Description of Additional Supplementary Files

**Supplementary Data 1** 

**Description:** Detailed clinicopathological characteristics of NPC patients (n=106)

**Supplementary Data 2** 

**Description:** H&E staining images of 47 tumors for bulk sequencing

**Supplementary Data 3** 

**Description:** Somatic mutational events identified by WES in this cohort

Supplementary Data 4

**Description:** Sanger sequencing validation of candidate mutations

**Supplementary Data 5** 

**Description:** 48-drug screening results (42 PDOs)

Supplementary Data 6

**Description:** First-line CRT screening results (20 PDOs)

**Supplementary Data 7** 

**Description:** 48-CRT screening results (8 PDOs)

**Supplementary Data 8** 

**Description:** Gene cohorts with subtype-differentiated expressions

Supplementary Data 9

**Description**: Sanger sequencing validation for CRISPR-Cas9 KO experiment

**Supplementary Data 10** 

**Description**: Formulation of tissue dissociation buffer and organoid culture medium

**Supplementary Data 11** 

**Description:** Summary of sequencing coverages

**Supplementary Data 12** 

**Description:** Drug library used for high-throughput screening (146 drugs)

## **Supplementary Data 13**

**Description:** sgRNA oligos used for CRISPR-Cas9 KO experiment