October 8, 2024

Stephen Yoder
Chief Executive Officer
Pieris Pharmaceuticals, Inc.
225 Franklin Street, 26th Floor
Boston, MA 02110

Re: Pieris Pharmaceuticals, Inc.
Amendment No. 1 to Registration Statement on Form S-4
Filed September 23, 2024
File No. 333-281459

Dear Stephen Yoder:

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

Please respond to this letter by amending your registration statement and providing the requested information. 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 any amendment to your registration statement and the information you provide in response to this letter, we may have additional comments. Unless we note otherwise, any references to prior comments are to comments in our September 6, 2024 letter.

Amendment No. 1 to Registration Statement on Form S-4
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.

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.

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.

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.

Certain Unaudited 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.

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

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.

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.

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.

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.

Please contact Gary Newberry at 202-551-3761 or Vanessa Robertson at 202-551-
3649 if you have questions regarding comments on the financial statements and related
matters. Please contact Lauren Sprague Hamill at 303-844-1008 or Laura Crotty at 202-551-
7614 with any other questions.

Sincerely,

Division of

Corporation Finance

Office of Life

Sciences

cc: Joseph Walsh