

We are a specialist in Protein production and Immunotherapeutics*

Developing Innovative Immunotherapeutics

Process development: From Gene to Product offering complete cGMP Production

As one-stop-shop we offer a wide range of services for

- Feasibility studies
- Strain development
- Optimized fermentation of your protein
- Development of the downstream production process
- Development of a full set of analytical methods
- Innovative technologies for further improvements
- cGMP consulting
- Full cGMP production in a state-of-the-art facility
- Quality management and quality operations incl. batch release

Profit from our expertise to develop new Immunotherapeutics - offering the cutting edge in fighting

- cancer
- inflammation
- auto-immune diseases
- and possibly more

a spin-off of  **Fraunhofer**
IME

... one of the largest research organizations in the world
with an annual budget of well over 1 billion US\$

Pharmedartis

FOUR BUSINESS SEGMENTS

Pharmedartis GmbH is a biotechnology company founded by experienced scientists of the Fraunhofer Institute for Molecular Biology and Applied Ecology (IME) in Aachen, Germany. We provide innovative solutions for the production, characterization and modification of proteins. While we now emphasize on biopharmaceuticals we still like to serve our roots in supporting the Feed, Food and Fine Chemicals companies. Following a hybrid business model Pharmedartis is active in four segments:

1. Feasibility studies and Process development

According to your special needs we select the appropriate production system. You select from a broad spectrum of production systems (bacteria, yeasts or mammalian cells). Upon your request we are aiming to optimize the strain. An in-depth analysis of all process parameters such as media constitution, fermentation strategy, up-scaling or development of purification strategies will lead to an optimized production process. Based on the latest technologies we can develop a full set of analytical methods for you.



40 L pilot fermentation

source: Fraunhofer/IME

2. Production of recombinant proteins and peptides

Using our proprietary strains of *Hansenula polymorpha* and *Arxula adenivorans* or the protocol of periplasmic expression in *E. coli* we are able to produce your protein at high efficacy and in accordance with regulatory and economic requirements. Several other production systems such as mammalian cells or plant cell lines are also available. We are also prepared to employ your own systems as well.

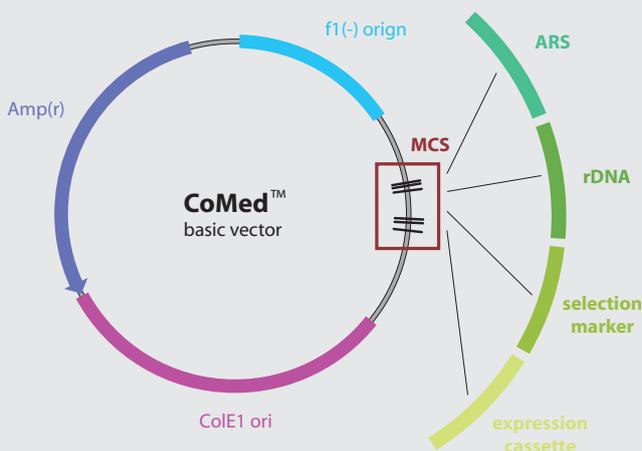
A broad range of fermentation equipment (1 L - 350 L) is available to supply you with product according to your desire. Selecting from the various options for down-stream processing (AEX, CEX,

IMAC, Protein A, gel filtration) we are able to purify the protein to your special needs. While offering our clients a direct cost advantage, we wish to participate in the mutual benefits. Pharmedartis is not always the typical fee-

Pharmedartis is a full-service provider to the Biotech and Pharma industry offering as one-stop-shop everything from gene to product including cGMP produced clinical trial APIs up to phase III.

for-service provider, but offers innovative models for your development and production needs.

Based on its broad technology platform and backed by co-operations within the Fraunhofer network Pharmedartis offers its clients tailor-made solutions for their specific requirements as well as additional services such as the preparation of cell banks, peptide mapping, protein modification or development of analytical methods.



Selected module elements

Module 1: ARS, HARS, CEN

Module 2: rDNA elements from *A. adenivorans*, *H. polymorpha*

Module 3: LEU2 (*A. a.*, *S. c.*), dLEU2, URA3 (*S. c.*), TRP1 (*S. c.*, *A. a.*), kanMX, hph

Module 4: promoter, MCS, MOX or TEF, terminator
 promoter: TEF1 (*A. a.*, *A. g.*), TPS1 (*H. p.*), NR (*H. p.*), GAP (*S. c.*, *H. p.*), AOX (*H. p.*, *P. p.*), FMD (*H. p.*)

ARS: Module 1 - replication in yeast

rDNA: Module 2 - genome integration

selection Marker: Module 3 - transformant selection

expression cassette: Module 4 - gene expression

3. Intellectual Property and Licensing

Pharmedartis holds a strong and expandable portfolio of patents in regards to protein production. In particular the **CoMed™** system, for which patent protection was recently filed, will be established as a new standard for the development of industrial production processes. We offer **CoMed™** for use in the development and production of recombinant proteins for various applications such as Biosimilars or novel Immunotherapeutics. In addition Pharmedartis has covered its expertise in the field of Immunotherapeutics by five patent families.

4. Development of new drugs and diagnostics

Patent protected developments of innovative Immunotherapeutics and Immunodiagnostics.

FEASIBILITY STUDIES

One of the first steps in the development of Biopharmaceuticals is the selection of the expression host. A key lesson learned over the last 20 years is the need to find at an early stage of the development process the right combination of gene of interest, vector system and host organism. This combination must allow for the efficient production of your targeted protein.

Pharmedartis supports you in a combined effort to establish a process of high quality acceptable to the regulatory authorities and easy and cost-effective to implement.

The long history of unpredictable misfortune in selecting an appropriate expression host has led Pharmedartis' scientists to develop a new – first in its class – decision tool for cost-effective and reliable selection of yeast expression hosts.

The **CoMed™** vector system permits rapid and reliable evaluation of major yeast expression systems. It features a variety of universal rDNA targeting sequences and numerous strong promoters. The variety of available selection markers offers great flexibility, but will also be constantly expanded. *Hansenula polymorpha*, *Pichia pastoris*, *Saccharomyces cerevisiae*, *Arxula adenivorans* and *Yarrowia lipolytica* are being tested on a routine basis. Many more can be evaluated on demand.

Proprietary strains of *Hansenula polymorpha* and *Arxula adenivorans* are available. To interested parties we grant a restricted license on the **CoMed™** system.

Working with Pharmedartis using its unique concept, its innovative production methods as well as the small and affordable feasibility studies, representing state-of-the-art technology, will offer a significant advantage for you. In addition we can offer a broad range of sophisticated technologies such as DNA sequencing, microarray technology, 3-dimensional imaging, confocal microscopy, fluorescence and radioisotope image detection, high-throughput cell screening, flow cytometry, cell sorting, real time analysis of biomolecular interactions, protein crystallography, electrospray mass spectrometry, MS/MS protein identification or thermal analysis (e.g. DSC) to be implemented in your project.



GMP fermentation volume of 350 L

source: Fraunhofer-IME

Pharmedartis develops complete production processes and welcomes licensees.

Pharmedartis develops complete processes for innovative recombinant proteins for all applications.

cGMP MANUFACTURE

GMP compliance is mandatory for the production of biotechnological APIs even for clinical trials. Efficient production of biotechnological APIs under cGMP regulation requires a highly specific knowledge base, difficult to establish at small biotech and even mid-sized fully integrated pharmaceutical companies. In addition, establishing cGMP manufacturing capacities demands enormous capital investment and years in design and construction as well as recruitment of appropriate personnel and establishment of efficient organizational structures.

The most appropriate and now generally accepted solution to bridge this gap is to utilize Contract Manufacturing Organizations (CMOs) specialized on cGMP for biotechnological APIs. Clearly choosing the best partner for your specific needs is crucial for the economic success of your product.

However, key requirements are our uncompromising focus on quality, flexibility and sound scientific base: all provided by Pharmedartis and its partner, the Fraunhofer IME.

Pharmedartis develops innovative and cutting-edge Immunotherapeutics fighting cancer, inflammation and auto-immune Diseases.

Fraunhofer has granted its spin-off Pharmedartis the exclusive marketing rights for its newly built state-of-the-art GMP facility in Aachen, Germany.

DEVELOPMENT OF NOVEL IMMUNOTHERAPEUTICS

Pharmedartis investigates methods to improve the generation of cytokines. This will open up completely new areas of clinical applications.

The new Immunotherapeutics to be developed by Pharmedartis will tackle major indications, but it is also planned to develop therapies for niche markets with major unmet needs. The project progress driven by Pharmedartis will usually not go beyond phase II of clinical development. It is even preferred by Pharmedartis to find partners for development or total out-licensing as early as end of phase I. Pharmedartis will also out-license its tool-box of human toxins for specific immunotherapy in several additional indications. In addition, Pharmedartis already has several projects of completely new recombinant Immunotherapeutics (apoptotic substances, immunokinases and recombinant immunotoxins) and Immunodiagnostics underway, for which it already has applied or will apply shortly for patent protection.

Interested?

We welcome to work with you, prepare answers and solutions tailor-made to your needs. From the very beginning you will have only one primary contact person to address all your specific matters.

You may visit us at any time and also have a look around the Fraunhofer IME, one of the leading Research Institutes in Germany. Please contact us at:

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source: Fraunhofer-IME