Legends for Supplemental Figures:

Supplemental Figure S1: Comparison of serum glutamate levels in African Americans and Caucasian Americans with metastatic-castrate resistant prostate cancer.

Mean plot of serum-glutamate levels for normal individuals and patients with primary or metastatic castrate-resistant PCa, stratified by race. The effect of clinical status of the patients, race and their interaction on the log-transformed serum measurements was assessed using two-way ANOVA. Comparisons between the race and patient-type combinations are made using Tukey pair-wise comparisons. A significant racial difference for serum glutamate levels was observed in the mCRPCa patients ($P = 0.037$). The transformed 95% confidence interval for the mean serum glutamate in African American patients with mCRPCa was (55.50 - 82.26) and for Caucasian Americans it was (44.96 - 50.93).

Supplemental Figure S2: Immunohistochemical staining of metabotropic glutamate receptor 1 (GRM1) in selected non-malignant prostatic tissues. Tissue sections were stained as described in "Materials and Methods". The quality of specimens was determined based on H&E staining of serial sections. A, Normal glands show intense nuclear staining in basal cells and absence of staining in cytoplasm of the luminal acinar cells. B, BPH, intense nuclear staining in basal cells and absence of staining in luminal acinar cells. C, intense cytoplasmic and nuclear staining are seen in an area of basal cell hyperplasia (left). D, intense cytoplasmic staining is noted in a representative image of high-grade prostate intraneoplasia. Original magnification, x 200.
Supplemental Figure S3: Immunohistochemical staining of metabotropic glutamate receptor 1 (GRM1) in selected prostate cancers.

Tissue sections were stained as described in “Materials and Methods”. The quality of specimens was determined based on H&E staining of serial sections. **A**, moderate to intense cytoplasmic staining with perinuclear enhancement is noted in Gleason score 7 (4+3) tumor with a typical cribriform plate. **B**, intense cytoplasmic staining in a ductal adenocarcinoma (4+4). **C**, intense cytoplasmic staining of prostate cancer cells metastasized to abdominal wall. **D**, intense cytoplasmic staining of prostate cancer cells scattered in soft tissue attached to bone. Original magnification, x 200.

Supplemental Figure S4: Effect of BAY36-7620 on prostate cancer cells proliferation

**A-C**, Cells were seeded at 500 (PC-3, DU145, LNCaP) per 200 µl/well in 24 replicates in 96-well plates in their complete medium. After 3 days, cells were incubated in their maintenance medium in the presence or absence of BAY36-7620 (a non-competitive GRM1 antagonist) for 2, 4, or 6 days. The media were refreshed every 48 h. Cell proliferation was measured by adding 20 µl MTS solution per well for 1 h and measuring the absorbance at 490 / 630 nm. Data represented the average of three independent experiments ± SEM. Statistical significance ($p < 0.001$) between the control and treatment groups was evaluated by one-way ANOVA test with Bonferroni adjustment.

Supplemental Figure S5: Scratch-wound migration assays.

Prostate cancer cells were grown to 30% confluency in a 6-well plate in their complete medium. Cell monolayers were scratched with a rubber cell scrapper, washed to remove debris and cultured in their maintenance medium supplemented with or without riluzole or BAY36-7620 at 10 or 25 µM and incubated for 2, 4, or 6 days. Representative photomicrographs were taken at
4 days using a 10 objective on an Olympus microscope. Experiments were performed in triplicate and repeated three times independently.