



Scaling up success: Novel enzymes produced by antibiotic-free fermentation technology are now in a routine supply.

Greifswald (Germany) & Seraing (Belgium), April 27, 2023 – Enzymicals and Syngulon present an update about their non-exclusive license agreement of May 2020 on the use of Syngulon's antibiotic-free technology to produce enzymes. After successful completion of an R&D phase and the start of largescale production, the developed enzyme products are now in a routine commercial stage. The expansion of internal production capacities as well as the extension of the use of the technology to new products is currently being planned.

Enzymicals AG, a German enterprise focusing on industrial biocatalysis and Syngulon SA, a Belgian synthetic biology company developing original genetic technologies using bacteriocins, announced in April 2022 the start of the antibiotic free large-scale production of enzymes for a world leading diagnostics company. Demonstrating successful scale-up is particularly important in the biotechnology sector, as a key purpose of innovation in this industry is to achieve large-scale impact on sustainability and green transformation. This success story is now extended by the establishment of routine production of these products and their positioning in the competitive environment.

Recombinant protein production has revolutionized the biotechnology industry, providing a reliable source of valuable proteins for medical, industrial and research purposes. However, traditional recombinant expression systems often rely on the use of antibiotics as selection markers, which have negative impact on the environment like the spreading of antibiotic resistance. Syngulon's technology addresses this challenge and offers advantages over antibiotic selection. Enzymicals is active in industrial enzyme technology since more than a decade providing proven solutions for enzyme development and process scale-up of cell-free manufacturing. The two companies recognized that by combining their strengths, they can bring novel enzyme products to market more efficiently having a unique selling point in sustainable production.





The collaboration partners successfully scaled up the antibiotic-free production of recombinant enzymes up to a 500-liter fermentation scale followed by a downstream process adapted to process the respective quantities of biomass in the required quality. The use of the bacteriocin-based selection marker technology, combined with smart process engineering and a metal-chelate affinity-based purification system, were key to achieve the desired quantities in the required quality and purity. Fundamental basis for this was the careful selection of suitable sequences with high catalytic activity and promising producibility in the initial R&D phase and their seamless integration into bacteriocinbased vectors systems. Finally, a high yield of the target enzymes while reducing the overall production cost makes the process more efficient and cost-effective. The enzymes are now in a routine supply stage which means that the customer can rely on consistent quality and delivery times.

Dr. Erik de Vries, CEO of Enzymicals AG, states: "The biotechnology industry is constantly evolving, with new technologies and approaches emerging all the time. One of the keys to success in this industry is collaboration between different companies with complementary strengths and expertise. In this example, Syngulon focused on providing efficient selection marker technology and Enzymicals on enzyme and process development with scale-up. We successfully joined forces to bring novel enzymes to commercial production scale."

Guy Hélin, CEO of Syngulon SA, added: " It is always a pleasure to witness how our versatile, antibioticfree selection technology can be adapted to a range of industrial contexts, from industrial biotech applications to pharmaceuticals, including the production of enzymes. Our fruitful and synergistic collaboration with Enzymicals is an excellent example. Following the implementation phase, they are now fully autonomous in their use of our technology.."

In conclusion, the use of antibiotic-free expression systems is the future of recombinant protein production. These systems provide a safer, more responsible and more sustainable alternative to traditional methods, while still delivering high yields of recombinant protein. By choosing this expression strategy, companies can demonstrate their commitment to the environment and public health, while still achieving their protein production goals. Enzymicals and Syngulon are pioneers in this field with their respective competences and are happy to support you in your projects.





About Syngulon

Syngulon is a synthetic biology startup developing original genetic technologies. The team of scientists works in collaboration with different academic partner laboratories including a.o. UCLouvain, ULB, ULiège, UNamur in Belgium, INRAE in France and Imperial College, UCL in UK. R&D programs of Syngulon are supported by the Walloon Region of Belgium.

Syngulon's selection technology expands the capacity for selection of microorganisms. Synthetic biology uses the concept of "bioengineering" to improve or modify existing genetic systems to create microbes with desired behaviors, and Syngulon uses this approach to develop its selection technology (with issued patents in EU, USA, India, China and Brazil). It is based on bacteriocins, ribosomally-produced peptides naturally made by most bacteria to kill competitive microbial species. Syngulon owns the largest collection (PARAGEN) of natural and synthetic bacteriocins.

About Enzymicals

With technologies, products and offerings for the industrial implementation of cell-free manufacturing (also known as biocatalysis), Enzymicals supports the global industry to enable the change to biologically-inspired production concepts.

Enzymicals is your experienced partner for industrial biocatalysis from g to ton-scale with more than a decade of experience. Our experts offer their expertise in the use of enzymatic processes for complex chemical synthesis, from initial catalyst-lead finding to process optimization and scale-up. Core working principles are high quality R&D, professionalism and customer satisfaction. By this our company adds value with tailor-made enzymes, customized chemicals and individual process solutions and enables greener and safer manufacturing procedures.