UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

DIVISION OF
CORPORATION FINANCE

December 2, 2024

Christopher Whitten Bernard
Chief Executive Officer
Metsera, Inc.
3 World Trade Center
175 Greenwich Street
New York, New York 10007

Re: Metsera, Inc.
Draft Registration Statement on Form S-1
Submitted November 4, 2024
CIK No. 0002040807

Dear Christopher Whitten Bernard:

We have reviewed your draft registration statement and have the following comments.

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 a comment applies 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 this letter and your amended draft registration statement or filed registration statement, we may have additional comments.

Draft Registration Statement on Form S-1

Prospectus Summary
Overview, page 1

1. Please revise here and on page 119 to explain what you mean when you say that your lead candidate, MET-097i, is "BLA-eligible," and explain the significance of a product candidate being so eligible with the FDA. Also, given that your disclosure that MET-097i is in ongoing Phase 1/2 trials, revise to explain when companies typically make a BLA application (e.g., following successful completion of all required clinical trials and at same time the company seeks marketing approval).
2. We note your disclosure that you are advancing a "broad, scalable and combinable portfolio of injectable and oral NuSH analog peptides" and that your pipeline includes

"clinical-stage" injectable and oral GLP-1 RA analog peptides, as well as multiple complementary peptides that "can be combined with GLP-1 RAs." Here and throughout where appropriate, please revise as follows:

- Clarify that your pipeline includes both clinical-stage and early preclinical stage product candidates. Likewise, revise the subsections on pages 6 and elsewhere throughout captioned "Other pipeline programs" to clarify that the programs described are in preclinical stages.
- To the extent that the scalability and combinability of your product candidates is currently aspirational, please so state. For example, we contrast certain of your other disclosures that you "plan" to develop MET-233i to be administered in combination with other peptides, including MET-097i if you are first able to establish sufficient results in your Phase 1 trial of MET-233i as a monotherapy.
- If true, balance this disclosure by explaining that the data you have generated to date from MET-097i "supporting combinability" is preliminary and limited to preclinical data, and that you have yet to initiate any clinical trials of any combination therapies.
- As appropriate, revise the Summary, Risk Factors and Business sections to describe how the development of combination therapies differs from the development of single agent therapies, and whether such development may present more or different challenges than development of single agent therapies, or otherwise advise.

3. We note your disclosure that MET-097i, your most advanced product candidate, is a "subcutaneously injectable" GLP-1 RA that you are developing for the treatment of obesity and overweight. In this regard:
   - Please revise the Summary and Business where appropriate to explain how you intend for MET-097i and any other of your subcutaneous injectable product candidates to be delivered and administered. In this regard, we note certain references throughout to "disposable injector devices" and "cartridge-based injectable drug product units" that lack sufficient context.
   - Revise to disclose whether you anticipate that any of your injectable product candidates may be regulated by the FDA as drug-device combination products. As appropriate, explain the implications of drug-device combination product classification with respect to the regulatory approval process, including how this process differs from the process of obtaining FDA approval for drugs or biologics alone, or otherwise advise.
   - If material, please add summary risk and risk factor disclosure discussing any risks or challenges related to your development of MET-097i and any other injectable product candidate if the FDA may consider such candidate(s) to be a drug-device combination product, or otherwise advise.

4. In the appropriate places in the Summary and Business sections, please revise to disclose the location(s) of all completed, ongoing, and planned clinical trials of your product candidates. Also, as appropriate, revise your risk factor disclosure on pages 10 and 29 to clarify whether you are currently conducting trials outside the United States. In this regard, we note your disclosure that you have initiated a Phase 1

trial prototype compound MET-002, a predecessor peptide to MET-224o, following your Clinical Trial Application being approved by Health Canada in October 2024. We also note your disclosure on page 25 stating that you and your collaborators are "currently conducting" clinical trials in foreign countries.

The Obesity and Overweight Market, page 2

5. Please revise the Summary and Business sections where appropriate to:
   - Disclose your development and regulatory approval plans for each of your product candidates, including clarifying the initial estimated patient population(s) for which you are developing each candidate in each indication (e.g., adults versus children), and the jurisdiction where you plan to first seek regulatory approval.
   - Revise your discussion of the market opportunity for your product candidates by separately disclosing your best estimate of prevalence and incidence figures for obesity and overweight in the patient population(s) you intend to treat in any jurisdiction(s) where you plan to seek regulatory approval. In this regard, we note that on page 2, you provide prevalence figures for obesity and overweight worldwide, in Southeast Asia and the Americas. You also provide an estimate that in 2020, obesity and overweight "affected more than 70% of adults in the United States," and that "nearly half of Americans are projected to have obesity by 2030.

The Evolving Obesity and Overweight Treatment Landscape, page 3

6. You state that the GLP-1 RA market has experienced rapid commercial success, is expected to continue to grow in the future, and that third-party market research reports estimate that GLP-1 RAs represented approximately $36 billion in global sales in 2023 and could reach $170 billion by 2030. In this regard:
   - Please revise here and in Business to separately provide past and future estimated sales figures for GLP-1 RAs in the patient population(s) you intend to treat in any jurisdiction(s) where you plan to seek regulatory approval.
   - Balance your statements here and elsewhere pertaining to market size by disclosing that you do not have any products approved for commercial sale and discussing the regulatory steps you must take before receiving such approvals. Explain that your product candidates are in the early stages of U.S. clinical development, that it will take years to develop and commercialize them, and that even if you are successful in obtaining regulatory approval, there can be no assurance as to your ability to penetrate the obesity and overweight market, and if so, to what extent.

7. Please balance your statements here and elsewhere pertaining to the tolerability of currently approved products with disclosure about the TEAEs that you have observed in your Phase 1/2 clinical trial of MET-097i.

Our Approach, page 4

8. We note the statement that your MINT peptide library was developed through over 20 years of iterative and empirical discovery work. Please clarify which entities conducted this discovery work.

9. Please revise this section here and in Business as follows:
   - Explain what prodrugs and antibody peptide conjugates are, and why you believe developing these technologies could reduce injection frequency. Disclose the status of your development of these technologies, and identify any material steps that will need to be taken in order to utilize them either alone or in combination with your product candidates.
   - Explain what you mean by "dose titration" and "re-titration."

MET-097i, page 5

10. Please revise this section here and in Business as follows:
   - On pages 6 and 124, you state your belief, based on preliminary results from your ongoing Phase 1/2 clinical trial of MET-097i, that the observed half-life provides "clinical validation" of your HALO half-life extending platform. Please revise to clarify that this "validation" does not mean that your product candidates will demonstrate safety or efficacy, and disclose that product candidates developed with the HALO platform have yet to be evaluated in a completed clinical trial.
   - On pages 6 and 125 you state your belief that observed change in body weight from baseline in the same ongoing trial "is consistent with, or better than the highest titrated study arms of similar Phase 1 trials for marketed and clinical-stage GLP-1/GIP RA compounds." Please tell us whether any differences in the "similar" third party Phase 1 trial protocols, patient populations, dosages, or other factors could lead to material differences in measured change in body weight. Also, balance your statement by explaining that there are risks in drawing conclusions as to the performance of MET-097i relative to that of any other therapy given the absence of head-to-head trials, and disclose that the results from clinical trials of a competitor’s product candidate in the same class may not predict the results of clinical trials of your product candidates.

Our Pipeline and Programs, page 5

11. We note that the pipeline table should graphically demonstrate the current status of your product candidates and clearly show the material trial phases you will need to complete before marketing your products. The table should be a reflection of the narrative disclosure in the prospectus and should not be used to prematurely project or imply successful completion of the stages required prior to regulatory approval and commercialization. A narrative discussion is more appropriate for the next steps or aspirational plans for your product candidates, such as the completion of a particular trial phase.
   - As appropriate, please revise to shorten the progress arrows, by product candidate and indication, to reflect the actual status of your pipeline candidates as of the latest practicable date. As currently drawn, the gray "in process" portion of the arrows could inappropriately create the impression of further candidate progress.
   - Your disclosure on page 1 and in footnote 2 to the pipeline table appears to indicate that you have two parallel oral peptide development programs underway: (1) the ongoing Phase 1 formulation optimization trial of MET-244o (prototype peptide formulation), and (2) IND- and CTA-enabling preclinical studies of MET-

244o (optimized formulation). Since you are not currently conducting a Phase 1/2 clinical trial of either oral formulation, please tell us whether presenting the ongoing studies/trials for each oral formulation separately in the pipeline table would be more appropriate. We note in this regard that the progress arrow for "MET-244o/MET-002" could be interpreted as indicating that you have completed all preclinical work for MET-244o, rather than that you "plan to complete" such studies. Please ensure your arrows clearly align with your narrative disclosure.

- Revise the heading of the eighth column to remove the reference to "current status," as the progress arrows themselves should reflect the current status of each product candidate. In this column, you may instead identify the single next anticipated material milestone for each product candidate.
- Please revise to qualify your statement regarding the next anticipated milestone with respect to the MET-097i + MET-233i combination program. In this regard, we note that sufficient safety might not be established in the MET-233i Phase 1 trial.
- Please tell us your consideration of removing the columns captioned "HALO Half-Life Extending Platform" and "Global Rights" from the pipeline table. We do not object to discussion of these topics in the supporting narrative disclosure.

12. Please explain to us why your MET-AMYo oral amylin analog program, for which you have not yet identified a lead candidate, is currently sufficiently material to your operations so as to warrant being highlighted in the pipeline table. Similarly, explain the same with respect to each of the "next-generation combination" programs. To the extent that you believe these programs are material, please revise the Business section to explain each program and the respective identified product candidate(s) in greater detail, including a discussion of relevant pre-clinical work that has been conducted or is in process. In this regard, your disclosure in the Business section concerning the preclinical work should support the positioning of the arrows in your pipeline table, as well as the next material step reflected in the "Anticipated Milestones" column. Alternatively, revise to remove any pre-clinical program that is not currently material to your business. We do not object to your narrative discussion of such programs in the Summary and Business sections.

MET-233i, page 6

13. We note your statements here and on page 125 that MET-233i "has a potentially class-leading half-life amongst known amylin analogs in development and is the only candidate suitable for monthly dosing," as well as the statements on pages 8 and 127 that your goal is to develop "potentially best-in-class injectable and oral therapies." Please remove these and any similar statements throughout, as such statements are speculative in light of the current regulatory status of your product candidates and the uncertainty involved in clinical development. Further, such statements could be read to imply that your product candidate is effective or likely to be approved, and such determinations are solely within the authority of the FDA and comparable regulatory bodies.

Our Strategy, page 8

14. Please revise your disclosure in this section and in Business as follows:
    - Balance your statement of belief that your product candidates "have the potential to outperform current approved products and development-stage product candidates on tolerability, efficacy, convenience, and scalability" by disclosing, if true, that you have not conducted head-to-head clinical trials of any of your product candidates against currently approved products, your product candidates are in the early stages of U.S. clinical development, that it will take several years to develop and commercialize them, and that even if you are successful in obtaining regulatory approval, there can be no guarantees as to outperformance of other therapies on any of tolerability, efficacy, convenience or scalability.
    - Balance references to your team's "track record" in drug development and your belief in your ability to "develop multiple product candidates to global regulatory approvals, to manufacture at commercial scale, and to commercialize effectively in major markets." Disclose, if true, that the past experience of your individual team members is not necessarily predictive of the future success of your company, that as an organization you have not successfully obtained regulatory approval or commercialized any products in any jurisdiction, that you may not obtain approval for any product candidates in any jurisdiction, and that even if you are successful in obtaining any regulatory approvals, there can be no guarantees as to your ability to manufacture your product candidates at commercial scale.

Risk Factors
We currently rely on third parties for the manufacture and shipping of our product candidates for clinical development..., page 35

15. We note your disclosure that you entered into a Development and Supply Agreement with Amneal Biopharma Solutions Private Limited in October 2024. Pursuant to this agreement, among other things, you are obligated to pay up to $100 million over four years for the construction of two new greenfield manufacturing facilities in India for the manufacture of drug substances and drug products, which Amneal will use to manufacture peptide drug substances and injectable peptide products for you and drug substances and drug products for itself and its other customers. Please revise to disclose the estimated timeline for completion of these facilities. Also disclose, if true, that there can be no assurance that your investment in these manufacturing facilities will be recouped.

Our current amended and restated certificate of incorporation provides..., page 81

16. Please revise to disclose that the federal forum provision may result in increased costs to shareholders to bring a claim.

Participation in this offering by our existing stockholders and/or their affiliated entities may reduce the public float..., page 81

17. You disclose that "[t]o the extent certain of our existing stockholders and their affiliated entities participate in this offering, such purchases would reduce the non-affiliate public float of our shares, meaning the number of shares of our common

stock that are not held by officers, directors, and controlling stockholders." Please revise your disclosure throughout the filing, including your prospectus summary, to clarify whether and to what extent existing stockholders and their affiliates have indicated an interest in purchasing shares in your offering.

Use of Proceeds, page 88

18. Please revise to disclose an estimate of how far in your development and commercialization of MET-097i, MET-233i and MET-244o the proceeds from this offering will allow you to reach with respect to each product candidate, including specific phases of any preclinical and clinical trials. If material amounts of other funds are expected to be necessary to accomplish the specified purposes for which net proceeds are intended to be used, provide an estimate of the amounts of such other funds and the sources thereof.

Unaudited Pro Forma Combined Financial Information
Note 3- Consideration Transferred and Purchase Price Allocation, page 98

19. We note your disclosure stating that the identifiable intangible assets you acquired consist of two in-process research and development, or IPR&D, assets which were assigned aggregate fair values of $67.0 million and are indefinite-lived until the programs can begin to be commercialized. Please expand your disclosure to clearly identify, describe, and separately quantify each acquired intangible asset, as well as all material assumptions used to determine their fair value.

20. We note you allocated $42,916 of the purchase price of Zihipp, Ltd. to contingent consideration. Please expand your disclosure to explain the method and material assumptions used to estimate the fair value of the contingent consideration, or cross-reference to where this information can be located in your filing.

Management's Discussion and Analysis of Financial Condition and Results of Operations
Results of Operations, page 103

21. We note your disclosure, on page 101, stating that you track your external research and development expenses on a program-by-program basis, but you do not track your internal research and development expenses on a program-by-program basis. Please expand your disclosure, for the periods presented, to provide a breakdown of your research and development expense by program or product candidate and by type of internal expense. Additionally, expand your disclosure to separately discuss any material changes, from the prior period, between product candidate or program expenses and between internal expenses.

Business, page 119

22. Throughout this section, please revise the discussion of your completed, ongoing and planned clinical trials to clearly specify the primary and secondary endpoints, and how they were or will be measured.

Phase 1/2 clinical trial of MET-097i, page 143

23. We note the use of p-values on page 147. Please revise to briefly explain how "p-

value" is used to measure statistical significance and the relevance of statistical significance to the FDA's evidentiary standards for drug approval.

In vivo effectiveness of MET-097i and MET-233i, page 153

24. You state that a head-to-head repeat dose study of MET-097i and MET-233i versus CagriSema found statistically significant superiority from the combination versus CagriSema. Please revise to disclose p-values. Also, revise to qualify the following statement on page 155: "We plan to initiate a clinical trial of MET-097i in combination with MET-233i after sufficient evidence of clinical safety has been established in our MET-233i Phase 1 trial."

Licensing, Partnerships and Collaborations, page 165

25. Please revise your disclosure regarding the license agreements with D&D to identify the product candidate or platform to which the licensed materials and property relate.

26. We note your disclosure that you entered into an Amended and Restated Research and Collaboration Agreement with D&D and its wholly-owned subsidiary, Neuraly, Inc. in March 2025. Please confirm whether you have described all material terms of this agreement, and file this collaboration agreement in accordance with Item 601(b)(10) of Regulation S-K, or otherwise advise.

27. With respect to each agreement discussed in this section, please revise to disclose the following material terms:
    - Duration of agreement and royalty term. Where an agreement may remain in effect until the expiration of the last-to-expire royalty term, please revise to clarify when the patents underlying the royalty term are expected to expire.
    - Applicable royalty rates. In the event a range is provided in place of the actual royalty rate, such range should be specified within ten percentage points. In this regard, we note that certain references to "tiered mid-single digit to low double digit percentage royalties" should be revised so that the upper bound of such a range is more specific.
    - Aggregate amounts paid or received to date under agreements. For example, with respect to the Imperial License Agreement, we note your disclosure elsewhere in the prospectus that during the nine months ended September 30, 2024, you achieved an initial development milestone and paid $6.3 million toward such milestone and issued a note payable to related parties with a principal balance of $5.9 million.
    - Aggregate future potential milestone payments to be paid or received. In this regard, if material, please revise to disclose the amount of the annual license fee under the Imperial Agreement. Also, please update the amounts you may be obligated to pay Imperial at an exchange rate on the most recent practicable date.

Intellectual Property
Patent Rights, page 169

28. We note your disclosure that you own or license 41 issued patents. Please disclose the specific product candidates or product candidate groups to which these patents relate

and clarify, if true, that there are no issued patents covering the product candidates that you are currently developing.

Executive and Director Compensation, page 193

29. Please include the information required by Item 402 of Regulation S-K with your next amendment.

Consolidated Financial Statements of Metsera, Inc.
Consolidated Statements of Redeemable Convertible Preferred Stock and Stockholders' Deficit, page F-5

30. We note, during your fiscal year ended December 31, 2023, you issued 2,500,000 shares of common stock. Please expand your disclosure to explain to whom the stock was issued and why there is no dollar amount associated with the issuance.

General

31. Please supplementally provide us with copies of all written communications, as defined in Rule 405 under the Securities Act, that you, or anyone authorized to do so on your behalf, have presented or expect to present to potential investors in reliance on Section 5(d) of the Securities Act, whether or not they retain copies of the communications.

Please contact Tracie Mariner at 202-551-3744 or Lynn Dicker at 202-551-3616 if you have questions regarding comments on the financial statements and related matters. Please contact Lauren Sprague Hamill at 303-844-1008 or Chris Edwards at 202-551-6761 with any other questions.

Sincerely,

Division of Corporation Finance
Office of Life Sciences

cc: B. Shayne Kennedy