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December 10, 2024

VIA ELECTRONIC MAIL

Dr. Javier Szwarcberg
Spruce Biosciences, Inc.
2001 Junipero Serra Blvd. Suite 640
Daly City, CA 94014

Re: Covenant Not to Sue

Dear Dr. Szwarcberg:

We represent Neurocrine Biosciences, Inc. and write with respect to Spruce's two recent losses to Neurocrine at the Patent Trial and Appeal Board. As you know, in Final Written Decisions on U.S. Patent Nos. 10,849,908 and 11,007,201, the PTAB found all challenged claims invalid because they lacked an adequate written description. That decision was so decisive that the Board did not even reach the numerous other grounds for invalidity. As the PTAB concluded: "a person of ordinary skill in the art would not have recognized, either from the express disclosures of the ['908/'201] Specification or from the knowledge of the prior art, the 'structure, formula, chemical name, physical properties, or other properties, of species falling within the genus' of claimed CRF₁ receptor antagonists."

Other Spruce patents suffer from the same defects. For example, U.S. Patent Nos. 11,344,557 and 12,115,166 share the same specification and are likewise broadly directed to use of a genus of CRF₁ receptor antagonists. *See also, e.g.* U.S. Patent No. 11,304,950 (method of treatment using a genus of CRF₁ receptor antagonists even though only single patient, single compound data disclosed for TART). And Spruce is pursuing counterparts of these patents in jurisdictions around the world, each with similar infirmities.

Spruce is clearly targeting Neurocrine with a global portfolio of invalid patents and applications directed to Neurocrine innovations that predate Spruce's existence. Neurocrine will not condone such targeted interference with its business, and intends to vigorously defend its innovations and ensure its ability to bring the first new treatment to CAH patients in 70 years. Neurocrine has already incurred significant fees and costs invalidating the '908 and '201 Patents. And Neurocrine has just filed a Notice of Opposition to European Patent No. 3784233.

We ask that Spruce provide in writing, by December 18, 2024, a covenant not to sue Neurocrine (and its licensees) on any of its U.S. patents and their foreign counterparts (now and in the future) with claims directed to CRF₁ receptor antagonists, including crinecerfont. Such

SPRUCE – EXHIBIT 2003

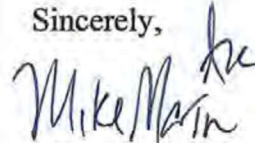
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patents include, but are not limited to those claiming priority to U.S. Provisional Application Nos. 62/545,406, 62/822,815, and 62/663951.

We also ask that, by December 18, 2024, Spruce commit in writing not to challenge the PTAB's recent decisions, at the PTO or Federal Circuit. Otherwise, Neurocrine will institute additional proceedings—in both courts and administrative agencies—to invalidate Spruce's defective patents in the US and abroad, and seek recovery of its fees and costs in doing so.

Sincerely,

A handwritten signature in blue ink that reads "Mike Morin". The signature is stylized, with a large "M" and a cursive "Morin".

Mike Morin
of LATHAM & WATKINS LLP

cc: Darin Lippoldt, Esq., Chief Legal Officer, Neurocrine Biosciences, Inc.
Michael Rosato, Esq., Partner, Wilson Sonsini Goodrich & Rosati