

# Commercializing Antibodies

In light of favorable demographic trends projected over the next few years, considerable growth rates can be expected in the future for innovative drugs. Of ever-increasing importance is the role played by therapeutic antibodies for the treatment of a variety of diseases such as cancer, inflammation or autoimmune diseases. Another important market for the use of MorphoSys' HuCAL<sup>®</sup> antibodies are new antibody research applications.

## Commercial Application of HuCAL<sup>®</sup>



### Commercializing the HuCAL<sup>®</sup> technology with collaboration partners

MorphoSys offers different types of business models through which partners can access the HuCAL<sup>®</sup> technology. Within the scope of the collaborations, the technologies are used for the development of human antibodies in the areas of research, diagnostics and therapeutics.

### Developing and commercializing a proprietary product portfolio

MorphoSys is currently developing therapeutic antibodies in the areas of cancer and inflammation. The aim is to obtain a partner prior to the start of clinical development.

### Exploitation of HuCAL<sup>®</sup> in research – Antibodies by Design

MorphoSys initiated a new business unit, Antibodies by Design. The aim of Antibodies by Design is to establish the HuCAL<sup>®</sup> technology as an industrial standard for making research antibodies.

## Possible Uses of Antibodies

Antibodies are part of the body's principal defense mechanism. They are themselves proteins and each individual has more than one billion different antibodies. An antibody is able to recognize and bind to a specific molecular structure on a potentially disease-related target. This binding process triggers a number of physiological reactions which can protect, or can be used to protect, humans against disease in a number of different ways. Antibodies can thus be applied as:

Antibodies are proteins naturally produced by humans and form a key element of the immune system.

- **Therapeutic substances**, since antibodies, when administered to the human body, can
  - (1) bind to and block the disease-related target from negatively affecting healthy structures in the body,
  - (2) transport a therapeutic “effector function”, where the effector can, for example, act upon cancer cells expressing the disease-related target by triggering their death;
- **Diagnostic substances**, whereby the antibody can identify certain structures on a disease-related target and can, for example, if combined with a radioactive marker, reveal the location and severity of the disease;
- **Tools assisting the research and development of drugs** by detecting and isolating proteins, determining where these proteins are distributed and made in the body, and mapping which molecules they interact with, in order to ultimately determine biological function.

Antibodies are therefore indispensable reagents for the advancement of the understanding of diseases, and the development of either conventional small-molecule (chemical) drugs or antibody therapeutics.

## The Market for Antibodies

The market for therapeutic antibodies is estimated to grow at more than 30% over the next several years. In 2003 annual sales amounted to over 5 billion US\$.

The success of biotechnology in medical research as well as in the development and manufacture of drugs is now well established. Moreover, the pressure to innovate is very high: of the 30,000 diseases known today, only 10,000 can be treated adequately.

Antibodies play an important role in the pharmaceutical industry. Today, roughly 20% of the biotechnological products on the market are antibodies. Therapeutic antibodies are the fastest-growing class of drugs in the pharmaceutical market. With global sales growth rates of more than 30%, the importance of antibodies in modern medicine continues to increase. In 2003, the number of approved antibodies increased from 12 to 16, and more than 200 therapeutic antibodies are currently in clinical development.

The continuing success of antibodies is due to several main factors. First, technological advances now allow fully human antibodies to be generated with relative ease. Being fully human, these antibodies have very few side effects and are ideally suited to use in certain diseases such as cancer. Second, the recently completed decoding of the human genome will allow for a better understanding of diseases, and thus additional points for therapeutic intervention using drugs such as antibodies. Last but not least, antibodies have well-understood properties and can be rapidly made against virtually any target.

Currently 16 antibodies are on the market and more than 200 therapeutic antibodies are in clinical development—a clear sign of the potential of therapeutic antibodies.

Product	Origin	Indication	Approved
OKT3	Murine	Transplant rejection	1986
ReoPro	Chimeric	Cardiovascular	1994
Rituxan	Chimeric	Cancer	1997
Zenapax	Humanized	Transplant rejection	1997
Simulect	Chimeric	Transplant rejection	1998
Remicade	Chimeric	Inflammation/ autoimmune diseases	1998
Synagis	Humanized	Virus infection	1998
Herceptin	Humanized	Cancer	1998
Mylotarg	Humanized	Cancer	2000
Campath	Humanized	Cancer	2001
Zevalin	Murine—radiolabeled	Cancer	2002
Humira	Human (PCR library)	Inflammation/ Autoimmune diseases	2002
Bexxar	Murine—radiolabeled	Cancer	2003
Xolair	Humanized	Cancer	2003
Raptiva	Humanized	Inflammation/ autoimmune diseases	2003
Erbitux	Chimeric	Cancer	2003

## The MorphoSys Strategy

The Company's strategy is to commercialize its proprietary HuCAL<sup>®</sup> technology for the development of antibodies as therapeutics, diagnostics and research reagents. Thereby MorphoSys can create significant value and support the future growth of the Company.

The MorphoSys business strategy is based on its proprietary antibody technology HuCAL<sup>®</sup>. This technology makes it possible to produce fully human antibodies which can be easily optimized. HuCAL<sup>®</sup> is distinguished from other antibody technologies by its unique ability to systematically improve the functional characteristics of the antibodies. Additionally, these antibodies can be easily optimized, labeled, or formulated in different formats.

The goal of systematically optimizing active substances for use as drugs has been pursued in drug development for decades. MorphoSys technologies now enable this systematic optimization process for antibodies. The use of HuCAL<sup>®</sup>, the leading technology in this field, allows MorphoSys and its partners to develop better, wholly novel antibodies for use as drugs.

MorphoSys intends to become profitable by providing high value-added services relating to therapeutic antibody generation as well as target discovery for pharmaceutical and biotechnology companies. MorphoSys has recently added proprietary antibody products to its offering. In this way, the Company will add significant value to its current capabilities, and at the same time deliver what the industry currently desperately seeks—more novel therapeutic products to combat disease.

### **Key elements of the Company's business strategy include:**

#### **1. Commercializing MorphoSys' HuCAL<sup>®</sup> technology with collaboration partners**

To accelerate drug discovery and develop new, premium-priced drugs, pharmaceutical companies require new technologies for discovering active substances, as well as methods for identifying new disease-associated target molecules against which those drugs can be directed. MorphoSys exploits the full potential of antibodies as research tools and products in their own right by making them rapidly and reliably available through its HuCAL<sup>®</sup> GOLD library. MorphoSys believes that HuCAL<sup>®</sup> GOLD is superior to competing technologies and thus believes it can establish HuCAL<sup>®</sup> GOLD as an industry standard for antibody generation.



MorphoSys offers its partners support in order to identify specific antibodies

In addition to licensing its HuCAL<sup>®</sup> technology, MorphoSys commercializes its proprietary technology and expertise by collaborating with pharmaceutical and biotechnology companies in the areas of therapeutic antibody generation and target validation. Through licensing and collaboration agreements with companies that are developing antibody-based therapeutics and are seeking to outsource a portion of their research functions, MorphoSys offers a combination of the use of its technologies and the support of its scientists in order to identify antibodies with certain characteristics and to optimize their specificity and affinity to the defined target on its customers' behalf.

MorphoSys has expanded its HuCAL<sup>®</sup> technology with further technology platforms and services. MorphoSys works in close cooperation with several of its partners in the high-throughput generation of antibodies. MorphoSys generates antibodies for these partners and, on request, performs additional investigations and characterization of these antibodies. The results enable the collaboration partners to carry out further research more quickly to develop and market a therapeutic product.

MorphoSys intends to further expand both forms of collaboration with partners in order to generate revenues, e.g. through up-front payments, annual payments, research and development contributions as well as milestone and royalty payments.

## 2. Developing and commercializing a proprietary product portfolio

MorphoSys intends to build value by developing its own product portfolio. The Company is currently developing proprietary therapeutic antibodies in the areas of cancer and inflammation, and intends to continue to invest in new programs in these areas. In this regard, the Company aims to demonstrate efficacy in animal experiments for its antibody candidates before seeking a development partner. In contrast to the business described with collaboration partners, the Company carries all the costs of development prior to partnering. However, the level of payments in the form of up-front fees, milestones and royalties that can be reached on outlicensing typically exceed those possible in the partner-initiated business.

### 3. Exploitation of HuCAL<sup>®</sup> in antibody research—Antibodies by Design

In 2003, MorphoSys initiated a new business unit, Antibodies by Design, in order to more fully exploit the commercialization of the HuCAL<sup>®</sup> technology in antibody research applications. The aim of Antibodies by Design is to establish the HuCAL<sup>®</sup> technology as an industrial standard for making research antibodies. More specifically, the unit's current focus is on producing custom-generated research antibodies for potential partners, on a per antibody basis. In this capacity, Antibodies by Design can supply a client with high-affinity antibody reagents within eight to twelve weeks—significantly faster than other technologies currently can.

#### Antibodies by Design Management Team



**Dieter Lingelbach**  
Senior Vice President



**Joanne Crowe**  
Senior Director  
Marketing & Sales



**Dr. Achim Knappik**  
Senior Director  
Research & Development

### Future Growth Opportunities

Through collaborations concluded with pharmaceutical and biotechnology companies such as Pfizer, Bayer, Centocor and Schering, MorphoSys generates short-term revenue from license fees for access to technology, research support, and payments for completed work. In the medium term, the Company benefits from performance payments for the achievement of so-called milestones. In the long term, there is additional growth potential: if a product derived from the HuCAL<sup>®</sup> technology is approved for the market, MorphoSys has a stake in the revenue in the form of royalties.

By developing its own therapeutic antibodies, MorphoSys has extended its business model, and thereby its future growth prospects. In MorphoSys' proprietary programs, the aim is to obtain a partner prior to the start of clinical development who will assume responsibility for the further clinical development and commercialization of the products. Higher user fees and royalties are to be expected for outlicensing such product candidates than through fee-for-service deals, and as such offer the Company's shareholders greater value and upside.