

## News Release

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### **MilliporeSigma Awarded Canadian CRISPR Nickase Patent for Foundational Genome-Editing Technology**

- **Patent covers paired Cas9 nickase technology to advance gene therapy and research, reduce off-target effects**
- **Marks MilliporeSigma's 12<sup>th</sup> CRISPR patent overall**
- **Actively licensing CRISPR-related patents to interested parties**

Burlington, Massachusetts, March 4, 2019 – [MilliporeSigma](#), a leader in genome editing, today announced that the Canadian Patent Office has allowed MilliporeSigma's patent application directed to the use of paired CRISPR nickases in eukaryotic cells. The patent provides an important and more specific solution for scientists who need accurate methods when developing treatments for difficult-to-treat diseases that ultimately reach the patient.

"This patent allowance marks another advancement in safety for CRISPR-enabled therapeutics, as it covers technology that improves CRISPR's ability to fix diseased genes while not affecting healthy ones," said Udit Batra, CEO, MilliporeSigma. "MilliporeSigma has been at the forefront of genome-editing innovation for 15 years and this allowance further expands our foundational CRISPR cutting and integration intellectual property to help scientists advance gene therapy research."

CRISPR technology is a core competency for MilliporeSigma. As both a user and supplier of genome-editing technology, MilliporeSigma supports research with genome editing under careful consideration of ethical and legal standards. Its parent company, Merck KGaA, Darmstadt, Germany, has established an independent, external [Bioethics Advisory Panel](#) to provide guidance for research in which its businesses are involved, including research on or using genome editing, and has



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defined a clear operational [position](#) taking into account scientific and societal issues to inform promising therapeutic approaches for use in research and applications.

This Canadian patent marks MilliporeSigma's second in Canada and the 12<sup>th</sup> worldwide. Similar patents were granted in Australia and Europe in late 2018. This latest patent covers paired nickases, which drive specificity through a highly flexible and efficient approach to reduce off-target effects.

Paired nickases are two CRISPR nickases targeted to a common gene target that work together by nicking or cleaving opposite strands of a chromosomal sequence to create a double-stranded break. This process can include an exogenous or donor sequence for insertion in the same manner as MilliporeSigma's CRISPR integration technology. The requirement of two CRISPR binding events greatly reduces the chances of off-target cutting at other locations in the genome.

MilliporeSigma's CRISPR integration patent portfolio includes granted patents in Australia, Canada, China, Europe, Israel, Singapore and South Korea. These CRISPR patents are for chromosomal integration or cutting of the sequence of eukaryotic cells and insertion of a DNA sequence, to make a desired genomic change.

MilliporeSigma is licensing its entire patent portfolio for all fields of use.

MilliporeSigma was the first to offer custom biomolecules for genome editing globally (TargeTron™ RNA-guided group II introns and CompoZr™ zinc finger nucleases), driving adoption of these techniques by researchers all over the world. MilliporeSigma was also the first to manufacture arrayed CRISPR libraries covering the entire human genome, accelerating disease cures by allowing scientists to explore more questions about root causes.

In addition to basic genome-editing research, MilliporeSigma supports development of gene- and cell-based therapeutics and manufactures viral vectors. MilliporeSigma has a dedicated genome-editing group aimed at advancing research in novel modalities — from genome editing to gene medicine manufacturing — further solidifying the company's commitment to the field.



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### **About the Life Science Business of Merck KGaA, Darmstadt, Germany**

The Life Science business of Merck KGaA, Darmstadt, Germany, which operates as MilliporeSigma in the U.S. and Canada, has 20,000 employees and 60 manufacturing sites worldwide, with a portfolio of more than 300,000 products enabling scientific discovery. Udit Batra is the global chief executive officer of MilliporeSigma.

Merck KGaA, Darmstadt, Germany completed its \$17 billion acquisition of [Sigma-Aldrich](#) in November 2015, creating a leader in the \$125 billion global life science industry.

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. For more information about Merck, KGaA, Darmstadt, Germany, visit [www.emdgroup.com](http://www.emdgroup.com).