Editas Medicine Presents Data from Multiple Therapeutic Discovery Programs Emerging from its Genome Editing Platform at the ASGCT Annual Conference

May 18, 2015 4:07 AM ET

Cambridge, Mass., May 18, 2015 -- Editas Medicine, a leading genome editing company, today announced data from several emerging therapeutic discovery programs, as well as data from advancements in its technology platform. Together these data demonstrate the breadth of research underway at Editas Medicine to translate the promise of genome editing technology into new medicines. The data were presented at the 18th Annual American Society of Gene & Cell Therapy (ASGCT) Meeting in New Orleans.

"The data we presented at ASGCT highlight important advances in both our platform and our research programs," said Katrine Bosley, CEO, Editas Medicine. "We've made significant progress in the design and optimization of more efficient and more specific CRISPR/Cas9 molecules, and in delivering them to cells using several different technologies. We've applied these improvements across a number of early programs and are committed to developing a broad pipeline of medicines."

Each of the scientific posters from the ASGCT conference are available on the Editas Medicine website.

Summary of ASGCT Presentations

- Leber congenital amaurosis genome editing: A mutation in an intron of the CEP290 gene leads to a form of Leber congenital amaurosis (LCA10), a rare retinal disease that causes severe vision loss. Editas scientists designed guide RNAs (gRNAs), paired them with the *Staphylococcus aureus* Cas9 protein and used a single adeno-associated virus (AAV) vector to achieve delivery and correction of the CEP290 mutation in primary patient fibroblast cells.
- Gene conversion of the hemoglobin locus: Several CRISPR/Cas9 construct variants were evaluated *in vitro* to target the human hemoglobin beta gene (HBB) in the region mutated in sickle cell anemia. The construct containing the *Streptococcus pyogenes* D10A nickase isoform with selected gRNAs drove *in vitro* editing to approximately 30 percent of the HBB locus through gene conversion by the hemoglobin delta (HBD) locus. This suggests a potential therapeutic approach to treat sickle cell anemia in which correction of the sickle-cell mutation may be achievable through CRISPR/Cas9-mediated gene conversion.
- Cleavage efficiency characterization of *Staphylococcus aureus* Cas9 isoforms : Both the wild-type and nickase isoforms of *S. aureus* Cas9 are effective tools for genome editing with similar editing properties but distinct genome targeting properties from the more widely used *S. pyogenes* Cas9. The smaller size of the *S. aureus* gene allows for AAV delivery of this protein along with multiple gRNAs and required regulatory elements.
- Functional characterization Cas9 ribonucleoprotein complexes: A potential delivery approach for CRISPR/Cas9-based therapeutics is cationic lipid-mediated delivery of purified Cas9 protein with *in vitro* produced gRNA in a ribonucleoprotein (RNP) complex. Editas scientists evaluated the impact of gRNA length and base composition on the binding and formation of RNP complexes in an *in vitro* setting and found subtle differences in the thermal stability, the efficiency and the specificity of different compositions.
- **Development of effective delivery options for T-cells editing:** Researchers evaluated delivery via electroporation of RNA and RNP complexes and also assessed the functionality of different Cas9 protein variants in human T-cells. Efficient editing was achieved using *S. pyogenes* and *S. aureus* Cas9 proteins with both delivery approaches.
- **Robust genome editing of hematopoietic stem cells:** Several strategies were tested to deliver CRISPR/Cas9 molecules to primary human hematopoietic stem cells (HSCs). For selected approaches, Cas9 gene-edited HSCs maintained both viability and *ex vivo* hematopoietic colony-forming potential, similar to unedited cells.

About Genome Editing

Genome editing enables sequence-targeted modifications of DNA. Recent advances in this field have made it possible to modify almost any gene in the human body with the ability to directly turn on, turn off or edit disease-causing genes. This

has the potential to address diseases that have previously been intractable to traditional gene therapy, gene knock-down or other genome modification techniques.

The CRISPR (clustered, regularly interspaced short palindromic repeats)/Cas9 (CRISPR associated protein 9) system, the newest genome editing approach, uses a protein-RNA complex composed of an enzyme known as Cas9 bound to a guide RNA molecule that has been designed to recognize a particular DNA sequence. The RNA molecules guide the Cas9 complex to the location in the genome that requires repair. CRISPR/Cas9 uniquely enables highly efficient knock-out, knock-down or selective editing of defective genes in the context of their natural promoters, unlocking the potential to treat the root cause of a broad range of diseases.

About Editas Medicine

Editas Medicine is a leading genome editing company and part of a transformational new area of health care – genomic medicine. The company was founded by pioneers and world leaders in genome editing bringing specific expertise in CRISPR/Cas9 and TALENs technologies. The company's mission is to translate its proprietary technology into novel solutions to treat a broad range of genetically driven diseases. For more information, visit <u>www.editasmedicine.com</u>.

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