

Spero Therapeutics, Inc.
675 Massachusetts Avenue, 14th Floor
Cambridge, Massachusetts 02139

March 24, 2021

VIA EDGAR

United States Securities and Exchange Commission
Division of Corporation Finance
100 F Street, N.E.
Washington, D.C. 20549
Attention: Alan Campbell

RE: Spero Therapeutics, Inc.
Registration Statement on Form S-3 File No. 333-254170
Request for Acceleration of Effectiveness

Ladies and Gentlemen:

In accordance with Rule 461 promulgated under the Securities Act of 1933, as amended, Spero Therapeutics, Inc. (the "Company") hereby requests acceleration of the effective date of the Registration Statement on Form S-3 (File No. 333-254170) (the "Registration Statement"), so that it may become effective at 4:00 p.m., Washington, D.C. time on March 29, 2021 or as soon as possible thereafter.

The Company hereby authorizes Matthew J. Gardella, Esq. of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. to orally modify or withdraw this request for acceleration.

The Company respectfully requests that it be notified of such effectiveness by a telephone call to Mr. Gardella at (617) 348-1735 and that such effectiveness also be confirmed in writing. Any questions regarding this request may be addressed to Mr. Gardella.

Very truly yours,

SPERO THERAPEUTICS, INC.

/s/ Satyavrat Shukla

Satyavrat Shukla
Chief Financial Officer

cc: Spero Therapeutics, Inc.
Ankit Mahadevia, M.D., President and Chief Executive Officer
Tamara Joseph, Esq., Chief Legal Officer

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.

Matthew J. Gardella, Esq.
Matthew W. Tikonoff, Esq.
Lewis J. Geffen, Esq.