Hematopoietic Progenitor Kinase 1 (HPK1) Inhibition Enhances Antibody Secretion, Pro-inflammatory Cytokine Production and Proliferation of Primary Human B Cells

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CONCLUSIONS

- NDI-101150 is a highly potent and selective inhibitor of HPK1 achieving sub-nanomolar biochemical potency and greater than 1000-fold selectivity for the HPK1 family.
- HPK1 inhibition results in dose-dependent decreases in primary B cell, a subset of PE knockdown in B cells, followed by an increase in b2m expression in B cells and a decrease in non-specific B cell proliferation.
- HPK1 inhibition results in increased antigen-specific antibody production in response to immunization with KLH.
- NDI-101150 reduces human IgG antibody titers in the DOHH2 xenograft model, which includes B-cell proliferation.
- NDI-101150 is currently being evaluated in a Phase I human multicenter open label phase 1/2 trial (NCT04905942) for use in combination with standard of care in patients with relapsed/refractory multiple myeloma.