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Successful Genome Editing in Mammalian Cells with BRAIN-Metagenome-Cas (BMC), BRAIN-Engineered-Cas (BEC)

- Major milestone achieved: genome-editing in mammalian cell lines
- Potential to target very large addressable markets
- BEC, BMC well suited for different application fields

Zwingenberg, Germany, April, 4th 2022 – BRAIN Biotech AG has achieved a major milestone successfully demonstrating genome editing in mammalian cell lines with its proprietary CRISPR-Cas genome editing nucleases BRAIN-Metagenome-Cas (BMC), BRAIN-Engineered-Cas (BEC). This is expected to pave the way to potentially employ BRAIN's genome editing technology in very large addressable markets such as animal livestock, cell line development, pharmacology and therapeutics. The company will continue to develop this technology jointly with partners for a magnitude of end markets and applications.

These BRAIN-developed genome-editing nucleases are already today successfully employed in customer projects within the BioScience division and are utilized for the optimization of highly efficient microbial producer strains which power the biological production in so called microbial cell factories. Together with partners this proprietary genome editing nucleases are currently advanced for applications in agriculture, pharmaceutical cell lines, marine applications and industrial producer strains.

BRAIN-Engineered-Cas (BEC) and BRAIN-Metagenome-Cas (BMC) are different types of nucleases which differ in their general protein structure and their mode of action to target DNA. Hence, they can address different markets and applications most effectively. In July 2021 BRAIN had announced the identification of around 2,000 so far untapped additional Class 2 CRISPR nucleases which have been identified *in-silico* and have the potential to be deployed for genome editing. BEC and BMC are the lead nucleases which are currently developed for genome editing in several applications.

The Head of R&D at BRAIN Biotech, Dr. Michael Krohn, shares his excitement: "I really have to thank our scientific team for achieving this very important milestone. The dedication and speed by the team to drive forward scientific breakthroughs makes me really optimistic also for the next development steps. Genome-Engineering is widely regarded as one of the most influential technologies of this century for advanced healthcare, nutrition and sustainable production. To take an active part in this revolution greatly motivates the entire team and creates significant partnership and business opportunities. We will not only continue to build our portfolio

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of genome-editing nucleases and broaden the space of application but also invest in RNP target cell delivery systems and consumables to allow customers a convenient application of our technology."

Chief Financial Officer Lukas Linnig emphasized with a view to the economic potential: "From the very beginning we have stated that the BEC/BMC technology has the potential to become transformational for BRAIN and its stakeholders. Today we already employ our proprietary genome editing technology within our BioScience unit having generated a unique selling point for our scientific services to industrial partners. In addition, we create milestone and royalty upside for our contract research and producer strain business. With the activation in and editing of mammalian cell lines we will now open up an entirely new chapter. The largest addressable markets are pharmacology and therapeutics. We can now jointly develop solutions and products together with partners for these very attractive end markets. In order to grant our proprietary genome-editing technology the maximum scientific attention and the financial means to grow significantly, we will push ahead and create a separate legal entity during the coming months."



Metagenomics samples were selected using rational bioprospecting and the DNA of all microorganism living in those habitats was isolated.



To perform genome editing, the BEC protein loaded with a specific gRNA is introduced into the target cell.



The native repair mechanism of the target cell repairs the DNA that was targeted by the BEC protein in a non-perfect way leading to small insertions or deletions inside the genome. This mechanism can be used to knock-out genes.



The isolated DNA was sequenced using state of the art next generation sequencing techniques and analyzed to identify novel genome editing tools



With the help of a specific spacer sequences incorporated inside the gRNA the BEC protein can be programmed to find and bind a specific region on the genome of the target cell.



The targeted DNA can be repaired by the integration of a repair fragment that researchers can design to precisely integrate genes of interest into the genome.



The selected metagenomics sequences were optimized by protein engineering to enhance the genome editing activity and specificity and one best performing prime candidate was selected (BEC).



If the programmed spacer sequence perfectly matches the DNA sequence present in the genome the BEC protein precisely cuts the DNA at the predefined position.



The BEC protein can be used to specifically knock-out or knock-in genes to optimize the genome of a variety of organisms.

Illustration: BRAIN Genome Editing, from discovery to the optimized organism © BRAIN Biotech

About BRAIN Biotech

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BRAIN Biotech AG ("BRAIN") is a leading European industrial biotechnology specialist with a focus on nutrition, health and the environment. As a technology and solutions provider the company supports the biologization of industries with bio-based products and processes. From contract R&D with industrial partners to advancing own disruptive incubator projects and customized enzyme products, BRAIN's broad cutting-edge biotech expertise and its agile teams are key to success.

BRAIN Biotech AG, Germany, is the parent company of the international BRAIN Group. The Group develops and distributes B2B specialty products, including enzymes and bioactive natural compounds. BRAIN also optimizes microbial production strains and develops processes for precision fermentation up to industrial scale. The BRAIN Group has its own fermentation or production facilities in Continental Europe, UK and the US, which together with the associated biotechnological solution competency complete the value chain within the group.

As a Participant of the United Nations Global Compact, BRAIN Biotech AG is committed to aligning strategies and operations with universal principles on human rights, labour, environment and anticorruption and to actively advance common societal goals. Our products and services target at least five of the UN SDGs directly.

Since its IPO in 2016, BRAIN Biotech AG is listed in the Prime Standard of the Frankfurt Stock Exchange (ISIN DE0005203947 / WKN 520394).

Contact Investor Relations Michael Schneiders Head of Investor Relations & Sustainability Phone: +49 6251 9331-86 Email: mis@brain-biotech.com

Media Contact Dr. Stephanie Konle PR & Corporate Communications Phone: +49 6251 9331-70 Email: stk@brain-biotech.com

Follow BRAIN Biotech on Twitter (@BRAINbiotech) and on LinkedIn (BRAIN Biotech AG)

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BRAIN Biotech AG does not undertake any obligation to update or revise any forward-looking statements.