Reviewer's report

Title: Effects of BIS076 in a model of osteoarthritis induced by anterior cruciate ligament transection in ovariectomised rats

Version: 3  Date: 9 February 2015

Reviewer: Nicole Walsh

Reviewer's report:

The authors have attempted to address most of the reviewers concerns, however a few issues are still a concern.

Major Compulsory Revision:

1) Although the quality of the images shown in figure 1 are improved, the histology is still poor and raises questions. This reviewer is not convinced by the quality of the histology shown in Figure 1 is still poor. The Safranin-O stained images in Figure 2 show better quality histology, but it looks like this has been overstained (an with no counterstain) making it difficult to determine the extent of proteoglycan loss (which is one component of the OARSI histologic scoring system). NB the methods also still state that histologic scoring was performed on HE sections only.

2) Clarification of animal groups. The authors have clarified the experimental groupings. This has highlighted that their sham control animal is both sham for ovariectomy and ACLT surgery. Since they are looking at the effects of BIS076 on preventing OA-like joint damage, the most appropriate “sham” control would have been ovariectomy + Sham ACLT. The absence of this control prevents the determination of what bone is lost due to the ovariectomy and what alterations are due to ACLT.

3) MicroCT analysis of bone structural changes. The review agrees that T2 treatment does improve metaphyseal bone structure, however the evidence for similar changes in the epiphysis is not strong (not even a trend in change). Therefore the suggestion that treatment does improve epiphyseal bone structure should be removed.

Minor Essential Revision:

1) MicroCT methodology: The authors have provided most of the details for their microCT analysis, but have neglected to include details of the thresholds and algorithms used to binarise their images in CTANalyser for determination of structural properties. These should be included.

Level of interest: An article of limited interest

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests'