

Pieris Pharmaceuticals, Inc.
225 Franklin Street, 26th Floor
Boston, MA 02110

October 15, 2024

VIA EDGAR

United States Securities and Exchange Commission
Division of Corporation Finance
Office of Real Estate & Construction
100 F Street, NE
Washington, D.C. 20549

Attention: Gary Newberry
Vanessa Robertson
Lauren Hamill
Laura Crotty

**Re: Pieris Pharmaceuticals, Inc.
Amendment No. 1 to Registration Statement on Form S-4
Filed August 9, 2024
File No. 333-281459**

Ladies and Gentlemen:

This letter sets forth the response of Pieris Pharmaceutical's, Inc. (the "**Company**") to the comments of the staff of the Division of Corporate Finance (the "**Staff**") of the Securities and Exchange Commission (the "**Commission**") set forth in your letter dated October 8, 2024, with respect to the above referenced Amendment No. 1 to Registration Statement on Form S-4.

Concurrently with the submission of this letter, the Company is filing Amendment No. 2 to the Registration Statement on Form S-4 (the "**Second Amended Registration Statement**"). Capitalized terms used but not otherwise defined herein shall have the meanings ascribed thereto in the Second Amended Registration Statement.

Set forth below is the Company's response to the Staff's comments. For the Staff's convenience, we have incorporated your comments into this response letter in italics.

Prospectus Summary

The Companies

Palvella Therapeutics, Inc., page 11

1. *We note your response to prior comment 7, which we reissue with respect to the third and fourth bullets. Please revise both the Summary and Business sections to balance your disclosure with respect to Palvella's QTORIN platform by stating, if true, that clinical trials of QTORIN rapamycin targeting other indications (i.e., Gorlin Syndrome and pachyonychia congenita) failed to meet their respective primary endpoints, which may affect Palvella's ability to conduct clinical programs for other QTORIN-based product candidates and that the QTORIN platform may never result in the regulatory approval of any product candidate.*

Response: The Company acknowledges the Staff's comment with respect to the third bullet of prior comment 7 and respectfully advises that Palvella believes that there is no connection between its previous clinical trials of QTORIN rapamycin targeting other indications (i.e., Gorlin Syndrome and pachyonychia congenita) failing to meet their respective primary endpoints and Palvella's ability to conduct clinical programs for other QTORIN-based product candidates. Additionally, Palvella believes that such results do not create an increased likelihood or preclude regulatory approval of other QTORIN-based product candidates. Pachyonychia congenita ("PC"), Gorlin Syndrome ("GS") and microcystic lymphatic malformations ("microcystic LM") are unique diseases with unique genetic mutations that, in turn, have unique disease pathophysiologies. Palvella believes that its ability to conduct a Phase 3 clinical trial in microcystic LM, and its potential to receive regulatory approval, is independent of previous results in its other clinical trials. However, the Company is transparent about the results of these studies and believes these results reflect the risks that are inherent in clinical drug development, as discussed on page 65.

The Company acknowledges the Staff's comment with respect to the fourth bullet of prior comment 7 and has revised the disclosure on pages 11, 222 and 226 of the Amended Registration Statement.

2. *We note your response to prior comment 8, which we reissue in part. Please further revise both the Summary and Business sections to highlight your selection of "novel endpoints or other key clinical trial design features, such as choice of control" used or to be used in your ongoing and planned clinical trials of QTORIN rapamycin for various rare disease indications. In this regard, we note your disclosure on page 62 that such clinical trial features "could delay or prevent regulatory approval for Palvella's product candidates." Your revisions should:*

- *Explain what you mean by "baseline-controlled" study and how such a clinical trial differs from a placebo-controlled trial;*
- *Explain the clinical endpoints of your ongoing and planned clinical trials; and*
- *Explain the novelty and/or the subjective nature of your choice of control and selected endpoints.*

Response: The Company acknowledges the Staff's comment and has revised the disclosure on pages 12, 226, 234, 237, and 238 of the Second Amended Registration Statement.

Support Agreements, page 17

3. *We note your response to prior comment 12; however, we are unable to locate responsive disclosure in the registration statement. Therefore, we reissue the comment.*

Response: The Company acknowledges the Staff's comment and has revised the disclosure on pages 18 and 179 of the Second Amended Registration Statement.

Risk Factors

The articles of incorporation of the combined company will generally provide...., page 58

4. *We note your response to prior comment 15, which we reissue in part. Please revise your disclosure to expressly state whether the exclusive forum provision in the articles of incorporation of the combined company will apply to actions arising under the Securities Act or Exchange Act. If so, make conforming revisions in your related risk factor disclosures and disclose that risk to shareholders related to this provision may include increased costs to bring a claim. If not, please ensure that the exclusive forum provision in the governing documents states this clearly, or tell us how you will inform investors in future filings that the provision does not apply to any actions arising under the Securities Act or Exchange Act.*

Response: The Company acknowledges the Staff's comment and has revised the disclosure on pages 59, 112, and 314 of the Second Amended Registration Statement.

Certain Unaudited Financial Projections of Palvella, page 144

5. *We note your response to prior comments 21 and 24 and that the summary financial projections table covers a period through 2038. Please revise this section to include the information contained in your response letter indicating that Palvella's expected patent protections were tied to the length of the period projected in the table. As appropriate, clarify any material assumptions underlying this basis for the presentation period. Additionally, to the extent material, disclose the "high-level projections" that Palvella provided to Stifel for 2039 and 2040 for purposes of conducting the discounted cash flow analysis.*

Response: The Company acknowledges the Staff's comment and has revised the disclosure on page 148 of the Second Amended Registration Statement. Palvella Management believes projections for 2039 and 2040 are immaterial as they are substantially more uncertain than the Palvella Projections through 2038. As a result, such projections were not included.

6. *We note your response to prior comment 23, which we reissue in part. Please further revise your discussion of the material assumptions that underlie the financial projections table as follows:*

- *Please revise to explain how Palvella management arrived at the probability of regulatory approval for QTORIN rapamycin for each indication, as applicable.*
- *Clearly disclose any assumptions as to which indication(s) were assumed to have received approvals, the year(s) approval is received, and the regulatory jurisdiction(s). In this regard, we note that the bulleted list of assumptions now included on page 145 only appear to relate to QTORIN rapamycin for treatment of microcystic LM. If the probability of approval for the CVM indication was not assessed or was assessed to be 0 during the period presented, please expressly state as such, and explain the reason(s) why.*
- *With respect to line items such as total net sales, please specifically address the growth rates and clearly identify the material product revenue stream(s) underlying the projections.*
- *Revise to clarify what, if any, consideration the Pieris Board gave to the separate possibility that Palvella's product candidate may not successfully complete clinical trials in some or all indications.*
- *Additionally, discuss whether the projections factored in the possibility of FDA approval of new competitive products*

Response: The Company acknowledges the Staff's comment and has revised the disclosure on pages 146 and 147 of the Second Amended Registration Statement.

7. *We note your response to prior comment 24 and reissue the first bullet thereof. With regard to the length of the projections, please disclose the basis for projections beyond year five, including whether the forecasts reflect more than simple assumptions about growth rates, or whether, for example, the forecasts reflect straight line growth assumptions.*

Response: The Company acknowledges the Staff's comment and has revised the disclosure on page 148 of the Second Amended Registration Statement.

Pieris' Business
Strategic Partnerships, page 221

8. *We note your revisions in response to prior comment 28. With respect to the Pfizer Collaboration Agreements, please revise the description of the tiered royalties to disclose a royalty range within ten percentage points. Also, you disclose that the royalty term may terminate upon the last-to-expire patent on a country-by-country and product-by-product basis. Please revise to clarify when these patents are expected to expire.*

Response: The Company acknowledges the Staff's comment and has revised the disclosure on page 224 of the Second Amended Registration Statement.

Palvella's Business
QTORIN Rapamycin for the Treatment of Microcystic LM, page 228

9. *We note your response to prior comment 31, which we reissue with respect to the second and third bullets. Please revise to disclose the substance of any material FDA comments or guidance received related to Palvella's NDA or bridging strategy. In this regard, we note your disclosure on page 71 that the FDA recommends that bridging to support an NDA for the treatment of microcystic LM be done in a relative bioavailability study comparing the pharmacokinetics of a topical product applied under maximal use conditions and the approved oral drug. Notwithstanding any FDA recommendation(s), explain the rationale for Palvella's plans to bridge QTORIN rapamycin and the approved oral rapamycin product based on cross-study comparison between pharmacokinetic data from the prescribing information for the approved product rather than in a relative bioavailability study.*

Response: The Company acknowledges the Staff's comment and has revised the disclosure on pages 237 and 238 of the Second Amended Registration Statement.

10. *We note your response to prior comment 32, which we reissue in part.*

- *In light of your disclosure on page 67 that the design of a clinical trial can determine whether its results will support approval of a product, please further revise Palvella's Business section to summarize the substance of any material comments or guidance that the FDA provided with respect to each of the following Phase 3 clinical design features: proposed patient population, choice of control, dosing, and endpoint selection.*
- *Notwithstanding any FDA recommendation(s), explain Palvella's rationale for designing a baseline-controlled study rather than a placebo-controlled trial. Similarly, explain Palvella's rationale for employing a dynamic assessment that uses a comparative rating scale as the primary and key secondary endpoints.*
- *Consistent with the disclosure on page 68, discuss any surrounding uncertainty related to Palvella's use of these approaches, explain whether, and if so why, Palvella's Phase 3 trial design may be susceptible to objection, and what additional trials or testing could be required.*

Response: The Company acknowledges the Staff's comment and has revised the disclosure on pages 237 and 238 of the Second Amended Registration Statement.

Sincerely,

PIERIS PHARMACEUTICALS, INC.

/s/ Stephen Yoder

Name: Stephen Yoder

Title: Chief Executive Officer

Cc: William C. Hicks, Esq., Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
Marc D. Mantell, Esq., Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
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