

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

May 9, 2025

Scott Burrows Chief Financial Officer Spyre Therapeutics, Inc. 221 Crescent Street Building 23 Suite 105 Waltham, MA 02453

> Re: Spyre Therapeutics, Inc. Form 10-K for the fiscal year ended December 31, 2024 Filed February 27, 2025 File No. 001-37722

Dear Scott Burrows:

We have limited our review of your filing to the financial statements and related disclosures and have the following comment.

Please respond to this letter within ten business days by providing the requested information or advise us as soon as possible when you will respond. If you do not believe our comment applies to your facts and circumstances, please tell us why in your response.

After reviewing your response to this letter, we may have additional comments.

Form 10-K for the fiscal year ended December 31, 2024

Management's Discussion and Analysis of Financial Condition and Results of Operations, page 81

Results of Operations, page 88

- 1. We note the discussion of research and development (R&D) expenses, including external and internal components, on page 89. Please revise your disclosure in future filings to provide:
 - i) a breakout of external R&D expenses by program and functional area or indication, or state that such information cannot be tracked on those bases and the reason(s) therefore:
 - ii) a breakout of internal costs by function, type or category; and
 - iii) a discussion of the factor(s) impacting the changes in these disaggregated amounts for the periods presented.

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We note this information is particularly relevant to investors as your candidates are being evaluated to address multiple indications and given your expectation that you will invest "significant funds" into R&D in order to advance your product candidates through clinical trials (per pages 40 and 42). As part of your response, please provide what this disclosure would have looked like had it been included in your December 31, 2024 Form 10-K.

In closing, we remind you that the company and its management are responsible for the accuracy and adequacy of their disclosures, notwithstanding any review, comments, action or absence of action by the staff.

Please contact Jenn Do at 202-551-3743 or Kevin Vaughn at 202-551-3494 with any questions.

Sincerely,

Division of Corporation Finance Office of Life Sciences