

March 17, 2021

Ankit Mahadevia, M.D.
President and Chief Executive Officer
Spero Therapeutics, Inc.
675 Massachusetts Avenue, 14th Floor
Cambridge, Massachusetts 02139

Inc.

Statement on Form S-3

2021

Re: Spero Therapeutics,
Registration
Filed March 11,
File No. 333-254170

Dear Dr. Mahadevia:

This is to advise you that we have not reviewed and will not review your registration statement.

Please refer to Rules 460 and 461 regarding requests for acceleration. 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 Alan Campbell at 202-551-4224 with any questions.

Sincerely,

Division of Corporation Finance

Office of Life Sciences

cc:
Esq.

Matthew J. Gardella,