April 24, 2019

The Honorable Alex Azar II
Secretary
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

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[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.

the technology at this time. These issues, which must be addressed before proceeding, include 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,

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