CLINICAL STUDY PROTOCOL AMENDMENT

A Randomized, Double-Blind, Vehicle-Controlled, Parallel Group Phase 2a Study to Determine Safety, Tolerability, Pharmacokinetics, and Pharmacodynamic Activity of NFX-179 Gel in Subjects with Cutaneous Neurofibromas

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<td>Protocol/Amendment Date</td>
<td>01-APR-2021</td>
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<td>Amendment No.</td>
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<td>Supersedes</td>
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INVESTIGATOR COMMITMENT:

I will provide copies of the protocol, any subsequent protocol amendments and access to all information provided by NFlection to the investigational center staff under my supervision. I will discuss this material with them to ensure that they are fully informed about the Investigational Medicinal Product and the study protocol.

I agree to conduct this clinical study according to the attached protocol, except when mutually agreed to with NFlection in writing. I also agree to conduct this study in compliance with all local regulatory requirements, Good Clinical Practices, as well as with the requirements of the appropriate Institutional Review Board(s)/Ethics Committee(s) and any other Institutional requirements.

Printed Name of Investigator

____________________________________

Signature of Investigator

____________________________________

Date
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1 AMENDMENT HISTORY
Revised protocol 1 footer date: 24-JUL-2020
Previous amendments: Amendment 2, footer date 25-MAR-2021

2 AMENDMENT SUMMARY
The following section of the NFX-179-NF1-201 revised protocol (footer date 24-JUL-2020) as modified by amendment 2 (footer date 25-MAR-2021) and with a final NFlection Therapeutics approval signature date of 27-JUL-2020 is amended:
- Section 8.3.3 Efficacy analyses.

3 AMENDMENT RATIONALE
This protocol change is made to allow for Target cNF Tumors that are found not to be qualifying neurofibromas to be excluded from sensitivity analyses of efficacy results.

4 PROTOCOL CHANGES
Section 8.3.3 Efficacy analyses:

Previous paragraph 1:
“…Tumor volume is the primary measurement of interest; however, the ruler measurements of tumor length and height will also be analyzed as described below.”

Changed paragraph 1:
“…Tumor volume is the primary measurement of interest; however, the ruler measurements of tumor length and height will also be analyzed as described below. Any Target cNF Tumors confirmed not to be qualifying neurofibromas based on histological evaluation of the excised tissue may be excluded from sensitivity analyses of efficacy results.”