**Author’s response to reviews**

**Title:** Identification of cryptolepine metabolites in rat and human hepatocytes and metabolism and pharmacokinetics of cryptolepine in Sprague Dawley rats

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**RESPONSE TO REVIEWER COMMENTS**

**COMMENT 1:** Please include a title page as the first page of your manuscript where you list the full names, institutional addresses and email addresses for all authors. The corresponding author should be indicated.

 RESPONSE: Recommended changes have been effected in the manuscript.

**COMMENT 2:** Please can you clarify if the Sprague Dawley rats were euthanized at the end of the experiment and if so please provide a statement regarding this in the Methods section including the method used.
RESPONSE: Rats were euthanized by cardiac puncture at the last blood collection time point.

COMMENT 3: We note that your experimental protocol was approved by the Novartis Institutes for Biomedical Research Cambridge Institutional Animal Care and Use Committee. Please could you clarify whether all experiments took place at Novartis Institute for Biomedical Research – Cambridge?

RESPONSE: All in vivo experiments took place at Novartis Institute for Biomedical Research – Cambridge. However, in vitro experiments took place at Novartis Institute for Biomedical Research – Basel, Switzerland.

COMMENT 4: We note that you used Cryptolepine in your study, please could you clarify whether Novartis produces this drug. If so, this should be declared in the Competing interests section. Please note that as per our editorial policies receiving reimbursements, fees, funding, or salary from an organization that may in any way gain or lose financially from the publication of the manuscript, either now or in the future should be declared in the Competing interests section. Please see our editorial policies for more information https://www.biomedcentral.com/getpublished/editorial-policies#competing+interests

RESPONSE: As indicated in the manuscript (material and method section), cryptolepine hydrate was purchased from Sigma Aldrich (St. Louis, MO). Cryptolepine is not a Novartis product.

COMMENT 5: We note that you state that your study received no external funding, please could you clarify whether your study received any internal funding. All sources of funding for the research reported should be declared in the Funding section.

Please note that if your study received any commercial sources of funding, as a standard, we require that all commercial sources of funding are also declared in the Competing interests section.

RESPONSE: The study was funded by Novartis Pharma under the Next Generation Scientist Program.
COMMENT 6: Please provide a list of all the abbreviations used in the manuscript. This list should be placed just before the Declarations section. All abbreviations should still be defined in the text at first use.

RESPONSE: All abbreviations have been included and defined at first use.

COMMENT 7: Please clarify whether the chemical structure images in figures 1 and 2 are your own or taken from another source.

If taken from another source please acknowledge the source in the figure legend, and if it is under copyright also state the written permission given to use and adapt it.

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RESPONSE: These images are my own and were not taken from other sources. Figure 1 for instance was drawn with ChemBioDraw Ultra.

COMMENT 8: Thank you for attaching your authorship change form. I can now confirm that your change in authorship has been approved, please remove the form from the file inventory as it is no longer required.

RESPONSE: This has been removed from the file inventory.