April 24, 2019

Secretary Alex Azar II
U.S. Department of Health and Human Services
200 Independence Avenue S.W.
Sixth Floor
Washington, D.C. 20201

Dear Secretary Azar,

We write as scientific, industry, and bioethics leaders who are committed to translating the promise of gene editing into medicines to help patients in need, to express our views strongly condemning the recent reports of the birth of CRISPR-edited infants in China and to urge you to take action.

While we are still waiting for all of the facts to be independently verified, we find the recent reported actions of Dr. Jiankui He[1] to be deeply troubling. These reports indicate that Dr. He used CRISPR-Cas9 gene editing in human embryos to alter the *CCR5* gene with the reported intention of inducing HIV resistance and that two edited embryos were implanted and resulted in the birth of twin infant girls. In addition, it has been reported by He and confirmed by the Chinese government that a second edited pregnancy is ongoing.[2] The alterations induced by Dr. He in these two girls would be expected to have been introduced into human germline cells, which would make the changes heritable and therefore passed on to future generations. Dr. He proceeded without clear medical need, in a surreptitious manner lacking any meaningful public or scientific community discussion or consensus, and without any regulatory approval.

From our perspective, performing human germline clinical experimentation of this kind is currently irresponsible, and we condemn it in the strongest possible terms. Although we recognize the great scientific advancement represented by gene editing technologies[3] and their potential value for an improved understanding and possible treatment of human disease, we strongly believe the editing of human embryos that results in births carries serious problems for which there are no scientific, ethical, or societal consensuses. As a result, we contend that such human genetic manipulation should be considered unacceptable and support a binding global moratorium until serious scientific, societal, and ethical concerns are fully addressed.

From a scientific perspective, we believe that too many important scientific questions remain unanswered for human embryo editing to be a safe and acceptable therapeutic application of the technology at this time. These issues, which must be addressed before proceeding, include

[1]Associated Press. (2018, November 26). Chinese researcher claims first gene-edited babies. *AP News*. Retrieved from https://www.apnews.com/4997bb7aa36c45449b488e19ac83e86d.

[2]Associated Press. (2019, January 21). China says doctor behind gene-edited babies acted on his own. *AP News.* Retrieved from https://apnews.com/19c395ef2d3148b1a8ae0ab8be5375b0.

[3]Maeder, M. L., & Gersbach, C. A. (2016). Genome-editing technologies for gene and cell therapy. *Molecular Therapy, 24*(3), 430-446.

but are not limited to: optimizing the efficiency and precision of on-target modification, defining and minimizing off-target mutations, preventing on- and off-target mutation mosaicism, and understanding how novel on- and off-target mutations might interact with existing human genetic diversity when these new alterations are passed on to future generations. In addition, in our opinion, human embryo experiments of the type performed by Dr. He pose major ethical concerns, because research subjects would include not only embryos and children, but also future generations of descendants.

Finally, we consider it essential to develop effective social and policy mechanisms for carrying out broad and deep discussions of human clinical germline alteration to better understand and balance the individual, familial, societal, and species-level rights, needs, interests, and values affected by this rapidly advancing science. Clinical germline gene editing is appropriately prohibited in the United States, across much of Europe, in China, and in many other countries around the globe. Before this status quo is revisited, it is vital that extensive discussions and engagement take place among all major stakeholders, including members of the scientific, medical, patient, caregiver, policy, legal, ethical, and faith communities. These stakeholders need to determine together whether, and under which conditions, clinical germline gene editing should take place in the years ahead; however, to date, there have not been enough efforts to meaningfully engage each of these different groups on the subject of human clinical germline editing. To allow for a process of genuine public engagement with diverse stakeholders to take place, we strongly support practical and actionable steps to enable the development of a binding global moratorium limiting clinical testing of germline gene editing in humans, as well as effective and easily accessible mechanisms for reporting potential violations. We consequently urge the Administration to convene these diverse stakeholders as the next step in this critical process of engagement and national dialogue on these complex issues.

Potential of gene editing in somatic cells

We wish to note that, in contrast to embryo editing that results in births, we believe applying gene editing methods to somatic cells has the potential to make tremendous contributions to the study, understanding, and treatment of human disease. In somatic cells, certain types of gene editing will likely have important scientific and medical applications, including their use to treat patients living with genetic disorders such as sickle cell anemia, beta-thalassemia, blindness, muscular dystrophies, and hemophilia, as well as cancer and many other diseases. Although clinical trials will be required to demonstrate the efficacies of these approaches, we believe that current scientific methodology is sufficient to define and correct the inevitable issues related to safety and efficacy needed to move forward in the clinic. We also have confidence that international regulatory bodies, building on their decades of work overseeing gene therapy clinical trials as well as early trials of gene editing using zinc finger nucleases, are well positioned to oversee future trials of therapeutic somatic cell gene editing. We consider it unlikely that somatic cell gene editing will give rise to new or unique ethical concerns substantially different from those associated with other forms of research and therapeutics that have already been well discussed.

Summary and Closing Thoughts

Somatic cell gene editing technologies represent transformative scientific advancements that have potential to improve our understanding and treatment of human diseases. We strongly believe, however, that the editing of human embryos that results in births carries serious ethical problems for which there are no scientific, ethical, or societal consensuses. Therefore, we contend that such genetic manipulation in human embryos that results in births should be considered unacceptable and support a binding global moratorium unless and until diverse stakeholders have the opportunity to broadly and deeply discuss and reach a societal consensus on these challenges.

Lastly, we place significant value on transparency and true engagement around gene editing. As such, we stand ready to help policy leaders work through any topics related to the field. Should you have any questions, concerns, or insights you would like to discuss or share with us, please contact David Barrett, Executive Director of the American Society of Gene & Cell Therapy, at dbarrett@asgct.org, phone 414-278-1341. We would be delighted to pull together members of this group to speak with you further.

Thank you for your time and attention on this important topic.

Sincerely,

Burt Adelman, M.D.
Special Advisor
Novo Ventures

Charlie Albright, Ph.D.
Chief Scientific Officer
Editas Medicine

Lori Andrews, J.D.
Distinguished Professor of Law
Chicago-Kent College of Law, Illinois Institute of Technology

George Annas, J.D., M.P.H.
William Fairfield Warren Distinguished Professor
Director of the Center for Health Law, Ethics & Human Rights
Boston University School of Public Health, School of Medicine, and School of Law

Paul S. Appelbaum, M.D.
Dollard Professor of Psychiatry, Medicine, & Law
Director, Center for Research on Ethical, Legal & Social Implications of Psychiatric, Neurologic & Behavioral Genetics
Columbia University College of Physicians & Surgeons

Usman Azam, M.D.
President and Chief Executive Officer
Tmunity Therapeutics, Inc.

David Barrett, J.D.
Executive Director
American Society of Gene & Cell Therapy

Jean Bennett, M.D., Ph.D.
F.M. Kirby Professor of Ophthalmology
Perelman School of Medicine at the University of Pennsylvania

James W. Burns, Ph.D.
President and Chief Executive Officer
Casebia Therapeutics

Daniel Callahan, Ph.D.
President Emeritus
The Hastings Center

Michele Calos, Ph.D.
Professor, Department of Genetics
Stanford University School of Medicine
President
American Society of Gene and Cell Therapy

Paula M Cannon, Ph.D.
Distinguished Professor
University of Southern California
Treasurer
American Society of Gene and Cell Therapy

Alexander M. Capron
University Professor
Scott H. Bice Chair in Healthcare Law, Policy and Ethics
Co-Director, Pacific Center for Health Policy and Ethics
University of Southern California

Toni Cathomen, Ph.D.
Professor of Cell and Gene Therapy
Director, Institute for Transfusion Medicine and Gene Therapy
Medical Center - University of Freiburg

André Choulika, Ph.D.
Chairman and Chief Executive Officer
Cellectis Group

Marinee Chuah, Ph.D.
Professor - Deputy Director, Department of Gene Therapy & Regenerative Medicine
Vrije Universiteit Brussel

Giuseppe Ciaramella, Ph.D.
Chief Scientific Officer
Beam Therapeutics

Cindy Collins
Interim Chief Executive Officer
Editas Medicine

Kenneth Cornetta, M.D.
Director, National Gene Vector Biorepository
Clinical Professor of Medical and Molecular Genetics
Indiana University School of Medicine

Beverly L. Davidson, Ph.D.
Professor, Pathology and Laboratory Medicine
Perelman School of Medicine at the University of Pennsylvania
Director, Raymond G. Perelman Center for Cellular and Molecular Medicine
Children's Hospital of Philadelphia

Philippe Duchateau, Ph.D.
Chief Scientific Officer
Cellectis Group

John Evans
Chief Executive Officer
Beam Therapeutics

Terence R. Flotte, M.D.
Provost and Dean
University of Massachusetts Medical School

Theodore Friedmann, M.D., M.A.
Professor of Pediatrics, School of Medicine
University of California, San Diego

Guangping Gao, Ph.D.
Professor, Microbiology & Physiological Systems
Penelope Booth Rockwell Professor in Biomedical Research
Co-Director, Li Weibo Institute for Rare Diseases Research
Horae Gene Therapy Center and Vector Core Scientific Director, UMMS-China Program Office
University of Massachusetts Medical School
President-Elect
American Society of Gene and Cell Therapy

Charles Gersbach, Ph.D.
Associate Professor
Duke University

Michael A. Grodin, M.D.
Professor, Center for Health Law, Ethics & Human Rights
Boston University School of Public Health

Rachel Haurwitz, Ph.D.
President and Chief Executive Officer
Caribou Biosciences, Inc.

Helen Heslop, M.D., D.Sc. (Hon.)
Dan L. Duncan Chair
Director, Center for Cell and Gene Therapy
Baylor College of Medicine, Houston Methodist Hospital, and Texas Children's Hospital

Tim Hunt, J.D.
Senior Vice President of Corporate Affairs
Editas Medicine
Chair, Government Relations Committee
American Society of Gene & Cell Therapy

Rosario Isasi, J.D., M.P.H.
Assistant Professor (Research)
The Dr. John T. Macdonald Foundation Department of Human Genetics
University of Miami Leonard M. Miller School of Medicine

Sheila Jasanoff, J.D., Ph.D.
Pforzheimer Professor of Science and Technology Studies
Director, Program on Science, Technology and Society
Harvard Kennedy School

J. Keith Joung, M.D., Ph.D.
Pathologist and Professor of Pathology
Massachusetts General Hospital and Harvard Medical School
Member, Board of Directors
American Society of Gene and Cell Therapy

Sekar Kathiresan, M.D.
Director, Center for Genomic Medicine
Massachusetts General Hospital

Mark A. Kay, M.D., Ph.D.
Dennis Farrey Family Professor
Departments of Pediatrics and Genetics
Associate Chair for Basic Research (Pediatrics)
Stanford University

Patricia A. King, J.D.
Professor of Law Emeritus
Georgetown University

David R. Liu, Ph.D.
Vice-Chair of the Faculty
Broad Institute of MIT and Harvard
Investigator
Howard Hughes Medical Institute
Professor of Chemistry and Chemical Biology
Harvard University

Ruth Macklin, Ph.D.
Distinguished University Professor Emerita
Albert Einstein College of Medicine

Maritza McIntyre, Ph.D.
Independent Consultant
Advanced Therapies Partners, LLC
Chair, Clinical Trials and Regulatory Affairs Committee
American Society of Gene and Cell Therapy

R. Scott McIvor, Ph.D.
Professor of Genetics, Cell Biology and Development
Center for Genome Engineering
University of Minnesota

Richard Morgan, Ph.D.
Senior Vice President of Immunogenetics
Editas Medicine
Member, Board of Directors
American Society of Gene and Cell Therapy

Kiran Musunuru, M.D., Ph.D., M.P.H.
Associate Professor of Cardiovascular Medicine and Genetics
Perelman School of Medicine at the University of Pennsylvania

Vic Myer, Ph.D.
Chief Technology Officer
Editas Medicine

Luigi Naldini, M.D., Ph.D
Director, SR-Tiget, San Raffaele Telethon Institute for Gene Therapy
Professor of Tissue Biology and Gene and Cell Therapy
Vita-Salute San Raffaele University Medical School
Chair, Genome Editing Committee
American Society of Gene and Cell Therapy

Eric N. Olson, Ph.D.
Professor and Chair of Molecular Biology
Director of the Hamon Center for Regenerative Science and Medicine
University of Texas Southwestern Medical Center

Anthony Philippakis, M.D., Ph.D.
Venture Partner
GV

Laurent Poirot, Ph.D.
Vice President, Immunology Division
Cellectis Group

Stephen J. Russell, M.D., Ph.D.
Richard O. Jacobson Professor of Molecular Medicine
Mayo Clinic College of Medicine
Vice President
American Society of Gene and Cell Therapy

Michel Sadelain, M.D., Ph.D.
Director, Center for Cell Engineering
Memorial Sloan Kettering Cancer Center
Weill-Cornell Medical College

David Schaffer, Ph.D.
Hubbard Howe Jr. Distinguished Professor
Chemical and Biomolecular Engineering, Bioengineering, Molecular and Cell Biology, and the Helen Wills Neuroscience Institute
Director, Berkeley Stem Cell Center
University of California, Berkeley

David J. Segal, Ph.D.
Professor, Genome Center, Biochemistry and Molecular Medicine, Pharmacology, and MIND Institute
University of California, Davis

Albert Seymour, Ph.D.
Chief Scientific Officer
Homology Medicines, Inc.

Erik J. Sontheimer, Ph.D.
Professor and Vice Chair
RNA Therapeutics Institute
University of Massachusetts Medical School

Barry Ticho, M.D., Ph.D.
Chief Medical Officer
Stoke Therapeutics

Bruce E. Torbett, Ph.D., M.S.P.H.
Co-Director of the HIVE Center
Co-Director of the San Diego Center for AIDS Research
Associate Professor, Scripps Research
Chair, Ethics Committee
American Society of Gene and Cell Therapy

Jacques P. Tremblay, Ph.D.
Professor
Department of Molecular Medicine
Laval University

Arthur Tzianabos, Ph.D.
President and Chief Executive Officer
Homology Medicines, Inc.

Fyodor D. Urnov, Ph.D.
Deputy Director
Altius Institute for Biomedical Sciences

Thierry VandenDriessche, Ph.D.
Professor
Director, Department of Gene Therapy and Regenerative Medicine
Vrije Universiteit Brussel

Daniel F. Voytas, Ph.D.
Professor
Department of Genetics, Cell Biology & Development
Director, Center for Precision Plant Genomics
University of Minnesota

James Wilson, M.D., Ph.D.
Director, Gene Therapy Program
Perelman School of Medicine at the University of Pennsylvania

Feng Zhang, Ph.D.
Core Member
Broad Institute of MIT and Harvard
Investigator
McGovern Institute for Brain Research at the Massachusetts Institute of Technology
James and Patricia Poitras Professor of Neuroscience
Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology
Investigator
Howard Hughes Medical Institute

Cc: Dr. Francis Collins, Director, National Institutes of Health
Dr. Norman Sharpless, Acting Commissioner of Food and Drugs, U.S. Food and Drug Administration
Senator Lamar Alexander, Chairman, Senate Committee on Health, Education, Labor, and Pensions
Senator Patty Murray, Ranking Member, Senate Committee on Health, Education, Labor, and Pensions
Congressman Frank Pallone, Chairman, House Committee on Energy and Commerce
Congressman Greg Walden, Ranking Member, House Committee on Energy and Commerce