United States Senate Committee on Health, Education, Labor and Pensions

Hearing on Gene Editing Technology: Innovation and Impact

Written Testimony of

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Chairman Alexander, Ranking Member Murray, and Members of the Committee, thank you for the opportunity to testify today about genome editing technology.

I am Katrine Bosley, CEO and President of Editas Medicine. At Editas Medicine, we are committed to harnessing the power and potential of CRISPR genome editing to develop medicines for patients with serious diseases where other technologies have not been able to help. We are only focused on applying our CRISPR genome editing platform to cells that cannot pass on changes to future generations. Our company was founded four years ago in Cambridge, Massachusetts, and we have built a team of over 100 people to tackle the deep scientific challenges of turning this exciting – but young – technology into medicines. We are one of a small number of companies in this field of genome editing, and we believe we are on the brink of a truly exciting new era of medicine, powered by genome editing technologies.

There are a few times in our lives when science astonishes us, when we are suddenly able to do something that seemed like science fiction just the day before. This is one of those

moments. Our DNA is at the root of who each of us is – that unique combination of genes that makes you who you are. But sometimes there are mistakes in DNA – mutations in genes that can cause many different kinds of serious diseases. There are over 6,000 genetically defined diseases, and, according to the National Organization for Rare Disorders (NORD), 95 percent of them have no approved medicines. What if you could repair broken genes? What if you could address the root of diseases caused by mutations in DNA? How many patients could we help in the years ahead? This is the promise and possibility of gene editing.

My testimony today will focus on how innovative American researchers, universities, and companies are advancing new genome editing tools like CRISPR to translate the value of the Human Genome Project and its insights into a new class of transformative medicines that work at the level of the gene to treat serious diseases that afflict millions of Americans. The field of gene therapy and genomic medicine has been working toward this moment for decades, and this year marks the first time that some of these patients will have access to gene therapy products approved by the U.S. Food and Drug Administration (FDA). These gene therapy product approvals promise to be the first of many new genomic medicines that can address previously untreatable diseases and help patients move from chronic to durable treatments. Continued success in this field will depend in part upon Congress maintaining the robust, but flexible regulatory system over novel genetic technologies that has operated effectively since the first recombinant genetic research began over 40 years ago. Maintaining regulation that is both rigorous and science-driven not only protects patients, it also helps the American biotechnology industry flourish. Our industry leads the world by a very long measure, and sophisticated, highly-engaged regulators are a key and valued partner in this continuing success story.

At the outset, I want to remark that at Editas Medicine we are fully aware that genome editing in general, and CRISPR in particular, represents a fast-moving, potentially disruptive technology that often evokes great hopes and, at times, legitimate concerns. That is why we believe it is part of our mission and responsibility to engage with major stakeholders in a highly transparent and respectful manner. Our company, and many of our partners and collaborators in medicine and industry, applaud the Committee for convening this hearing and judiciously engaging in the science and policy implications of genome editing.

I understand that the Committee also convened a bipartisan staff briefing approximately a year ago with the American Society of Gene & Cell Therapy (ASGCT), and, therefore, has already benefitted from the insights of some of the world's leading genome editing experts. Today's hearing is another hallmark in this Committee's long and distinguished history of overseeing biomedical research and promoting the now-flourishing American biotechnology industry. From balanced oversight hearings of recombinant DNA technology in the 1970s to funding of the National Institutes of Health (NIH), overseeing and strengthening the FDA to last year's enactment of the 21st Century Cures Act, on a bipartisan basis you have thoughtfully helped develop a tremendous American ecosystem of innovation in service of patients. These forward-looking, bipartisan policies are now bringing forth unprecedented medicines that can transform, and often save, countless lives. For these reasons, I would like to thank the Committee for its historic and ongoing support.

This continued support will also be critically important for the United States to remain the global biotechnology leader and a beacon of hope for patients around the world. As the Committee is aware, developing medicines is a long, complex process that is riddled with setbacks and failure. At Editas Medicine, for example, we are a four-year old company with no

approved products to generate operating revenue. To date, we have raised approximately $500 million from investors and partners to fund our scientific discovery and clinical development of new medicines. We will need to raise significantly more capital before our first product is approved in the U.S. or Europe. This is a necessary and important undertaking for us to be successful in our ambitious goal to create these unprecedented medicines. We know how important this is – every week we receive letters and emails from patients and their families asking about our progress, and letting us know that they are paying close attention to everything we do. Patients are our motivation every day for discovering and developing CRISPR medicines.

I. What is Genome Editing?

In the world of medicine, the idea and the promise of genome editing is straightforward: *What if we could repair broken genes?* Our bodies depend on many intricate biological systems that follow instructions embedded within our genes. Even one mutation, which is a naturally-occurring change in our DNA that disrupts the function of a gene, can result in serious or life-threatening diseases. Most diseases caused by genetic mutations have no approved therapeutic options. Some of these diseases are well known: rare forms of blindness, sickle cell disease, cystic fibrosis, Huntington's disease, and hemophilia. Our goal in advancing genome editing is to repair these broken genes at the level of DNA.

CRISPR (pronounced "crisper") is an acronym for "Clustered, Regularly Interspaced, Short Palindromic Repeats," and refers to a recently developed genome editing technology that can revise, remove, and replace DNA. It is the latest in a series of genome editing technologies that can engineer molecules to cut DNA in a highly targeted manner, including zinc finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs), and meganucleases.

Beyond human health, genome editing can be applied to animal and plant DNA, as well as many organisms that are used in basic biological research. Applications in agriculture and animal health have the potential to deliver major advances to help feed the world. In basic research laboratories, the use of CRISPR technology is nearly ubiquitous. It is opening up a wide range of new ways to ask and answer essential biological questions. Researchers are using it to probe the internal workings of cells, to identify the actions of genes with unknown function, and to rapidly create new animal models of disease to enable testing and advancements of medicines of all kinds. Creative new applications of the technology keep emerging, and we are just at the beginning of seeing what can be achieved.

II. Innovative Researchers, Clinicians, and Companies Are Applying Genome Editing in Drug Development Programs to Meet Unmet Medical Needs of American Patients with Serious and Life-Threatening Diseases.

Mr. Chairman, it is simply impossible to overstate the needs of millions of American patients and their families who urgently need medical progress, treatments, and, wherever possible, cures. As we continue working to develop gene editing medicines to address this need, we are often asked what these medicines might look like. Genome editing medicines can take different forms, depending on what tissue in the body needs to be treated for a given disease. In some instances, the genome editing product could be administered directly to a patient. In these cases it could be a biological preparation (such as a viral or nanoparticle preparation to deliver the genome editing molecules) or edited cells (such as induced pluripotent stem cells, or iPSCs). The patient would receive the biological preparation or the cells as an injection, either systemically or to a specific tissue. In other instances, gene editing can be performed outside the

body on a patient's cells – for example, cells from the blood like T cells. In these cases, a patient's cells would be removed, then edited, and then given back to the patient via an infusion.

Editas Medicine is working to deliver new genomic medicines that realize the potential of CRISPR genome editing. Our most advanced program is focused on a rare disease called Leber's Congenital Amaurosis Type 10 (LCA10). This disease afflicts children with significant vision loss and blindness. We have initiated a natural history study in LCA10 to better understand the disease's progression and intend to use the insights learned from this study to inform clinical trials for our first product candidate in development, which is called EDIT-101. We aim to file an Investigational New Drug application with the FDA for this program by mid-2018. Our broader pipeline focuses on genetically-defined eye diseases, inherited blood disorders, and producing new cell therapies in immuno-oncology, along with our partner, Juno Therapeutics.

In addition to Editas Medicine, there are several leading biotechnology companies working to translate the promise of genome editing into medicines to help patients in need. These include CRISPR Therapeutics and Intellia Therapeutics, both of whom work on CRISPR technology, as well as bluebird bio, Cellectis, and Sangamo Therapeutics, who are pursuing drug development using other genome editing platforms. Editas Medicine and, to my knowledge, all of these companies are only focused on applying their technologies to cells that cannot pass on genetic information or any edits to future generations. As such, the editing is *non-heritable*, and only applied to somatic cells or cells that are derived from somatic cells.

Around the world, clinical trials with genome editing technologies are already underway in patients. Sangamo Therapeutics and Cellectis are two examples of companies whose ZFNs- and TALENs-based genome editing products are currently in clinical trials. Last October,

Chinese researchers were the first to inject a patient with CRISPR-edited cells in a clinical trial for lung cancer treatment. The CRISPR genome editing platform has yet to be used in a clinical trial in the United States or Europe, but U.S. companies are expected to initiate clinical trials soon.

III. Genome Editing to Treat Disease Falls Under a Robust and Comprehensive Regulatory System.

Those clinical trials are carefully regulated by Federal authorities. In September, FDA Commissioner Scott Gottlieb spoke to our common goals for intelligent oversight of the promising field of genome editing. He said, "…our principles for regulation allow and facilitate beneficial new innovation while making sure that FDA continues to meet its gold standard for safety and effectiveness."

Mr. Chairman, I believe this is an accurate description of the current, robust Federal regulatory framework that has guided clinical research and drug development involving recombinant genetic technology over the past 40 years. Genomic medicines developed with novel genome editing platforms like CRISPR have and will be subject not only to FDA review, but also public review by the NIH's Recombinant DNA Advisory Committee (RAC). The NIH's RAC dates back to the 1970s, and has afforded the American public with unique opportunities to review and comment on clinical trials and other information that would otherwise be deemed confidential by the FDA in its own, parallel review. This is appropriate for such novel technologies, and it has proven to be a strength of our existing regulatory framework. In conjunction with the NIH RAC, the FDA has overseen gene therapy development since the 1990s, and together, the two agencies will use this same framework to oversee potential clinical

applications of genome editing technology, including CRISPR, to treat human disease. With these agencies working in tandem with public advisory committees, local Institutional Review Boards (IRBs), and other oversight mechanisms, the United States possesses a rigorous, transparent, and flexible regulatory system that is pro-patient, pro-innovation, and has served as a model for the rest of the world.

As you know, the FDA has broad authority to uphold high standards of safety and effectiveness for any novel biological product, including genomic medicines. They have also had extraordinary success implementing a range of programs for collaboration with sponsors and expedited reviews, including the orphan drug, fast track, breakthrough therapy, priority review, accelerated approval, and the recently enacted Regenerative Medicine Advanced Therapy (RMAT) programs – all of which could expedite the availability of genomic medicines. Perhaps most importantly, in our experience, the Agency's leaders and scientific reviewers have also demonstrated a strong commitment to understanding the latest breakthroughs and to improving their regulatory science. I commend the FDA in particular for their outreach to leading academic and industry experts in genome editing. To date, the Agency has been forward-looking and thoughtful in starting early conversations about how they plan to integrate oversight of genome editing into their existing regulatory framework. As the field of genome editing continues to advance in the years ahead, these kinds of early, constructive, and collaborative engagements will be invaluable in keeping all parties aligned and focused on delivering important medicines to patients.

The European Union has also sought to understand and appropriately regulate this work. On October 18, the European Medicines Agency (EMA) gathered leading academics and companies together for an initial discussion around the oversight of clinical uses of genome

editing. I attended this meeting, and the discussion focused on their regulatory framework for gene therapies, how their Committee on Advanced Therapies (CAT) should think of genome editing medicines and setting standards under such a framework, and their appreciation of the importance of the EMA's regulatory science co-evolving with emerging technologies. While the EMA has demonstrated foresight on genome editing, it was my impression that the early engagement efforts of the FDA have brought the Agency to a closer familiarity with the leading edge of the field's rapid innovation. Like the FDA, the EMA is committed to learning and engaging with leading companies and researchers.

Our expectations for how genome editing medicines will be regulated are informed by the experience in the United States and Europe with genomic medicines technologies overall, including many years overseeing gene therapy clinical trials. In recent years, companies developing other genome editing technologies have initiated early clinical trials in the U.S. following reviews by the NIH RAC and the FDA.

IV. Recent NAS/NAM Report Endorses Existing Comprehensive Regulatory System.

We are fortunate to have authoritative, independent confirmation that genome editing will be carefully regulated under current law. In December 2015, the National Academies of Science and Medicine (NAS/NAM or Academies) co-hosted an international summit on human genome editing with the British Royal Society and the Chinese Academies of Science. The Academies spent three days exploring the scientific, social, and legal implications of genome editing, and offered a preliminary conclusion that clinical use of genome editing in somatic cells "can be appropriately and rigorously evaluated within existing and evolving regulatory frameworks…"

In February 2017, the Academies issued a comprehensive report titled “Human Genome Editing: Science, Ethics, and Governance.” Mr. Chairman, I encourage the Members and staff of this committee to review its analyses and its specific, actionable recommendations to rely on current regulations to facilitate progress. Critically, the report reaffirms that "clinical trials of genome editing in somatic cells for the treatment or prevention of disease or disability should continue, subject to the ethical norms and regulatory frameworks that have been developed for existing somatic gene therapy research and clinical use to treat or prevent disease and disability."

We agree strongly with this conclusion and the finding that the Federal government should continue to "use existing regulatory processes for human gene therapy to oversee somatic human genome editing research and uses." In short, the Academies' report confirms that current, multilateral Federal safeguards, standards, and oversight mechanisms, as well as long-standing guidelines in the research community, preclude the need for additional, potentially disruptive restrictions of genome editing research.

V. U.S. Companies Are Developing Non-Heritable, Somatic Cell Medicines, and Not Germline Modifications.

As I mentioned, U.S. companies are exclusively developing *non-heritable* gene edits to somatic cells, which cannot pass on their genetic information to future generations. Editas Medicine is not working on editing germline cells, and we have no plans to do so. Nevertheless, the NAS February 2017 report raised the prospects of one day permitting germline editing for clinical application if select criteria could be met. Though this topic is beyond my scope and expertise, I would like to share two thoughts. The first is that edited human cells of all kinds are under the FDA’s jurisdiction, and provisions in the Consolidated Appropriations Act of 2017 and

the Consolidated Appropriations Act of 2016 effectively bar the Agency from allowing clinical trials of products that cause germline modifications.

Second, that the Biotechnology Innovation Organization (BIO) recently issued a position statement that reflects its member company consensus on germline editing for clinical application:

> BIO views the science of germline genome editing as having not advanced sufficiently for clinical applications to be appropriate at this time. As scientific developments progress, BIO urges continued discussion and engagement on this topic with important stakeholders, including members of the patient, caregiver, regulatory, legal, academic, ethical, and faith communities, to determine if and under which conditions this status quo should be changed.

VI. Conclusion

Mr. Chairman, we are discussing this revolutionary translation of fundamental breakthroughs in the understanding of human genetics into innovative medicines thanks in great measure to the bipartisan commitment of Congress, including this Committee, and of successive administrations to fully fund the Human Genome Project. That historic achievement, in turn, would have been impossible without our country's extraordinary, decades-long commitment to basic research – a commitment that built a system of higher education that leads the world and is the envy of other nations; that secured a lion's share of Nobel Prizes and patents in the sciences and medicine; and that has created breakthroughs in high technology, computation, the Internet, and medicine.

To sustain this extraordinary success, I urge the Committee to continue its support of robust research funding through NIH; to maintain its oversight of the FDA and support the

Agency in its embrace of fast-moving scientific developments, including advances in genome editing; and, critically, to continue to support public dialogue about the tremendous promise and important challenges in the field of genome editing. I am greatly encouraged that this hearing exemplifies the National Academies' recommendation that "[p]ublic participation... be incorporated into the policy-making process for human genome editing."

Dr. Gottlieb recently said that this field holds “the promise of changing the contours of human illness and altering the trajectory of medicine and science” – what the late Chairman of this Committee, Senator Kennedy, once called "the century of life sciences." I have been in this industry for more than 25 years. I can say without equivoacation that it is hard to compare genome editing to any other field that I know. The implications for medicine and for patients who have as yet untreatable diseases; the scientific intensity as we work to overcome challenges translating the science into medicines; and the intensity of the public spotlight, given the profound implications of this technology, all make this field exceptional. We bear great responsibility to patients, to their families, and to society broadly. We take that very seriously. We are here for the long term, and want to listen and respectfully engage with all major stakeholders.

Thank you for the opportunity to testify today. I look forward to answering your questions.

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