INTRODUCTION

- Bcl-2 inhibitors (BBI) delay progression of the intrathoracic amyloid pathogenesis and promote tumor cell resistance to apoptosis.
- The Bcl-2 inhibitor venetoclax is approved for chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) as first-line therapy.

METHODS

- BBI-11417 (PCT0439302) is an ongoing phase I study to evaluate safety, tolerability, and antitumor activity of BBI-11417 in adults with B-cell malignancies (Figure 1).
- Daily dose escalation (DLE) or severity (CLL/SLL) and BBI-1147 best response to date (BRD) in patients with low tumor burden led to CLL.
- Dose-limiting toxicity (DLT) for each dose cohort was evaluated by a Bayesian logistic regression model.

RESULTS

- Of 57 patients, 32 (NHL, n=28; CLL/SLL, n=4) discontinued study treatment.
- The number of patients per cohort is estimated and may vary; MrD was assessed by flow cytometry in 6-cycle intervals (peripheral blood) and upon CR (peripheral blood and bone marrow).

CONCLUSIONS

- These initial results from BBI-11417 indicate that BBI-11417 monotherapy, at all tested doses up to 640 mg, was well tolerated without dose-dependent increases in toxicity.
- The risk of TLS was low and manageable in this study, with no clinical TLS observed.
- Initial antitumor activity of BBI-11417 was promising; responses were observed in patients with R/R CLL/SLL at lower dose levels.
- Preliminary antitumor activity was observed in patients with NHL, with BBI-11417 monotherapy; further expansion data are being generated.