

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

March 8, 2024

Cameron Turtle
Chief Executive Officer
Spyre Therapeutics, Inc.
221 Crescent Street
Building 23, Suite 105
Waltham, MA 02453

Re: Spyre Therapeutics, Inc.
Amendment No. 2 to Registration Statement on Form S-1
Filed March 1, 2024
File No. 333-276251

Dear Cameron Turtle:

We have reviewed your registration statement and have the following comment.

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.

Amendment No. 2 to Registration Statement on Form S-1 filed March 1, 2024

Management's Discussion and Analysis of Financial Condition and Results of Operations
Results of Operations

Comparison of the Years Ended December 31, 2023 and 2022, page 58

1. Please include an explanation for the increase in Other expense, net.

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.

Refer to Rules 460 and 461 regarding requests for acceleration. Please allow adequate time for us to review any amendment prior to the requested effective date of the registration statement.

Cameron Turtle Spyre Therapeutics, Inc. March 8, 2024 Page 2

Please contact Christine Torney at 202-551-3652 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 Jason Drory at 202-551-8342 with any other questions.

Sincerely,

Division of Corporation Finance Office of Life Sciences

cc: Branden Berns