Waldenstrom Macroglobulinemia is an indolent lymphoid malignancy that remains incurable with current therapies. Despite recent advances in understanding pathogenesis and genomic landscape of the disease, as well as therapeutic advances, there remains a need for developing novel agents. This is particularly important for patients with unfavorable mutational disease status, i.e. MYD88-wt, CXCR4-mut, p53-mut, as well as for patients experiencing relapses after current therapies.

Lipid rafts represent an attractive target to deliver therapeutic payloads due to their high prevalence on LPL cells. Iopofosine I 131 is a novel radiotherapeutic consisting of phospholipid ether delivery platform conjugated to radioactive iodine I 131. In the early phase 2A basket study, 6 out of 6 patients with relapsed and refractory WM achieved at least a major response with 1 patient with highly refractory bulky disease and MYD88-wt profile attaining a complete remission.

CLOVER WaM is a global phase 2B single arm study of Iopofosine I 131 that enrolled patients with at least 2 prior lines of therapy that could have included a BTKi. Patients with treated with 2 cycles of Iopofosine I 131 that was administered intravenously on days 1 and 15 of each cycle. The primary objective of the study was Major Response Rate (MRR) and secondary objectives included rate of overall, very good partial, and complete responses, duration of response and progression free survival (DOR, PFS), among others. The study enrolled 65 patients, of whom 55 were evaluable for efficacy endpoints. The overall response rate 80% with 56.4% of patients attaining major response (PR or better). At the median follow up of 8.8 months, the median DOR and median PFS were not reached. Toxicity profile in the overall safety population (n=65) was consistent with prior reports and known AE profile of Iopofosine, with most prominent toxicity being hematologic. Cytopenias were manageable and recovered in all patients. Further details of the study results will be