Reviewer’s report

Title: A small molecular agent YL529 inhibits VEGF-D-induced lymphangiogenesis and metastasis in preclinical tumor models in addition to its known antitumor activities

Version: 8 Date: 25 February 2015

Reviewer: Steven Stacker

Reviewer’s report:

- Minor Essential Revisions

The lack of balance on VEGF-C (Q2) in the introduction and the lack of an experiment addressing its activity does leave a gap in this study

The "few reports" of VEGF-D in tumor metastasis should include the original reference Stacker et al., Nature Medicine 2001.

Ref#38 is not the original reference for this fact. Debinski et al., Mol Med. 2001, 9:598-608

Page 11, the new sentence appears incomplete.

Rounding of the numbers from two-decimal places is suggested

Figure 7 is still quite confusing and does not adequately explain the different contributions of R2 and R3 on LEC and blood vessels. The diagram should as a minimum show the different contributions of R2 and R3 on LEC, and preferably compared to BEC on blood vessels.

Expressions like "the specific lymphangiogenic factor" will confuse readers about the specificity of VEGF-D and do not integrate the activity of VEGF-D seen on blood vessels by these workers and others. It will create an incorrect bias in the minds of the readers about the total activity of the factor.

Figure 7 is quite poor, and could provide so much more information and guidance to the readers.

Level of interest: An article whose findings are important to those with closely related research interests

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

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests:

I am a shareholder in Circadian Technologies and Ark Therapeutics, both companies are involved in developing therapeutics for the treatment of angiogenesis and lymphangiogenesis in cancer and other diseases