Seamless Therapeutics to Present New Data at ESGCT Demonstrating its Ability to Reprogram Large Serine Recombinases to Specific Target Sites in the Human Genome

-- Proprietary approach enables efficient and precise integration of gene-sized DNA cargo --
-- Seamless' zinc-finger dependent recombinases show superior target site specificity for gene editing --
-- Data will be presented in two presentations at the European Society of Gene & Cell Therapy Congress 2024 --

Dresden, Germany, and Lexington, MA, October 22, 2024 – Seamless Therapeutics today announced that it will be presenting new preclinical data, including human cell data, highlighting its unique platform's capabilities to reprogram large serine recombinases (LSRs) to target naturally occurring loci in the human genome. The company's recombinases are engineered to precisely excise, exchange, invert, or insert gene-sized DNA fragments in any target gene sequence, independent of the cell's natural DNA repair pathway. In addition, Seamless will be presenting data on its engineered zinc-finger dependent recombinases, demonstrating its ability to condition the activity of the company's recombinases to zinc-finger binding for LSRs and tyrosine recombinases (Y-SSRs). Both datasets are presented in poster sessions during the European Society of Gene & Cell Therapy Congress 2024, held from October 22 – 25, in Rome, Italy.

"The data that we will be presenting at the 2024 ESGCT Congress serve as an initial validation of our innovative approach and positions us at the forefront of next-generation gene editing technologies for developing therapeutics. We are showcasing our ability to program recombinases to recognize user-defined target sequences, bypassing the need for pre-inserted target sites and enabling seamless, efficient, and precise DNA sequence integration," said **Albert Seymour, Ph.D., Chief Executive Officer of Seamless Therapeutics.** "Our near-term objective is to translate these exciting findings into an *in vivo* model, paving our way toward progressing to the clinic. Long-term, we aim to demonstrate the technology's significant potential for creating a new class of therapeutics for indications affecting patient populations in areas of high unmet need."

Presentation Details:

P0670 - Reprogramming Large Serine Recombinases for Site-Specific Integration into Mammalian Genomes
Presenter: Teresa Rojo-Romanos, PhD, Co-founder and Head of Technology & Platform Development at Seamless
Poster Session: Poster Session IV
Presentation Date & Time: Thursday, October 24, 6:00 – 7:30 pm CEST.
Presentation Location: Concourse Level -1 and Mezzanine Concourse

Seamless' proprietary search motif enables identification of target sites in nearly all coding genes and putative human safe harbor sites, allowing for broad applicability that is not limited to pre-existing targets with high homology to wild-type recombinase recognition sites. Through directed evolution and rational design, the company engineered LSRs to recognize four natural selected target sites in the human genome. In the study, the engineered LSRs clones demonstrated high activity in bacterial cells, with good translation of activity to human cells. The selected engineered LSR, IntSTX-SH2, showed its ability to precisely integrate DNA sequences into the specific SH2 locus in human cells. Seamless further optimized the programmed LSR to IntSTX-SH2 2.0, resulting in a three-fold increase in activity as compared to the first generation and with the potential for further improvement. The company's pioneering approach for efficient and precise integration of gene-sized DNA cargo is advancing into *in vivo* studies, focusing on the liver as production site for metabolic enzymes.

P0590 - Zinc-Finger Dependent Recombinases for Precision Genome Editing
Presenter: Liliya Mukhametzyanova, Sr. Scientist at Seamless
Poster Session: Poster Session IV
Presentation Date & Time: Thursday, October 24, 6:00 – 7:30 pm CEST.
Presentation Location: Concourse Level -1 and Mezzanine Concourse

In this study, Seamless identified insertion sites for zinc-finger binding domains (ZFDs) within tyrosine recombinases (Y-SSRs) and LSRs as well as evolved variants. The zinc-finger-conditioned evolved variants were shown to be inactive without the DNA target site for the ZFD and reactivated if the DNA target site was present, ensuring that gene editing only occurs at the intended sites. The company's approach for evolving ZFDs improves the efficiency of recombinases and increases their specificity, broadening Seamless' suite of DNA editing techniques.

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About Seamless Therapeutics
Seamless Therapeutics is changing the paradigm of gene editing through a pioneering approach that has the potential to address unmet medical needs in patients with severe conditions. Our technology platform unlocks the reprogramming of recombinases, a highly versatile class of enzymes. We are applying our proprietary know-how to develop a pipeline of disease-modifying product candidates across a broad spectrum of indications to expand the therapeutic potential of gene editing.

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