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Merck KGaA, Darmstadt, Germany Receives First U.S. Patent for Improved CRISPR Genome-Editing Method

- **Proxy-CRISPR technology provides solution to improve genome editing and advance new possibilities for research**
- **Helps modify difficult-to-access regions of the genome, increasing genome coverage**

Darmstadt, Germany, February 19, 2019 – Merck KGaA, Darmstadt, Germany, a leading science and technology company and leader in genome editing, today announced that the United States Patent and Trademark Office has issued a formal notice allowing the Life Science business' patent application directed to its proxy-CRISPR technology.

"This is our first U.S. patent for CRISPR, and as a leading innovator of CRISPR technology, we will continue to collaborate with scientists around the world to ensure that the full potential of this powerful tool is realized, responsibly and ethically," said Udit Batra, member of the Executive Board and CEO, Life Science business of Merck KGaA, Darmstadt, Germany. "This is great news for researchers in the U.S., as they now have more gene-editing options that accelerate drug development."

Proxy-CRISPR is a new genome-editing technique that makes CRISPR more efficient, flexible and specific by opening up the genome for modification of DNA.

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The technology can help scientists modify regions of the genome which are difficult to access.

This U.S. patent allowance marks the 13th patent granted worldwide for the Life Science business of Merck KGaA, Darmstadt, Germany. Its CRISPR patent portfolio includes granted patents in Australia, Canada, Europe, Singapore, China, Israel and South Korea. Those patents are for CRISPR-related technologies covering foundational and alternative genome-editing methods.

To deploy the proxy-CRISPR method, two CRISPR systems are designed to target the genome in proximity to each other and work together. One CRISPR system opens a regional "door," pushing away blocking chromatin proteins, while the other walks through it to find the exact location for modification. Since the resulting modification requires two CRISPR binding events, the proxy-CRISPR method can enable twice the specificity of individual CRISPR systems.

The Life Science business of Merck KGaA, Darmstadt, Germany has received patents for its CRISPR paired nickase technology (cleaving opposite strands of a chromosomal sequence to create a double-stranded break) in Australia, Canada and Europe. Patents for the business' CRISPR integration technology (chromosomal cutting of the sequence of eukaryotic cells and insertion of a DNA sequence) have been granted in Australia, Canada, Europe, Singapore, China, Israel and South Korea. The Life Science business of Merck KGaA, Darmstadt, Germany, is licensing its entire patent portfolio for all fields of use.

CRISPR technology is a core competency for the Life Science business of Merck KGaA, Darmstadt, Germany, which has 15 years' experience with genome editing, spanning from discovery to manufacturing. The company recognizes that genome editing has resulted in major advancements in biological research and medicine. At the same time, the growing potential of genome-editing technologies has opened scientific, legal and societal concerns. As both users and suppliers of genome-editing technology, the businesses of Merck KGaA, Darmstadt, Germany support research with genome editing under careful consideration of ethical and legal standards. Merck KGaA, Darmstadt, Germany has established an independent, external [Bioethics Advisory Panel](#) to provide guidance for research in which its businesses

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are involved, including research on or using genome editing, and has developed, defined and transparently published a clear operational [position](#) taking into account scientific and societal issues to inform promising therapeutic approaches for use in research and applications.

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About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across healthcare, life science and performance materials. Around 51,000 employees work to make a positive difference to millions of people's lives every day by creating more joyful and sustainable ways to live. From advancing gene editing technologies and discovering unique ways to treat the most challenging diseases to enabling the intelligence of devices – the company is everywhere. In 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

The company holds the global rights to the name and trademark "Merck" internationally. The only exceptions are the United States and Canada, where the business sectors of Merck KGaA, Darmstadt, Germany operate as EMD Serono in healthcare, MilliporeSigma in life science, and EMD Performance Materials. Since its founding 1668, scientific exploration and responsible entrepreneurship have been key to the company's technological and scientific advances. To this day, the founding family remains the majority owner of the publicly listed company.