Eribulin is a pharmacologically and structurally optimized analog of the marine sponge natural product halichondrin B. Eribulin differs from both Vinca alkaloids and taxanes in its mode of binding to tubulin polymers and in its effects on microtubule dynamics.

- Its salt form, eribulin mesylate (Halaven®) is clinically used as an analog of the marine sponge natural product halichondrin B.

- Eribulin demonstrated potent cytotoxic activity in vitro, with 1% IC₅₀ values approaching 0% for most cell lines at the highest concentration tested.

- The median relative IC₅₀ for the PPTP cell lines was higher than that of the other PPTP cell lines (2.07 nM versus 0.14 nM, respectively, p=0.02), as illustrated by the green bars to the left in the COMPARE-LIKE graph below.

- The most sensitive cell lines, each with rIC₅₀ values < 0.1 nM, were all of lymphoid origin (3 ALL, 1 ALCCL, and 1 NHL), shown in the graph by bars to the right.

- The rIC₅₀ for the neuroblastoma cell lines was higher than that of the other PPTP cell lines (2.07 nM versus 0.14 nM, respectively, p=0.02), as illustrated by the green bars to the left in the COMPARE-LIKE graph below.

- The cell line panels showed distinctive median Relative In/Out% values, with the four rhabdomyosarcoma cell lines having a median value of only -38% (p=0.02 for comparison to non-rhabdomyosarcoma cell lines) and with the ALL cell lines that have a median value of -99% (p=0.005 for comparison to non-ALL cell lines).

- Of the cell lines with ABCB1 relative expression ≥ median panel expression had rIC₅₀ values (2.07 nM) greater than the other PPTP cell lines (2.07 nM versus 0.14 nM, respectively, p=0.01).

- Eribulin was tested at 1 mg/kg using a q4dx3 schedule repeated at day 21. It was well tolerated with only a 1.5% toxicity rate in the treated groups, not much higher than that observed for control animals (0.2%).

- Eribulin was highly active against a range of pediatric solid tumor and ALL xenografts, with objective responses observed in 18 of 35 (51%) solid tumor xenografts and 8 of 15 ALL xenografts.

- CR or MCR were observed in 1 of 2 Wilms tumor, 4 of 5 Ewing, 6 of 7 rhabdomyosarcoma, 2 of 4 glioblastoma, and 3 of 6 osteosarcoma xenografts. For the ALL panel, all 8 xenografts achieved CR or MCR.

- The overall activity profile of eribulin is similar to that for vincristine, but with eribulin appearing more active than vincristine for Ewing sarcoma (see above) and rhabdomyosarcoma (of 7 MCR for eribulin versus 2 MCR and 1 PR out of 7 for vincristine). Both vincristine and eribulin showed reduced activity against neuroblastoma xenografts, perhaps related to ABCB1 expression among neuroblastoma models.

- Published eribulin pharmacokinetic data suggest that murine (CF-1 strain) exposure at 1 mg/kg administered IV and human exposure at 1.4 mg/m² (the recommended phase 2 dose) are reasonably comparable.

- These results support evaluation of eribulin in children with relapsed/refractory cancers, and if robust single agent activity is observed then proceeding with further development for the cancers identified as clinically responsive.