TPS7097 **Poster Session**

A phase 1 trial of BTM-3566 in relapsed/refractory mature B cell lymphomas.

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Background: Relapsed/refractory (R/R) aggressive B-cell lymphomas, including diffuse large B-cell lymphoma (DLBCL) and mantle cell lymphoma (MCL), remain challenging to treat, particularly in patients who have exhausted approved therapies. BTM-3566, a novel compound demonstrated efficacy against diverse B-cell malignancies, with the most pronounced impact observed in DLBCL and MCL. BTM-3566 initiates the mitochondrial ATF-4-mediated integrated stress response (ISR) pathway via a unique mechanism governed by the mitochondrial protein FAM210B. In vitro, BTM-3566 induces apoptosis across multiple hematological and solid tumor cell lines with several in vivo models demonstrating tumor regression or significant tumor growth inhibition. This includes complete tumor regressions in DLBCL and MCL patient-derived xenograft (PDX) mouse models carrying genetic alterations linked to unfavorable prognosis such as double hit (DH) and triple hit lymphoma (TH) and MCL PDX models from patients previously treated with CAR T, rituximab, venetoclax and/or BTK inhibitors. **Methods:** This ongoing Phase 1, single-arm, open-label, multi-center trial is evaluating the safety, tolerability, and preliminary efficacy of BTM-3566 in adult patients with mature B-cell lymphomas. Eligible participants must have histologically confirmed mature B cell lymphoma that has progressed after at least two prior lines of systemic therapy. BTM-3566 is administered orally in two weeks cycles (7 days on, 7 days off). Primary endpoints include incidence of dose-limiting toxicities (DLTs) and treatment-emergent adverse events (TEAEs). Secondary and exploratory endpoints include objective response rate (ORR), duration of response (DoR), progression-free survival (PFS) pharmacokinetics and pharmacodynamic assessments. Enrollment is scheduled to start in Q1 2025 in US and Canada. Clinical trial information: NCT06792734. Research Sponsor: None.