

July 27, 2020

Preston Klassen, M.D.
President and Chief Executive Officer
Metacrine, Inc.
3985 Sorrento Valley Blvd., Suite C
San Diego, CA 92121

Re: Metacrine, Inc.
Amendment No. 2 to
Draft Registration

Submitted July 2,

CIK No. 0001634379

Statement on Form S-1
2020

Dear Mr. Klassen:

We have reviewed your amended draft registration statement and have the following comments. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure.

Please respond to this letter by providing the requested information and either submitting an amended draft registration statement or publicly filing your registration statement on EDGAR. If you do not believe our comments apply to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing the information you provide in response to these comments and your amended draft registration statement or filed registration statement, we may have additional comments.

Draft Registration Statement on Form S-1
Overview, page 1

1. Summary with disclosure that doctors recommend weight loss to treat liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) reduce fat in the liver, inflammation, and fibrosis, or Factor disclosure that the current standard of care is market penetration of MET409 and MET642 for the treatment of commercialized, please include this in your Summary.

Please balance your nonalcoholic fatty because weight loss can scarring. We note your Risk likely to present a major challenge to the NASH, if ever

2. that you "believe FXR agonists will become first-line

We note your disclosure

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monotherapy, as well as the backbone of combination therapy (emphasis added), for patients with NASH." Please provide your basis for this statement given that diabetes, obesity and metabolic syndrome appear to be the diseases with which NASH is associated and it appears that the current standard of care includes antidiabetic therapies, which

would appear to be the principal therapy in any potential combination with a therapy for

NASH.

3. Please revise here and throughout your prospectus to balance and provide the basis for your disclosure that "with our program, we believe we can be the leader [emphasis added] in developing best-in-class FXR agonist therapies for NASH and other GI diseases." We note your disclosure that other companies are in later stages of clinical trials for their FXR agonists than you and that "MET409 and MET 642 are FXR agonists, a class of drugs from which there are no approved therapies in the diseases for which we are currently pursuing clinical trials, and our initial target indication is NASH, for which there are no approved therapies." Further, please remove "best-in-class" and "first-in-class" therapy references (and similar phrases) found throughout your registration statement since these terms suggest that the product candidates are effective and likely to be approved.

4. We note your disclosure that "targeting FXR has demonstrated improvements in NASH in large-scale clinical trials, including reversal of fibrosis, which we believe makes this a well-established target (emphasis added) for the treatment of NASH patients." Please revise your disclosure to provide the basis for this belief given your disclosure that "MET409 and MET 642 are FXR agonists, a class of drugs from which there are no approved therapies in the diseases for which we are currently pursuing clinical trials, and our initial target indication is NASH, for which there are no approved therapies." We further note your disclosure on page 13 that the FDA recently denied accelerated approval for a competitor's product candidate based on the surrogate histologic endpoint of improvement of fibrosis as shown by liver biopsy with no worsening of NASH in lieu of clinical outcomes such as overall survival and time to transplant."

5. As safety and efficacy determinations are solely within the Food and Drug Administration's authority and they continue to be evaluated throughout all phases of clinical trials, please remove references to these terms, along with references to "potency," and any similar references in your prospectus.

6. We note your Summary disclosure on page 2 that you intend to pursue development of your FXR agonist product candidates for the treatment of Inflammatory Bowel Disease, or IBD, including Ulcerative Colitis, or UC, and Crohn's disease. Please provide us with your analysis as to why it is appropriate to include the lengthy Summary discussion of these indications and emphasis on the \$9 billion annual market opportunity for IBD given it appears your product candidates are preclinical for such indication. We note your disclosure that you plan to submit an IND for an undisclosed product candidate in 2022.

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7. We note your disclosure that "[i]n preclinical studies of our FXR agonists, we have observed improvement in colon inflammation on a level similar to that of biologics currently used for treatment. We believe an oral, once-daily therapy

with FXR agonists, such as those in our FXR program, could be an attractive treatment option for IBD patients." Efficacy is a determination that is solely within the authority of the FDA or similar foreign regulators. Additionally, comparisons to other available treatments require head-to-head trials. Please delete the statements indicating that your FXR agonists, which haven't been clinically tested for this indication are effective at treating IBD and remove any comparisons with third party treatments, including your perceived similarity to existing therapies currently used for treatment.

8. We note that the status arrows in your pipeline chart on pages 4 and 86 end at different locations within the columns. Please include a narrative that describes what the chart is depicting.

9. We note that your pipeline table includes the "MET409 or MET642" for IBD Monotherapy, as preclinical programs that you are exploring, but it appears you don't plan to file an IND for either of these candidates for such indication until 2022. As your narrative disclosure only briefly discusses these programs for any indication within the class of IBD, an IND is not planned until two years from now and you have not allocated any proceeds for their development in your use of proceeds section, please explain to us why you believe these programs are sufficiently material to your business to be included in your pipeline table. Your analysis should address specific product candidates and indications within IBD.

10. We note that your pipeline table includes "MET409 or MET642" for "other indications" as preclinical programs that you are exploring. As you only discuss these programs in general terms very briefly in the prospectus and you have not allocated any proceeds for their development in your use of proceeds section, please provide us your analysis supporting your determination to include a specific product candidate for a specific indication in this category in your pipeline table.

11. Please remove the last row of your pipeline table that generically references "inflammation and fibrosis targets" and then "NASH," neither of which are a summary of your research and development programs.

12. We note your disclosure that your lead candidate, MET409, completed Phase 1b clinical trial as a monotherapy in the Netherlands and that you plan to initiate a Phase 2a combination trial in the first half of 2021 of MET409 with an antidiabetic agent in patients with type 2 diabetes and NASH, and expect to report topline data in the first half of 2022. Please revise your disclosure to indicate whether you are conducting the Phase 2a trial in the United States and if so, whether you have submitted an IND to FDA. To the extent that you have submitted an IND, disclose when you submitted it and identify the IND sponsor(s) and the specific indications listed therein. Please disclose whether you believe that clinical data generated in the Netherlands will be accepted by the FDA and its

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foreign equivalent and therefore enable you to commence your planned

Phase 2a trials in the United States, without the need to repeat your Phase 1 clinical trial in the United States.

13. Please state when you plan to submit an IND in advance of your plans to initiate a Phase 2a, randomized, placebo-controlled trial of MET642 in patients with NASH in the first half of 2021.

14. We note your intent to expand the development of your FXR program into IBD. Please identify the product candidate and specific IBD indication referenced and state with more specificity when you plan to submit an IND and when you intend to initiate a Phase 2a clinical trial in IBD patients in 2022.

15. We note your Risk Factor disclosure that "...some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors product candidates. This is acutely relevant (emphasis added) for our development of MET409 and MET642 for the treatment of patients with NASH and IBD, diseases for which there are significant competition (emphasis added) for clinical trial subjects." Please consider whether this is material to your business and as such should be included on page 5, Risks Associated with Our Business.

We are an early stage biopharmaceutical company with a very limited operating history., page 12

16. We note that you disclose your results for the fiscal years ended December 31, 2018 and December 31, 2019, and for the six months ended June 30, 2020. Please expand your disclosure here and throughout your registration statement, where appropriate, to include results for the six months ended June 30, 2019.

Risk Factors

We are very early in our development efforts and we have limited experience conducting clinical trials in humans., page 15

17. We note your disclosure that "[t]o date, MET409 and MET642 have only been evaluated for safety and toxicology in animals for up to 13 weeks and 16 weeks, respectively, and their longer term toxicity is unknown." Please confirm that this is current information, as it appears to be inconsistent with your clinical development disclosures.

We rely, and intend to rely, on third parties to conduct our clinical trials and perform some of our research and preclinical studies., page 30

18. We note that you rely, and intend to rely, on third parties to conduct your clinical trials and perform certain other tasks. To the extent material, attach any agreements covering such relationships.

Use of Proceeds, page 64

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19. Please disclose how far into development (e.g., phase of clinical study) for each product candidate with a specific indication you anticipate the proceeds of this offering will allow. Expedited development and review programs, page 106

20. Please expand your disclosure to explicitly state that fast track designation does not guarantee an accelerated review by the Food and Drug Administration. Amended and Restated Certificate of Incorporation and Amended and Restated

21. Please provide amended bylaws that reflect your disclosures regarding the applicability of your exclusive forum provision to Exchange Act and Securities claims or revise your disclosure here and your risk factor to clarify that your bylaws do not explicitly address the Exchange Act or Securities Act.

You may contact Tracie Mariner at (202) 551-3744 or Kevin Vaughn at (202) 551-3494 if you have questions regarding comments on the financial statements and related matters. Please contact Courtney Lindsay at (202) 551-7237 or Celeste Murphy at (202) 551-3257 with any other questions.

FirstName LastNamePreston Klassen, M.D.
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Sincerely,

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