Supplementary Figure Legends

Supplementary Fig. 1:  Mutation rate and ploidy for each individual patient's primary and metastatic sample (cohort 1).  Each patient is designated by a different color with primary samples plotted on the left and metastatic samples on right of the graphs.  A) Plots depict the somatic mutation rate (mutations/megabase of DNA) of paired primary and metastatic gastric adenocarcinoma samples.  Lines connect the paired samples B) Computationally derived tumor ploidy from whole exome sequencing of primary and metastatic gastric adenocarcinoma samples.  Lines connect the paired samples, including the three samples where the metastasis but not the primary tumor had undergone genome doubling, marked with \*\*. The \* marks patients in whom both the primary and metastatic sample had undergone genome doubling.

Supplementary Fig. 2: Validation of genomic heterogeneity within primary tumor and between primary tumor and lymph node (LN) metastases detected by next generation sequencing (NGS) with fluorescent in situ hybridization (FISH) and immunohistochemistry (IHC). A) FISH confirmation of heterogeneous genomic calls for gene amplification of *MET, EGFR* and *CCND1* in distinct tumor areas. B) ERBB2 IHC demonstrates ERBB2 overexpression in primary tumor but its absence in LN metastases, results consistent with the NGS in this patients’ samples.

Supplementary Fig. 3: PANGEA: Platform clinical trial of molecularly driven therapies in patients with previously untreated GEA. This schematic shows the prioritized biomarker and treatment assignment algorithm used to assign patients to treatment arms. In cases where profiling of the metastasis and primary are discordant, the metastatic biopsy is used to guide therapy. Further, in cases of concurrent gene amplifications (*ERBB-2++*, *MET++*, *EGFR++*, *FGFR2++*), the highest absolute gene copy determines targeted therapy assignment.

Supplementary Fig. 4: Biomarker profiling of PANGEA where the biomarker profiling of the metastatic tumor did not lead to treatment reassignment relative to treatments assigned based upon the primary tumor. Results for distinct genes by next-generation sequencing, immunohistochemistry and FISH are shown for each sample. For EGFR, assessment of protein level by mass spectrometry is also shown for select cases.