

From license to large scale manufacturing

Taking you to the next step

Our CMO service

- Efficient transfer of biomanufacturing processes into GMP production
- Integrated fermentation and purification process development
- Development of robust, reproducible and scalable processing methods
- Cell banking
- GMP production



With over 15 years experience in the contract manufacturing of pharmaceutical-grade biological APIs, Novozymes guarantees technical and regulatory support to streamline your drug development pipeline.

Efficiency, traceability, reproducibility and flexibility

Operating as an independent CMO, we offer microbial fermentation and purification of biological compounds from preclinical up to commercial scale. The manufacturing operations are supported by process development, cell bank establishment and characterization, scale-up and optimization of biotechnology processes and process validation.

At our EMEA- and FDA-approved production facilities, all equipment, installations and procedures are validated and fully documented according to cGMP. We are authorized to produce biological material for medicinal purposes and are able to handle recombinant and native organisms as well as moderate risk class 2 pathogens. A separate cell banking facility is also available for spore-forming organisms.

Capacities ranging from 1 to 5000 liters enable us to run both large and small projects simultaneously, giving equal commitment to projects of all sizes.

Combined expertise for seamless transfer

With a flexible and fully transparent approach, Novozymes is your strategic partner throughout the lifetime of the development process and beyond. All of our standard operating procedures and programs can be easily adapted to your specific requirements to enable seamless transfer from discovery and research through to clinical trials and market supply.

Express your interest in albufuse™ today:

Email: albufuse@novozymes.com

Web: <http://biopharmaceuticals.novozymes.com>

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Both Novozymes Biopharma UK Limited and Novozymes Biopharma AB are wholly owned subsidiaries of Novozymes A/S based in Bagsvaerd, Denmark.

novozymes
Rethink Tomorrow

albufuse™
technology

HALF-LIFE EXTENSION
THROUGH ALBUMIN
FUSION

To discuss how we can bring your product to market, please refer to the contact details for Novozymes Biopharma AB at the back of this brochure



albufuse™ technology

HALF-LIFE EXTENSION THROUGH ALBUMIN FUSION

Enhance your active molecule with Novozymes

The key advantages of albufuse™ technology include:

- Increased half-life of the active molecule, resulting in:
 - Less frequent administration
 - Increased bioavailability
- Reduced dose rates
- Reduced side effects
- Possible reduction in immunogenicity
- No requirement for post-production chemical derivatization such as PEGylation
- Single source license for production and half-life extension technologies
- Competitive production costs

Injected biotherapeutics may be rapidly cleared from the circulation after administration, requiring high dose rates or frequent administration to maintain effective therapeutic levels. To overcome these problems, proteins and peptides can be genetically fused with albumin to enhance their bioavailability.

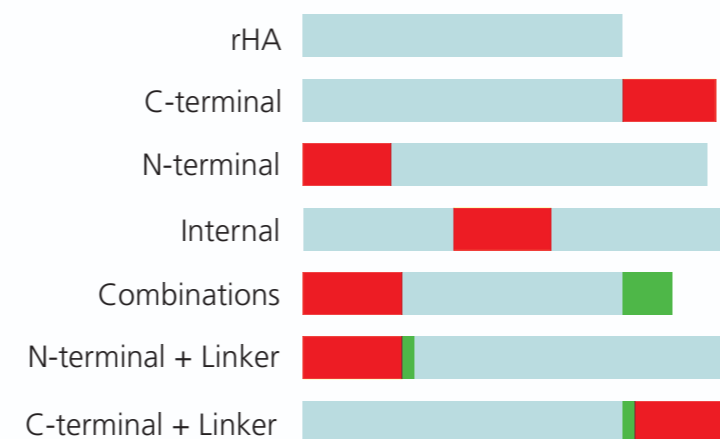
albufuse™ technology is proven to enhance active molecules in a range of pre-clinical studies and is being clinically evaluated in human therapeutic applications

Albumin fusion technology

Building on our proprietary expertise, Novozymes has developed albufuse™ technology to enable the genetic fusion of a client's target protein to albumin at the molecular level. The resultant moiety is secreted as a contiguous peptide linked via a peptide bond.

We have extended our capabilities in protein expression by engineering our yeast *Saccharomyces cerevisiae* to produce albumin fusion proteins (AFPs) in an animal component free system.

albufuse™ technology represents a simple but flexible platform for the production of proteins with extended circulatory half-life. The following schematic illustrates at a molecular level the possible construct fusion variants with recombinant human albumin (rHA).



albufuse™ technology offers a single step expression solution eliminating lengthy and costly post-production chemical processing such as PEGylation.

Demonstrable half-life extension

We have presented pre-clinical data that has demonstrated the extension of circulatory half-life of a number of therapeutically relevant proteins. Comparisons of fused vs. unfused molecules showed that all fusions were active and had a significantly extended half-life of between 5-74 fold i.v. and 4-12 s.c. administration.

In addition, scFv fusions have been shown to extend the *in vivo* residence time of the scFv whilst retaining their ligand binding properties.

One of our licensees (Human Genome Sciences Inc.) has also demonstrated the advantage of this fusion technology in the production of Albuferon™ – a fusion of albumin and interferon alpha. In human clinical studies Albuferon™ has been shown to be biologically active and has the potential to allow a less frequent dosing regime in comparison to a daily dosing regime for the unfused moiety.

Extensive technical expertise and support

Located in Nottingham, UK, our FDA and Health Canada inspected, cGMP-compliant manufacturing site has an 8000L fermentation capacity, which has been commercially producing recombinant albumin since 1995.

Novozymes' yeast based expression technology is the gold-standard in microbial protein expression and provides the perfect vehicle for our albufuse™ technology.

Our protein expression pedigree is one of the most impressive in the industry, producing Recombumin®: the only commercially available, cGMP recombinant human albumin approved for use in human therapeutics.

Our in-house technical capabilities include integrated teams responsible for:

- Molecular biology manipulation of yeast and protein engineering
- Fermentation
- Process development
- Analytical techniques

Proven track record in fusion technology

Using highly developed, commercially proven proprietary strains and a 2-micron plasmid, our expression system can be easily manipulated in direct response to our customers' requirements. We have successfully expressed over 50 fusions, secreted at a high level up to 5g/L. Those characterized to pre-clinical study stage include growth hormone, cytokines, endostatin, HIV inhibitory peptides, IL1-receptor antagonists, IL10 and IL11.

The latest key application for albufuse™ technology is in the increasingly important area of antibody fragment expression where our scientists have achieved high-level expression of scFv albumin fusions of >5g/L.

We have effectively partnered with all levels of the industry from pharmaceutical majors and healthcare companies to young biotech start-ups.

One-step licensing solutions

Access to albufuse™ technology is just a conversation away. Novozymes' extensive IP portfolio, encompassing albumin fusion and our core proprietary expression system, allows us to offer flexible licensing terms as part of our business model.

For albufuse™ technology we offer a single license package for expression and fusion technologies which avoids the extra costs and IP issues associated with alternative chemical based methods.

Take the first step to enhance your product and talk to us

For a portfolio of publications on yeast based expression technology visit our website: <http://biopharmaceuticals.novozymes.com>

To discuss the use of albufuse™ technology in your application please refer to the contact details for Novozymes Biopharma UK at the back of this brochure