News

Rentschler Biopharma and XL-protein demonstrate efficient production of a hyperactive PASylated DNase I with extended half-life

- Hyperactive DNase I modified with XL-protein's PASylation® technology demonstrated significantly extended systemic half-life in vivo, potentially offering improved treatment options for autoimmune diseases and cystic fibrosis
- Potential for high-yield manufacturing of other PASylated protein therapeutics in mammalian cell culture on Rentschler Biopharma's bioprocessing platform

Rentschler Biopharma SE, a leading global contract development and manufacturing organization (CDMO) for biopharmaceuticals, and XL-protein GmbH, a privately owned biopharmaceutical company located in Germany, announce a successful collaboration to manufacture a long-acting, hyperactive recombinant human deoxyribonuclease I (DNase I). Combining XL-protein's proprietary PASylation® technology and Rentschler Biopharma's expertise in bioprocess development, a process was developed with enhanced yield for a modified DNase I showing both strongly increased activity and an extended pharmacokinetic profile. This PASylated DNase I may open better treatment options for patients suffering from inflammation, chronic or autoimmune diseases.

"This highly successful collaboration was due to Rentschler Biopharma's strong expertise along the entire biopharmaceutical value chain ranging from cell line development, upstream and downstream processes to drug substance manufacturing in combination with XL-protein's know-how and longstanding experience in the design of proteins with enhanced stability using its proprietary PASylation technology. The strong results from this case study pave the way for high yield manufacturing of other PASylated proteins and peptide drugs using mammalian cell culture on Rentschler Biopharma's bioprocessing platform," said Thilo Grob, Vice President Process Science at Rentschler Biopharma SE.

Dr. Michaela Gebauer, Co-Managing Director at XL-protein, commented: "PASylation technology is compatible with efficient production in diverse expression hosts, and we now have shown that it can be applied to Rentschler Biopharma's robust high titer mammalian cell line development platform which also allows for native post-translational modification of recombinant human proteins. This success further demonstrates the strength and flexibility of our technology platform and its potential to support biopharmaceutical partners seeking to develop recombinant protein or peptide drugs with extended half-life and low immunogenicity."

Therapeutic DNase I has been used for more than 20 years to treat cystic fibrosis and holds the potential to be a promising treatment option for chronic as well as autoimmune diseases or inflammation. However, the short half-life of conventional DNase I requires high dosing frequency, which may result in low patient compliance and, in the case of cystic fibrosis, can lead to an elevated risk of lung infections. The improved DNase I manufactured collaboratively by Rentschler Biopharma and XL-protein has demonstrated both extended systemic half-life in an animal model and increased enzymatic activity. While its DNA-degrading activity is associated with a burden for the producing cell line, the high titer of recombinant proteinachieved in the bioprocess is a remarkable success. The clinical application of this PASylated hyperactive DNase I could potentially offer improved patient adherence and better quality of life.

About PASylated DNase I and PASylation® technology

PASylation® technology offers a biological alternative to PEGylation. The PASylated DNase I was generated using gene constructs encoding a hyperactive DNase I fused with an N-terminal PAS polypeptide comprising the small natural L-amino acids Pro, Ala and Ser in a defined sequence. The resulting modified DNase I demonstrated expanded hydrodynamic volume and a strongly extended pharmacokinetic profile in an animal model.

About Rentschler Biopharma SE

Rentschler Biopharma is a leading contract development and manufacturing organization (CDMO) focused exclusively on client projects. The company offers process development and manufacturing of biopharmaceuticals as well as related consulting activities, including project management and regulatory support. Rentschler Biopharma's high quality is proven by its long-standing experience and excellence as a solution partner for its clients. A high-level

quality management system, a well-established operational excellence philosophy and advanced technologies ensure product quality and productivity at each development and manufacturing step. In order to offer best-in-class formulation development along the biopharmaceutical value chain, the company has entered into a strategic alliance with Leukocare AG. Rentschler Biopharma is a family-owned company with about 1,100 employees, headquartered in Laupheim, Germany, with a second site in Milford, MA, USA. In Stevenage, UK, Rentschler Biopharma has launched a company dedicated to cell and gene therapies, Rentschler ATMP Ltd.

About XL-protein GmbH

XL-protein is a German biotech company commercializing its ground-breaking PASylation® technology, which enables the design of biopharmaceuticals with extended half-life and enhanced pharmacological action. Based on a strong proprietary technology position, XL-protein focuses at the preclinical as well as clinical development of PASylated proteins in diverse disease areas. XL-protein is engaged in a growing number of partnerships with international pharmaceutical and biotech companies at various levels.

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