AMENDED AND RESTATED
CLINICAL STUDY PROTOCOL RIDER
LCH-IV Study

This Clinical Study Protocol Rider ("Rider") is entered into as of the date of last signature (the "Effective Date") by and between **St. Jude Children's Research Hospital, Inc.**, operating in its capacity as the NACHO Operations Center ("St. Jude"), and **the NACHO Participating Site** signatory ("Consortium Member") pursuant to the existing Agreement (defined below) between them. Individually each is a "Party" and together are the "Parties."

WITNESSETH:

WHEREAS, the Parties desire for this Rider to constitute a complete amendment and restatement and fully supersede any Clinical Study Protocol Rider for the LCH-IV Study previously signed by St. Jude ("Prior LCH-IV Rider"); and

WHEREAS, institutions that are members of the North American Consortium for Histiocytosis ("NACHO") engage in research activities and services, including creation, implementation, and documentation of clinical research, testing, and trials through research study protocols approved by one or more Institutional Review Boards; and

WHEREAS, under the Consortium Agreement (NACHO) previously entered by and between St. Jude and Consortium Member (the "Agreement"), Consortium Member may choose to participate in a Study Protocol by executing a Rider for that Study; and

WHEREAS, the Study Protocol defined below will further the NACHO research objectives consistent with its mission; and

WHEREAS, the Consortium Member desires to participate in the Study Protocol under the terms and conditions of the Agreement; and

WHEREAS, NACHO shall permit the Consortium Member and the Site Investigator to participate in the Study Protocol, in exchange for the Consortium Member's execution of this Rider, and compliance with its terms and the terms of the Agreement; and

WHEREAS, Consortium Member will execute this Rider for Study Protocol entitled "**LCH-IV: International Collaborative Treatment Protocol for Children and Adolescents with Langerhans Cell Histiocytosis**" hereby incorporated by this reference as **Attachment A** (the "Study Protocol"); and

WHEREAS, Consortium Member has facilities, personnel, and support sufficient to perform and adhere to the Study Protocol, the terms of this Rider and the Agreement, and Good Clinical Practice Guidelines as set forth in Title 21 of the U.S. Code of Federal Regulations, or the Consortium Member country's national equivalent regulation; and

WHEREAS, St. Jude has facilities, personnel, and support to coordinate the Study Protocol with the Consortium Member.

NOW, THEREFORE, in consideration of the promises and covenants contained herein, the Parties agree as follows:

(1) Capitalized terms in this Rider shall have the same meaning as defined and used in the Agreement.

(2) This Rider constitutes a complete amendment and restatement and fully supersedes any Prior LCH-IV Rider. This Rider is governed by the terms and conditions set forth in the Agreement and the Study Protocol terms are binding upon St. Jude and Consortium Member in conduct of the Study Protocol.

(3) The Consortium Member shall participate in the Study Protocol with the attendant rights and obligations identified in the Agreement, Study Protocol, and this Rider.

(4) The Consortium Member represents that it has the expertise, time, and resources to conduct the Study Protocol, will conduct the Study Protocol in a timely manner and in accordance with this Rider, the Study Protocol, and NACHO's written instructions, and will collect and record Study Data accurately.

(5) In return for its performance of the Study in accordance with the Agreement, Study Protocol, and this Rider, Consortium Member shall be paid in accordance with the Study Budget attached and hereby incorporated as **Attachment B**.

(6) The Study Protocol is effective upon the Consortium Member's IRB approval. Consortium Member may not modify the Study Protocol, but may propose changes to NACHO and request exceptions to the Study Protocol, which must be approved in writing by NACHO before becoming effective.

(7) This Rider shall be effective as of the Effective Date and shall continue until the completion of the Study under the Protocol and closure of the Study database and completion of Consortium Member's obligations under the Agreement, or until earlier termination as provided in Section 2 Term and Termination of the Agreement.

(8) During the term of the Rider and for a period of two (2) years thereafter, NACHO shall promptly report to Site Investigator information that could directly affect the health or safety of Study Subjects or influence the Study Protocol, Study results, and information in site monitoring reports and data safety monitoring committee reports. The Site Investigator and Consortium Member shall be responsible for communicating the findings to Study Subjects and the Consortium Member IRB, as appropriate.

(9) Consortium Member shall conduct the Study in conformance with generally accepted standards of Good Clinical Practice Guidelines as set forth in Title 21 of the U.S. Code

of Federal Regulations and in accordance with applicable Federal, state, and local laws and regulations, or the Consortium Member country's national equivalent regulation.

(10) Consortium Member represents that:

(a) By signing this Rider that, to the best of its knowledge, (i) neither the Consortium Member nor any individuals who will perform any of the work described in the Agreement on behalf of Consortium Member are presently debarred, suspended, or declared ineligible by any Federal Agency or have voluntarily excluded themselves from participation in covered transactions, pursuant to Title 45, CFR, part 76, and (ii) no such individuals shall perform any work described in the Agreement; and

(b) It has a system for discovering these actions in the United States; and

(c) It will notify NACHO and St. Jude promptly of an actual disqualification, debarment, suspension, or other ban of the Consortium Member or any individuals who will perform any of the work described in the Rider on behalf of Consortium Member that comes to its attention during the course of the Study and for two (2) years thereafter (if in the case of a new drug application for five (5) years thereafter); and

(d) It and Site Investigator have no conflict of interest that would affect the conduct of the Study Protocol; and it shall notify NACHO and St. Jude promptly if it discovers a conflict of interest during the term of this Agreement; and

(e) It and Site Investigator will not enter into a financial security transaction based on Study Data or Study results.

[REMAINDER OF PAGE LEFT INTENTIONALLY BLANK]

IN WITNESS WHEREOF, the Parties have caused this Amended and Restated Rider for LCH-IV Study to be executed and delivered by their authorized representatives.

ST. JUDE CHILDREN'S RESEARCH HOSPITAL, INC./NACHO

By: _____ **Date:** 28 JUNE 2019
Name: Terrence Geiger, MD, PhD
Title: SVP & Deputy Director for Academic & Biomedical Operations

NACHO PARTICIPATING SITE

By: _____ **Date:** _____
Name: _____
Title: _____
Institution Name: _____
Address: _____
Phone: _____
Email: _____

Read and Understood by SITE INVESTIGATOR

By: _____ **Date:** _____
Name: _____
Title: _____

ATTACHMENT A

Study Protocol

The current version (as of the Effective Date of this Rider) for the Study Protocol entitled: **"LCH-IV: International Collaborative Treatment Protocol for Children and Adolescents with Langerhans Cell Histiocytosis"** is hereby incorporated as if attached hereto, and Site acknowledges and agrees that this exhibit shall automatically be updated to include updated versions of the Study Protocol as it is amended from time to time.

NOTE TO SITE PERSONNEL: When submitting to IRB and performing other Study activities, **please be sure to use the latest version of the Study Protocol**. Updated/amended versions are typically available from on the LCH-IV webpage of the NACHO website (https://www.nacho-consortium.org/). Please contact the LCH-IV National Coordinating Center at LCH-IVSupport@stjude.org for any questions.

ATTACHMENT B

Budget

Enrollment & Payment Schedule

Participants are to be enrolled in accordance with the Inclusion and Exclusion Criteria as listed in the Protocol. Payment will be made only for eligible, qualified participants.

Funds in the amount of $1,000 per case will be provided to Consortium Member as reimbursement for eligible participants enrolled on Stratum I of the LCH-IV: International Collaborative Treatment Protocol for Children and Adolescents with Langerhans Cell Histiocytosis.

Funds are subject to availability for participants enrolled trial wide on Stratum I only.

- 50% of the payment will be initiated at the time of receipt of data for participant enrollment.
- 25% of the payment will be made at the time of receipt of data for Week 24 response evaluation.
- 25% of the payment will be made at the time of receipt of data for Week 52 response evaluation.

No other funding is associated with or available for opening the Study or enrolling participants on Strata other than Stratum I of the Study.

Payment Instructions:

No invoices are required to be remitted for this Study. NACHO will initiate payments to Consortium Member in accordance with this Attachment B. All checks should reference the Site Investigator's name for reference purposes.

For sites receiving payment by USD check:

PAYEE INFORMATION	
Payable To	
Payee Mailing Address	
Email Address	
Attention	
Tax ID#	

For sites receiving payment by USD ACH Payment:

Payee Information	
Beneficiary Name //PLEASE INSERT THE NAME ON THE ACCOUNT//	
Payee Mailing Address	
Email Address //FOR QUESTIONS AND NOTIFICATION OF PAYMENT//	
Attention //FOR QUESTIONS AND NOTIFICATION OF PAYMENT//	
Bank Name	
Bank ACH Routing No:	
Bank ACH Account No:	
Tax ID#	