Phase 3

- **Phase 3 will be the first randomized trial for BCBM & LC under FDA / SPA**

Clinical Design	Phase 3 Criteria	Rationale
Indication	**Leptomeningeal Carcinomatosis (LC)**	▪ No approved standard of care ▪ Poor prognosis (2-3 months survival) ▪ FDA Orphan Designated
Sub-Population	**HER2- Patients**	▪ FDA required homogenous patient population for SPA ▪ Two-thirds of breast cancer patients are HER2- ▪ Prognosis for HER2- patients is ~1-4 months worse ▪ Phase 2 results indicate that relative increase in survival is larger in HER2- patients which will drive a more efficient, smaller Phase 3 trial
Primary Endpoint	**Overall Survival**	▪ mOS for LC patients can be as low as 4-6 weeks – a surrogate biomarker such as ORR is not needed ▪ OS is the ultimate primary endpoint of oncology studies and requested by the FDA
Schema	**Interim Analysis with Adaptive Trial Design**	▪ Cost effective study design enables interim cohort expansion – elimination statistical risk