Press release

Caszyme and Integra Therapeutics sign licensing agreement for novel CRISPR Cas12l nucleases

Stockholm, November 4, 2024. Caszyme (Vilnius, Lithuania), a pioneer in the development and application of CRISPR gene editing technology, and Integra Therapeutics (Barcelona, Spain), a company leading the way in creating advanced therapies based on next-generation gene-writing tools, today announced a licensing agreement for the use of Caszyme's **novel Cas12l nucleases to develop safer and more efficient gene and cell therapies**.

The agreement was unveiled at this year's BIO Europe, which is the largest partnering event for the biomedical industry in Europe, taking place this week in Stockholm. Over 2,800 companies attended from 60 countries, with more than 5,000 biopharma professionals in attendance.

Under the agreement, Integra Therapeutics will incorporate the genome editor **Cas12l** into its **FiCAT 2.0** **(Find and Cut-And-Transfer) gene-writing platform**, following successful *in vivo* and *ex vivo* studies, which yielded highly positive results in terms of safety and functionality in human cells. Caszyme will receive milestone payments up to 40 million. euros in addition to royalties on sales.

Cas12l is a unique CRISPR nuclease family with an effector size of approximately 850 amino acids that stands out for its small size and versatility. As the demand for efficient and safe gene-editing

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tools in therapeutic contexts continues to grow, these small nucleases represent a promising solution, combining efficacy with the practical advantages of reduced size. Caszyme-developed Cas12l shows great activity in human cells across multiple targets. Compared to other nucleases, Caszyme's Cas12l offers additional delivery possibilities, especially when combined with other effector domains. Moreover, smaller nucleases from non-pathogenic bacteria may be less immunogenic compared to their larger counterparts, further highlighting their therapeutic potential. The nucleases discovered by Caszyme exhibit different characteristics from Cas9 nucleases, which formed the foundation of the find module in FiCAT 1.0, expanding their potential applications in advanced therapies.

"Caszyme's goal is to enable therapeutic companies to develop novel, efficient and affordable gene editing modalities. This collaboration with Integra Therapeutics is a perfect alignment between two highly innovative European companies, and when successful, will help bring advanced gene editing based therapies to the market." said Dr Monika Paulė, CEO and Co-Founder of Caszyme.

Adding, Dr Giedrius Gasiunas, CSO and Co-Founder of Caszyme, said "the partnership will further Caszyme's core scientific aims – which are to develop novel, safer and smaller Cas12l nucleases that are more compatible with diverse delivery technologies, such as AAVs, mRNA and LNPs."

Dr Avencia Sánchez-Mejías, CEO and Co-Founder of Integra Therapeutics, added, "This agreement with Caszyme reaffirms our commitment with the excellence in technology development to delivery therapeutic solutions for patients with our gene-writing technology in the preclinical regulatory phase and highlights the success of the transnational project funded by the European Commission, which we launched in 2022 through Eurostars, in support of Europe's most innovative SMEs."

"The integration of Caszyme nucleases into our FiCAT 2.0 platform strengthens Integra Therapeutics' mission to develop the highest-quality gene and cell therapy products for the treatment of a wide range of genetic and oncological diseases. FiCAT 2.0 will set itself apart in the market by offering enhanced precision and efficiency," explained Dr Marc Güell, CSO and Co-Founder of Integra Therapeutics.

About Caszyme

Caszyme is a gene editing company which combines its deep experience and dynamic platform to

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deliver world class CRISPR solutions. Caszyme was established in 2017 by Dr. Monika Paule, Dr. Giedrius Gasiunas and Prof. Virginijus Šikšnys - a pioneer of CRISPR-Cas gene editing research. Over the last 7 years, Caszyme has rapidly advanced its excellence and capabilities as an enabling expert partner in CRISPR gene editing solutions, collaborating with multiple life science organizations aiming to enter the CRISPR field or expand their gene editing capabilities. Company has a long-term expertise in discovery and development of novel gene editing tools, proteins evolution and engineering, mRNA synthesis and optimization. Also Caszyme has developed a platform of unique CRISPR nucleases. This enables Caszyme partners across various industries effectively apply CRISPR gene editing technology and tools for their market-ready products. Currently, in the therapeutics field Caszyme aims to develop safer and more compact gene editing tools for treating genetic eye diseases in vivo as well as develops a CRISPR based diagnostics platform. More information: caszyme.com

About Integra Therapeutics

Integra Therapeutics is a biotechnology company developing next-generation gene-writing tools to improve the safety and efficacy of advanced therapies. It has developed the FiCAT gene-writing platform, currently in the preclinical regulatory phase. The company is also working on the first therapeutic product targeting a paediatric liver disease with no cure. Founded in 2020 as a spin-off from Pompeu Fabra University (UPF), the company is based in Barcelona and backed by international investors (AdBio Partners, Columbus Venture Partners, Invivo Capital and Takeda Ventures) as well as organisations from the health and biomedical sectors. More information: integra-tx.com

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