Reviewer's report

**Title:** Efficacy of c-Met inhibitor for advanced prostate cancer

**Version:** 1  **Date:** 3 July 2010

**Reviewer:** Anthony Joshua

**Reviewer's report:**

**Major Complusory Revisions**

1- Author JCG is an employee of Pfizer apparently, this needs to be declared in the conflicts of interest section

2-This is now the second paper in the literature to discuss the use of c-met inhibitors in prostate cancer, and the third c-met inhibitor in use. I refer the authors to Dai et al., and Munshi et al., for recent papers on the utility of c-met inhibition. The findings of these papers, in particular Dai et al., need to be incorporated into the paper. In particular, the differences between the characteristics of c-met inhibition found in prostate cancer cell lines

3- Most of the effects found with the compounds were at concentrations of 2.5um. How does this level relate to the serum level achievable? Or to the IC50 of these compounds on c-met?

4- The authors also need to further verify the effects of supposed c-met inhibition by (i) competing out the effect of drug with HGF and/or (ii) carrying out K/down of the c-met gene

5- The reductions of ki67 index should also be supported by assessments of apoptosis, unless there is a good reason not to carry out this assay

6- The authors need to add to the western blot Figure 1D, the effects of inhibition of downstream pathways of c-met, for example, are PI3k and MEK required for the effects of this axis?

**Minor Essential Revisions**

The results section of the abstract is written poorly and needs to be revised to more accurately convey to the reader a sense of what is in the manuscript, likewise the conclusion.

Please correct all CRPR to CRPC

The second paragraph of the background is written poorly. In particular, it is unclear in the latter two sentences of this paragraph whether the authors are referring to the current or previous manuscript. Use of the past tense here would clarify things

Results section, second paragraph. "After 3 hrs of treatment"

A point of interest from the authors previous studies is whether c-met inhibition could delay the time to androgen resistance. This issue is only addressed in a limited fashion in the current manuscript and the paper would achieve greater
impact if this clinically relevant issue was addressed

Discretionary Revisions
None

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare I have no competing interests