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Presentation before the ADVISORY PANEL TO BETTER UNDERSTAND AND MAKE RECOMMENDATIONS REGARDING THE IMPLICATIONS OF GENOME-EDITING TECHNOLOGY TO THE CITIZENS OF THE STATE

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Good morning, Senator Claxton, Representative Zager and members of the advisory panel, my name is Lon Cardon and I am president and CEO of The Jackson Laboratory. The Jackson Laboratory is an international genetics and genomics research institution, headquartered in Bar Harbor, with other Maine-based facilities in Augusta and Ellsworth. I joined the Jackson Laboratory at the beginning of this year, with half of my previous career spent in academia, searching for genes that cause human disease, and the latter half in the pharmaceutical industry, trying to turn those discoveries into treatments.

I'm pleased to have the opportunity to speak to you today and would like to thank you for your service to the Legislature and people of Maine, and for bringing this important conversation to the fore.

My colleague, Dr. Laura Reinholdt, Associate Professor at our Bar Harbor campus, appeared before this panel in August. She discussed the critically important use of gene editing in research using mouse models for human disease.

My presentation will provide a bridge to take gene editing from early "pre-clinical" research studies to the human patient, focusing on three things. First, I will discuss gene editing in the development of human therapeutics. Second, I will discuss The Jackson Laboratory Rare Disease Translational Center, which is already using this technology. Finally, I will address the panel's question of what Maine can do regarding gene editing now and in the future.

First, gene editing in the therapeutic context. As described by Dr. Reinholdt, gene editing has transformed basic research. Until this technology development, the field of genetics was passive: we had to wait until some new disease or symptoms occurred and then try to find the genes that might have caused it. Many important discoveries were made this way, but they were made by chance and took months, years to discover.

Now, with gene editing, that process has changed dramatically. We can design and create such variants overnight, and even hundreds or thousands of them. This level of speed and precision is transformative for biomedical research, and the technology has advanced so rapidly that early stage scientists, even high-school students, can learn to deploy the tools productively.

If basic biology research studies of a rare disease therapeutic are successful, one next goal is to translate those findings into a drug treatment for a human patient. Toward this aim, gene editing

provides a key advance in a series of technologies that have been progressing over the past few decades. To understand the potential of gene editing in therapeutics, it is useful to understand how we got to where we are.

In rare diseases and some others, the disease emerges because of a genetic defect that doesn't let the gene make the gene product that is necessary for the healthy state. The gene is effectively 'broken.' The earliest solution to this, over 20 years ago, was for scientists to make correct versions of the gene product outside the body – literally in manufacturing factories – and then inject them into the patient. The broken gene is still in the body, but we offset that by putting in some working parts to take over the load. These are so called 'gene or enzyme replacement' therapies and drugs are approved for a number of rare diseases.

The next generation of these therapies, which are appearing today in some neurological and blood disorders, use exactly the same principle, but instead of making the unbroken product outside the body in a factory, scientists use some tricks to help the body make it itself. The broken gene is again still there, but a therapeutic gene has been delivered to sit alongside the broken one to put some properly working copies in our bodies. This and related approaches is what many people refer to as "gene therapy."

'Therapeutic gene editing' is the next generation of this type of biomedicine. This is a substantial change because in this case, the goal is not to just add some working parts alongside the broken ones, but to target the broken gene itself. Here we are trying to repair or replace that broken copy itself. In some cases, gene editing could render a permanent change at the genetic level. This is about as good as it could get, if safe and effective.

Second, JAX Rare Diseases commitment. Disease therapies based on gene editing are still rare. This panel has already heard examples of how gene editing is being used in the treatment of sickle cell disease, and I believe we are at the beginning of other treatments to come, but it is still early, and like nearly all new approaches that can transform medicine, it takes time to understand how to use them safely and to their greatest benefit.

Getting in early to lead the basic research is why, within my first year at JAX, I established the Rare Disease Translational Center, and named my colleague Dr. Cat Lutz as vice president. Dr. Lutz is a proud alumnus of The University of Maine, where she earned a Ph.D. in biochemistry. Throughout her career she has been involved in major milestones in rare disease research, including the preclinical studies of what would become Spinraza, the first FDA approved therapy for Spinal Muscular Atrophy. If this Advisory Panel is planning to make recommendations regarding the formation of the Rare Disease Advisory Council, I suggest the panel recommend the appointment of a scientist like Dr. Lutz, who not only has an internationally recognized track record of research productivity, but has demonstrated experience working closely with rare disease stakeholders including patients, patient advocacy groups, physicians, and researchers.

Since 2016, The JAX Rare Disease Translational Center has worked with dozens of rare disease foundations and their associated research teams to generate, using CRISPR/Cas9 and other gene editing methods, custom mouse models of rare conditions in order to lay the groundwork for new therapeutic interventions. Now, the Rare Disease Translational Center is expanding its focus. Under Dr. Lutz's leadership, JAX will work with hospitals from the point of diagnosis and with pharmaceutical companies to conduct pre-clinical tests of new therapeutics. I believe rare disease is an area where the expertise and scale of The Jackson Laboratory can have a major impact, and in fact, it has a natural symmetry because the Jackson Laboratory has been working on rare diseases for almost its entire 93 year existence. The ability of this Center

to realize the aspirations of the genomic revolution to treat rare disease will rely in part on gene editing.

Third and finally, this panel has accepted the difficult task of making recommendations regarding the implications of gene editing to the citizens of Maine. You've considered difficult scientific, ethical, and financial questions and have come up with a number of actionable recommendations that could make a difference in Maine. I'll leave you with two recommendations.

I agree with other presenters who recommended the state of Maine increase investments in education and teacher professional development. Most of today's students will be tomorrow's consumers of the precision therapeutics developed and implemented using gene editing technology. Some of today's students will pursue careers that put them in direct contact with gene editing: research scientists, physicians, engineers, social scientists, genetic counselors, farmers, and others. Today's students will also drive innovation and become biotech entrepreneurs, creating products and services using gene editing and creating economic opportunity in the process.
I also urge this panel to support recommendations that increase access to teacher professional development in genomics, which combines genetics and computer sciences to enable data-intensive research in one or many genomes. Increasingly, genetics research is performed using only computational methods, and there is an abundance of genomic data and an urgent need to grow this digitally-capable workforce. Any recommendation by this panel to support education or teacher professional development will advance the Maine 10-year Economic Development Strategy to *Grow Local Talent* and prepare students and teachers for the digital economy in biomedicine.

Investments in education and teacher professional development should parallel investments into the biosciences economy, specifically research; otherwise Maine's support of STEM education will increasingly benefit other states. I urge this advisory panel to consider gene editing as an example of why it is important that Maine begin to make perennial investments into bioscience research and development. As has been shown by Mr. Whitney and Maine Technology Institute, competitive grant awards made by the $45 million Maine Technology Asset Fund (MTAF) 2.0 in 2017 have so far created over 5,300 jobs and $1.4 billion in economic impact across the state.

Through MTAF 2.0, JAX was awarded $12.5 million to initiate construction of a world-class mouse vivarium in Ellsworth—an award that JAX matched with over $240 million in additional investment. The Ellsworth vivarium dramatically extends our mouse production and services capacity, including development of highly specialized mouse strains using gene editing technology. As of the first quarter of 2022, JAX can attribute 262 new jobs to MTAF 2.0, and annual salaries of over $18 million. JAX's Ellsworth expansion, catalyzed by state investment, has indisputably created indirect economic impact; look no further than private investments in housing, childcare, and other ventures that are made possible by the economic durability of the biosciences sector, which will not only grow, but will become increasingly efficient through technology improvements like gene editing. Just as the 2012 discovery of CRISPR/Cas9[1] was funded by a combination of private and public grants, so too can state funding help leverage private and federal support which collectively will grow the Maine innovation economy.

[1] https://www.science.org/doi/10.1126/science.1225829

I'll close by again thanking you for inviting me to share my experience and suggestions on what Maine should do now and in the future. Science is too often removed from the public sphere and I'm pleased to be a part of today's proceeding.