Background: PR-104, a hypoxia-activated prodrug currently in clinical trial, is a water soluble
substrate of AKR1C3. PR-104 is activated upon aerobic metabolism by AKR1C3 to produce DNA interstrand crosslinks. Certain cancer cell lines display atypical aerobic cell
death sensitivity and the rhabdomyosarcoma cell lines exhibiting less sensitivity.

CONCLUSIONS

- PR-104 exhibited an activity pattern consistent with a cytotoxic response to the cell lines of
  the in vitro panel.
- The median IC50 for the in vitro panel was 16.5 μM with the ALL cells exhibiting greater
  sensitivity and the rhabdomyosarcoma cell lines exhibiting less sensitivity.
- PR-104 demonstrated broad activity against the xenografts of the in vivo panels.
- Objective responses were observed to PR-104 in the rhabdoid, Wilms, Ewing, rhabdomyosarcoma, ependymoma, glioblastoma, osteosarcoma and ALL panels.
- No correlation between AKR1C3 levels localized by IHC and PR-104 in vivo activity were
  observed.
- Further preclinical work to determine the in vivo dose response of PR-104 is ongoing.