AMENDMENT FOR DISTRIBUTION 10.0 - INDUCED PLURIPOTENT STEM CELLS (iPSC)
NIMH HUMAN GENETICS INITIATIVE DISTRIBUTION AGREEMENT

NOW, THEREFORE, it is mutually agreed that the National Institute of Mental Health (NIMH) Human Genetics Initiative Distribution Agreement signed by NIMH, the center for Genetic Studies, and _____ as the Receiving Institution is amended to include the following text in paragraph 14 under the section, Acknowledgement for Induced Pluripotent Stem Cells (iPSC) Sample Biomaterials and Clinical Data:

Biomaterials and phenotypic data were obtained from the following projects that participated in the NIMH Induced Pluripotent Stem Cells (iPSC) Genetics Initiative:

NIMH Study 92 -- Data and biomaterials in Study 92 were collected as part of a longitudinal study of epigenetics of schizophrenia, supported by National Institutes of Mental Health (NIMH) grants RC2MH089859 and RC2MH089973 to Vishwajit L. Nimgaonkar, M.D., Ph.D., University of Pittsburgh and Raquel Gur, M.D., Ph.D., University of Pennsylvania, respectively. This project was part of a network of three NIMH-supported Consortia: The 8-site Consortium on the Genetics of Schizophrenia (COGS); the 3-site Multiplex-Multigenerational Investigation (MGI); and the 8-site Project among African-Americans to Explore Risks for Schizophrenia (PAARTNERS). The consortium was complemented by investigators from Johns Hopkins University (PI: A. Feinberg, M.D., Ph.D.), Rutgers University (D. Fugman, Ph.D.), and the Southwest Foundation for Biomedical Research (PI: L. Almasy, Ph.D.). The study coordinators were Sue Clifton (University of Pittsburgh) and Amy Cassidy (University of Pennsylvania). The data managers were Joel Wood (University of Pittsburgh) and Kosha Ruparel (University of Pennsylvania).

NIMH Study 115 – Data and biomaterials collection were supported by the National Institutes of Health. The Principal Investigator of NIH grant DP1MH099904 was Dr. Ricardo Dolmetsch and the Co-Investigator was Dr. Joachim Hallmayer. The Principal Investigators of NIH grant R33MH087898 were Dr. Joachim Hallmayer and Dr. Ricardo Dolmetsch. Additionally, Dr. Hallmayer received supplementary funding for NIH grant R33M087898 to obtain biomaterials, diagnostic assessments and other data from subjects with Phelan McDermid Syndrome Foundation and their families. Dr. Hallmayer supervised the diagnostic data collection on all projects. The collection of data and biomaterials would not have been possible without the generous help of the Phelan McDermid Syndrome Foundation. Staff of the foundation offered invaluable assistance, support and guidance. Deepest gratitude is also due to the families and individuals with Phelan McDermid Syndrome who were our partners in this research.

NIMH Study 116 – The collection of data and biomaterials comes from two studies funded by the NIMH. The first project, *Biological Correlates of Altered Brain Growth in Autism*, was supported from 2009 to 2012 by the NIMH grant R01MH089176. Co-prinicipal investigators were Flora Vaccarino, M.D., Sherman Weissman, M.D., Mark Gerstein, Ph.D., and Elena Grigorenko, Ph.D., of Yale University. The second study, *Cellular and Genetic Correlates of Increased Head Size in Autism Spectrum Disorder*, is funded since 2009 by the NIMH grant R21/R33MH087879. Principal Investigator is Flora Vaccarino, M.D., Co-Investigators are Katarzyna Chawarska, Ph.D., and Anita Huttner, M.D.

NIMH Study 117 – We have generated induced pluripotent stem cell (iPSC) lines from patients with Fragile X Syndrome in order to study the neural development aspects of autism. Fragile X fibroblasts were obtained from Dr. Philip Schwartz who has recently launched an NIH-sponsored program to generate fibroblast and iPSC lines from patients with autism spectrum disorder as a resource for the research community.

The collection of data and biomaterials for NIMH Study 117 was supported by the National Institutes of Health grant number R33MH087925 entitled "Autism iPSCs for Studying Function and Dysfunction in Human Neural Development" to Jeanne F. Loring, Ph.D. (The Scripps Research Institute). Biospecimen collection was coordinated by Philip Schwartz, Ph.D. (Children's Hospital of Orange County) and Randi Hagerman, M.D. (University of California – Davis). Subjects enrolled in the study were diagnosed using the Autism Diagnostic Interview-Revised (ADI-R) and the Autism Diagnostic Observation Schedule (ADOS). The induced pluripotent stem cells were generated in Jeanne Loring's laboratory by Michael Boland, Ph.D. (RSRI).

NIMH Study 125 – Data and biomaterials generated in Study 125/Site 393 were funded by an NIMH grant to Dr. Herb Lachman (MH087840: Analysis of Glutamatergic Neurons Derived from Patient-Specific iPS Cells). The co-investigators on this grant included Dr. Deyou Zheng and Dr. Reed Carroll, both from the Albert Einstein College of Medicine. Patients and controls were recruited at the Albert Einstein College of Medicine and at the Child Psychiatry Branch, NIMH, directed by Dr. Judith L. Rapoport. We want to thank participating families and Dr. Robert J. Shprintzen, Ph.D., President and Chairman of the board of The Virtual Center for Velo-Cardio-Facial-Syndrome, Inc., for patient referrals at the Einstein site.

NIMH Study 127 – Data and biomaterials generated in Study 127/Site 717 were funded by a grant to Dr. Chang-Gyu Hahn (Target Identification and Validation for Negative Symptoms and Social Cognition in Schizophrenia: A Translational Study: funded by Pfizer via University of Pennsylvania – Pfizer collaborative alliance). The co-investigators and collaborators on this grant included Edward Brodkin, M.D. (Co-PI), Karin Borgmann-Winter, M.D. (Collaborator), Bruce Turetsky, M.D. (Collaborator) and Paul Moberg, Ph.D. (Collaborator), all from the University of Pennsylvania. Patients and controls were recruited at the University of Pennsylvania directed by Dr. Raquel Gur. We want to thank participating families and all clinical research staff contributing to this study.

NIMH Study 130 – Data and biomaterials were collected as part of an in vivo and in vitro study of simvastatin as a modulator of Wnt/GSK3 signaling, supported by National Institutes of Health grant R21MH093958. This study is based at Massachusetts General Hospital. The Principal Investigators were Roy H. Perlis, M.D., MSc and Stephen J. Haggarty, Ph.D.

NIMH Study 131 – Investigators using these cells should cite "Yoshimizu T, Pan JQ, Mungenast AE, Madison JM, Su S, Ketterman J, Ongur D, McPhie D, Cohen B, Perlis R, Tsai LH. Functional implications of a psychiatric risk variant within *CACNA1C* in induced human neurons. *Mol Psychiatry* 2015 Feb; 20(2):162-169. PMID: 25403839; PMCID: PMC4394050" and acknowledge NIMH R01MH091115 and P50MH106933. The principal investigators were Li-Huei Tsai, Ph.D., Bruce Cohen, M.D., and Roy Perlis, M.D., MSc.

NIMH Study 132 – The clinical data and collection of biomaterials for the genetics of childhood-onset schizophrenia has been funded through the intramural program at the National Institute of Mental Health, NIH. The Child Psychiatry Branch/NIMH in Bethesda, Maryland recruited all patients and controls. Principal Investigator is Dr. Judith L. Rapoport. The entire team at the Child Psychiatry Branch extends our gratitude to our patients and their families for making our research possible.

NIMH Study 143 – This work was supported by grants from the California Institute for Regenerative Medicine (CIRM) TR4-06747, the National Institutes of Health through the NIH

Director's New Innovator Award program (1-DP2-OD006495-01), an R21 MH093954 from NIMH; and a NARSAD Independent Investigator award. The prinicipal investigators are Drs. Alysson R. Muotri and Vias Duvvuri at UCSD.

NIMH Study 144 – This work was supported by grants from the California Institute for Regenerative Medicine (CIRM) TR2-01814 and TR4-06747, the National Institutes of Health through the NIH Director's New Innovator Award program (1-DP2-OD006495-01), an R01 MH100175-01 from NIMH and from the International Rett Syndrome Foundation (IRSF grant # 2915); a NARSAD Independent Investigator Grant, an NIMH Autism Center of Excellence Program Project; the work was supported by the Helmsley Trust, the JPB Foundation, the Engmann Foundation, a grant from the CDMRP Autism Research Program; a KL2 CTRI (KL2TR00099) and a Postdoctoral Translational Fellowship from Autism Speaks. The principal investigators are Drs. Alysson R. Muotri (UCSD); Eric Courchesne (UCSD); Alan Percy (University of Birmingham); Fred H. Gage (Salk); Daniel Geschwind (UCLA) and Anthony Wynshaw-Boris (Case Western Reserve University).

NIMH Study 158 – Data and biomaterials were collected as part of a proof-of-concept study that schizophrenia could be modeled in vitro using human induced pluripotent stem cells. This study was based at the Salk Institute for Biological Studies and later at Icahn School of Medicine at Mount Sinai. The Principal Investigators were Fred H. Gage, PhD and Kristen J. Brennand, Ph.D. Co-investigators included Anthony Simone, Jessica Jou, Chelsea Gelboin-Burkhart, Ngoc Tran N, Sarah Sangar, Yan Li, Yangling Mu, Gong Chen and Diana Yu (Salk Institute for Biological Studies). Study collaborators included Shane McCarthy and Jonathan Sebat. The early characterization of these hiPSCs occurred in the Gage Laboratory, and was partially funded by CIRM Grant RL1-00649-1, The Lookout and Mathers Foundation, the Helmsley Foundation as well as Sanofi-Aventis. Subsequent studies occurred in the Brennand Laboratory, and were supported by the Brain and Behavior Research Foundation and the New York Stem Cell Foundation. The investigators are very grateful to the patients who participated in this study.

NIMH Study 160 -- Data and biomaterials were collected as part of a study examining how common and rare variants of patients diagnosed with Childhood onset schizophrenia affect neuronal functional of human induced pluripotent stem cell derived neural cells. This study is based at the Icahn School of Medicine at Mount Sinai (ISMMS). The Principal Investigators are Kristen J. Brennand, Ph.D. and Brigham J. Hartley, Ph.D. Co-investigators included Seok Man Ho, Erin Flaherty, Aaron Topol, Nadine Schrode, Ph.D., Julia TCW, Ph.D. and Ifeanyi Obiorah, Ph.D. Study collaborators included Judith Rapoport, M.D. and Pamela Sklar, M.D., Ph.D. Initial and ongoing characterizations of the hiPCSs and subsequent derived neural cells is being performed in the Brennand Laboratory and is partially funded by the Brain and Behavior Research Foundation, NIH grants R01 MH101454 and R01 MH106056, and the New York Stem Cell Foundation.

Human induced pluripotent stem cells were generated and validated in efforts led by Kristen Brennand, Ph.D (ISMMS) from patients recruited as part of a longitudinal study of childhood-onset-schizophrenia directed by Judith Rapoport, M.D. (NIH) (Topol A, et al., *Cell Reports*, 2016). The investigators are very grateful to the patients who participated in this study.

NIMH Study 163 -- Study participants were consented and enrolled, data and biomaterials were collected, and cell lines were generated at Massachusetts General Hospital as part of an NIMH/NHGRI Center of Excellence in Genomic Science grant (P50MH106933). The Neurobank

PI is Roy Perlis, M.D., MSc; key MGH co-investigators included Hannah Brown, M.D., J. Niels Rosenquist, M.D., Ph.D., Steven Sheridan, Ph.D., and Jennifer Wang, Ph.D. The CEGS co-PIs are Isaac Kohane, M.D., Ph.D. and Roy H. Perlis, M.D., MSc.

NIMH Study 165 -- The work to develop the iPS cells developed in this project was supported by the National Alliance for Research on Schizophrenia and Depression, NIH (5T32MH15330, 5R33MH087874, and 5R21MH086703), Stanley Medical Research Institute, Maryland Stem Cell Research Fund, the International Mental Health Research Organization, and the American Medicial Research Foundation.

The investigators involved were C-H Chiang, Y Su, Z Wen, N Yoritomo, CA Ross, RL Margolis, H Song, G-I Ming, NA Sachs, A Sawa, SE Holmes, and LE DeLisi. At the time of the investigation, all authors were affiliated with the Johns Hopkins University School of Medicine, with the exception of LE DeLisi who was then at New York University.

The DISC1 family was originally ascertained by LE DeLisi. Identification of the mutation, reexaminiation of the family, and skin biopsies were performed by N Sachs, A Sawa, SE Holmes, N Yoritomo, CA Ross, and RL Margolis. Stem cell generation and characterization was performed by C-H Chiang, Y Su, Z Wen, H Song, and G-I Ming.

We would also like to thank the families who have participated in and contributed to these studies.

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DATED SIGNATURES

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Signature and **Date**, Principal Investigator

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Signature and **Date**, Receiving Institution's Authorized Representative

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Signature and **Date**, NIMH Center for Genetic Studies' Authorized Representative
Washington University in St. Louis

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Signature and **Date**, NIMH Center for Genetic Studies' Authorized Representative
Rutgers University

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Signature and **Date**, NIMH's Authorized Representative