHL Patients across All Dose Levels



Efficacy

- Efficacy outcomes were assessed using Lugano 2014 criteria.
- As of the data cutoff (Oct 21, 2025), the overall response rate (ORR) was 62.5% (20/32) across all dose levels, with a maximum duration of response (DOR) of 652 days.
  - ORR was 64.3% (9/14) in patients with prior IMiDs therapy (**Figure 1**).
  - ORR was 71.4% (15/21) in all NHL patients at DL3.
  - ORR was 75% (9/12) in FL and MZL subgroup (**Figure 2**).

Figure 2. Change in Tumor Volume in R/R FL & MZL Patients at DL3



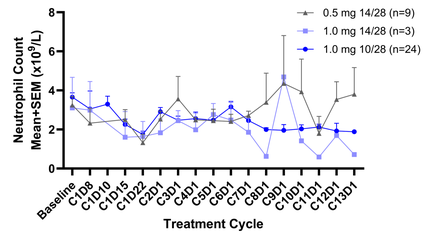
Safety

- Twenty patients (55.6%) reported Grade ≥ 3 treatment-related adverse events (TRAEs) **(Table 2)** .
- Neutrophil count decreased and other hematologic effects were the most common Grade ≥ 3 TRAEs.
- One dose-limiting toxicity (DLT) event (Grade 4 platelet count decreased) has been reported to date at DL3.

Table 2. Grade ≥3 TRAEs Occurring in ≥2 Patients

	DL1 (n=9)	DL2 (n=3)	DL3 (n=24)	Total (N=36)
Grade ≥ 3 TRAE , n (%)	4 (44.4)	3 (100)	13 (54.2)	20 (55.6)
Neutrophil count decreased	3 (33.3)	2 (66.7)	9 (37.5)	14 (38.9)
WBC count decreased	1 (11.1)	2 (66.7)	7 (29.2)	10 (27.8)
Lymphocyte count decreased	0	1 (33.3)	5 (20.8)	6 (16.7)
Platelet count decreased	0	1 (33.3)	3 (12.5)	4 (11.1)
Anemia	0	0	3 (12.5)	3 (8.3)
Pneumonia	1 (11.1)	1 (33.3)	1 (4.2)	3 (8.3)

Figure 3. Neutrophil Change over Time

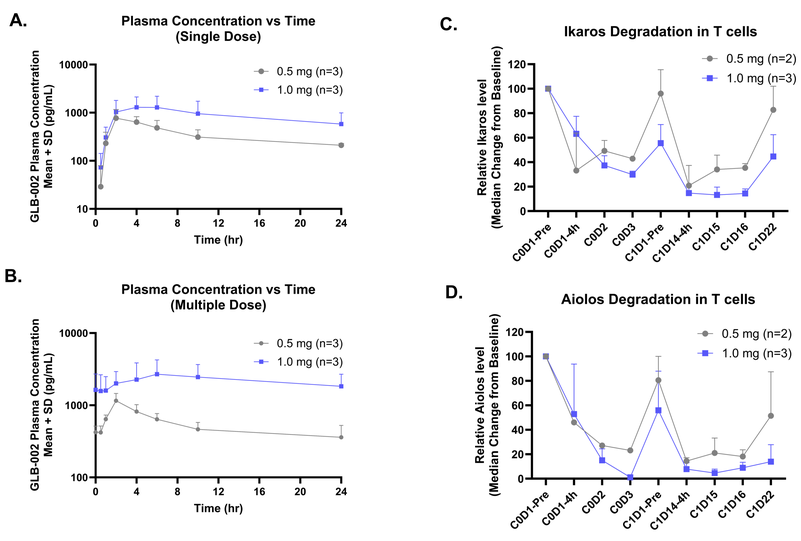


- Neutrophil counts were well-controlled across all 3 dosing regimens after long-term treatment (**Figure 3**).
- The potential RP2D (1.0 mg, 10/28) demonstrated the best safety profile while maintaining the intended therapeutic effect.

Pharmacokinetics and Pharmacodynamics

- GLB-002 demonstrated fast absorption and slow clearance at DL1 and DL2 (**Figures 4A & 4B**).
- GLB-002 induced time- and dose-dependent IKZF1/3 degradation in T lymphocytes (**Figures 4C & 4D**).

Figure 4. Pharmacokinetics and Pharmacodynamics Profile



CONCLUSION

- GLB-002 demonstrated a manageable safety profile and promising antitumor activities in R/R NHL patients.
- GLB-002 appears to overcome IMiDs resistance in NHL supported by preclinical data as well as similar level of response in patients with and without prior IMiDs treatment.

Reference

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2. *Carpio C, et al. Blood. 2020; 135: 996-1007.*
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