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 luminar 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.