Reviewer’s report

Title: Focal Segmental Glomerulosclerosis: Molecular Genetics and Targeted Therapies

Version: 1 Date: 17 February 2015

Reviewer: Laura Barisoni

Reviewer’s report:

The authors have nicely recapitulated the major issues and discoveries regarding FSGS. The manuscript is well organized.

The section “Is pathogenesis reflected in the histopathology of FSGS?” could be expanded, and the morphologic heterogeneity of FSGS, the current value of morphologic classifications and their relevance to pathogenesis discussed more in details.

The section on treatment of FSGS also needs an introduction. For example point 1. Discuss treatment of secondary FSGS, but there is no introduction to secondary forms prior this point.

The difference between primary and secondary is obviously critical for the clinical implications and treatment. How do we discriminate between the two? Do we currently use reliable criteria to declare FSGS primary or secondary? It the call based on evidence or opinion? How the community can better address these issues? FSGS secondary to what? Hyperfiltration, viral infection or genetic mutation? Are all suspected hyperfiltration mediated FSGS really secondary to hyperfiltration or the genetic background (APLO1) is really the cause and hyperfiltration a second hit mechanism?