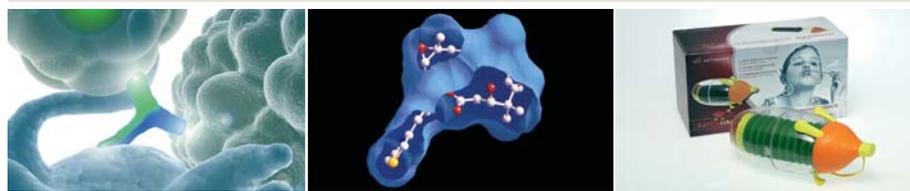


# informati - on

Ascenion Information Letter  
April 2008

## IP Value Becomes Tangible

For Ascenion and its partners, the past year has heralded a new era: The transfer of inventions from public research to industry has started to yield fruit in the form of therapeutic products.



In April, Activaero, a spin-out from the Helmholtz Zentrum München (formerly GSF) launched its innovative "Watchhaler®" inhalation device for children. In October, Bristol-Myers Squibb (BMS) gained marketing approval for Ixempra®, a new chemotherapeutic agent for the treatment of cancer originating from the Helmholtz Centre for Infection Research (HZI), and in December, Fresenius Biotech filed a market authorization application for removab® with the European Medicines Agency (EMA). Removab® is a novel trifunctional anti-cancer antibody that was designed by TRION Pharma, another spin-out from the Helmholtz Zentrum München and co-developed with Fresenius Biotech. If the EMA grants approval, the first antibody therapy "made in Germany" will hit the market.

For the inventors and research institutions, these successes will provide financial reward for the work they have done that is expected to range from 0.5 to 5 million Euros per year. This will increase public awareness that the

transfer of inventions from federally funded research brings tangible benefits – in the form of new companies, jobs and products that enhance people's lives. At the same time, it also becomes clear that it takes patience and perseverance to bring new inventions to market. Activaero and TRION Pharma were both founded in 1998, and HZI's epothilone technology, that forms the basis for Ixempra®, was licensed to BMS in 1997. These examples show that we need to think in decades. In selected cases, this means that we advise our partners to accept moderate short-term income in return for considerable long-term revenue potential. As a result, we have been able to build a pipeline of revenue-carrying agreements that should deliver a new stream of revenue in the above-mentioned range every few years. With the positive product news of 2007, we believe that our sustainable IP strategy will soon pay off for our partners and endorse an overall long-term perspective to technology transfer in Germany. Christian Stein, CEO of Ascenion

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## BioVaria 2008 – Germany's Next Top Technologies



Interview with Prof. Dr. Günther Wess,  
Scientific and Technical Director  
of the Helmholtz Zentrum München,  
keynote speaker at BioVaria 2008



**Q:** Before taking up the position of Scientific and Technical Director of the Helmholtz Zentrum München in November 2005, you held various leading positions in industry, most recently as head of drug development in Europe for Aventis and member of the discovery board of Sanofi Aventis. From the industry's perspective, what do you believe are the key issues in partnering with public research institutions?

The key issue has always been that there is not enough information exchange and interaction between industry and academia, in particular in Germany. There is definitely a lack of common understanding on opportunities that could be pursued as joint efforts. Too much research is still done in disciplinary silos, access to new technologies is not always guaranteed and critical capabilities like chemical biology are often missing.

**Q:** And from your current point of view as leader of an internationally renowned public research organization, what do you consider to be the major hurdles to forging deals with industry?

First, we need to identify more common ground and learn from each other. Cherry picking by industry is understandable but will

not help to improve the situation long term. Partnership should be based on fair sharing of risk and reward. Public research often needs to improve its IP position, and with a reasonable degree of effort could significantly increase the value of its research.

**Q:** What is your strategy for the Helmholtz Zentrum München to help overcome such hurdles?

To address the grand challenges in medicine, new styles of partnership between industry and public research are required. We therefore have to develop, implement and fund a new model for applied research co-operations. This will include, for example, staff exchanges between industry and academia, and equipping people with a broader skill base in science, management and leadership. As I already mentioned, we will have to learn from each other and discover common ground.

**Q:** Do you have any specific recommendations to industry, technology transfer professionals or policy makers to improve technology transfer in Germany?

Greatly increased funding of basic research is needed in Germany. Politics has to demon-

strate commitment and encourage global companies to open research facilities in Germany. Compared to the U.S. there is a huge funding gap for basic research in Germany. In addition, new models are needed to provide money for early applied research to help researchers reach a reasonable milestone that is attractive to industry.

**Q:** Given the plethora of partnering events around the world, why do we need BioVaria?

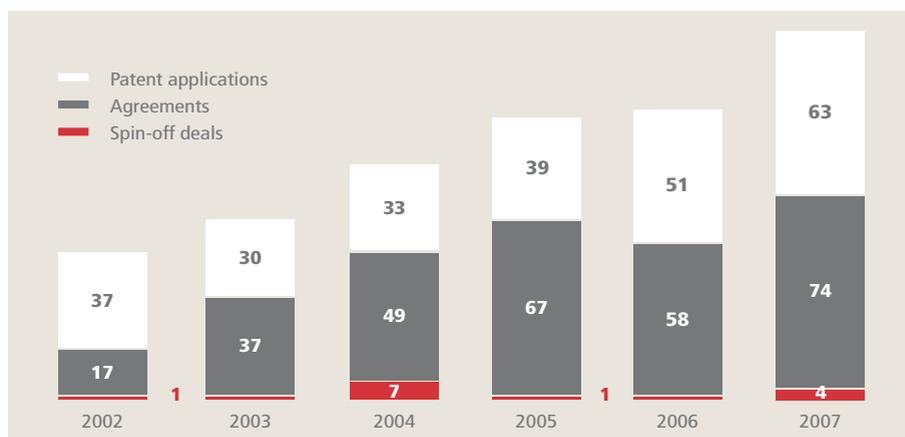
BioVaria is a partnering event tailored to the needs and problems faced by research here in Germany that I have just mentioned. Plus, in spite of global communication media, direct co-operation and regular face-to-face meetings greatly facilitate work flow and efficient collaboration.

**Q:** For all ditherers, can you provide a good reason to attend the event?

The conference provides a platform for public research organizations to present their innovative technologies and new therapeutic approaches. Industry representatives will have the opportunity to discuss these results directly with the inventors. Hopefully, this will lead to the establishment of successful cooperations.

## Ascension's Results in 2007

In terms of spin-off deals, agreements and patent applications, Ascension outperforms the European average according to ASTP standardized performance measures\* for technology transfer. More than 2 million Euros were earned in 2007, including revenues from licence, cooperation and material transfer agreements as well as proceeds from equity deals that were passed on to the Life-Science Foundation for the Promotion of Science and Research. With market approval of first therapeutic products originating from Ascension's partner institutions, the team expects a continuous increase in revenues in the coming years.



\* Performance per 1,000 research staff according to the Association of European Science and Technology Transfer Professionals (ASTP), most recent data from 2006

## Spinning Innovation

With three new shareholdings, three exits and two GO-Bio awards, Ascenion's spin-out activities and support have gained pace in recent months. In addition, a range of new funding tools spanning the whole spin-out process from initial business planning through the seed and start-up phase, may help getting new businesses professionally prepared and started. For further information on the funding landscape see our Newsletter Special on the 2nd Biotech-NetWorkshop at [www.ascenion.de](http://www.ascenion.de) or contact us directly.

### MedTherm: Heat-shock for tumours

It was the mid 1980s, when Prof. Rolf Issels, Medical oncologist and head of the clinical cooperation group "Hyperthermia" at the Helmholtz Zentrum München, began to explore the therapeutic value of regional hyperthermia (RHT), i.e. the heating of distinct areas of the human body to 40-44°C using electromagnetic waves.



It has long been known that these temperatures cause stress to all cells, but Issels and his team demonstrated that they also make malignant cells more susceptible to the body's immune defences, radiation and chemotherapy. In more than 20 years of intense research, the team has built a profound body of knowledge on RHT and its clinical effects and revealed new insights into the underlying biological mechanisms.

Last year, the positive outcome of a phase III clinical trial delivered final proof-of-concept: Soft tissue sarcoma patients showed improved response and disease-free survival when treated with RHT in combination with systemic chemotherapy in addition to surgery and radiation. These results gave impetus to the formation of MedTherm GmbH in late 2007. Key objectives are to broaden clinical research on RHT, increase its acceptance by statutory health insurances and integrate it into standard treatment schemes to the benefit of cancer patients. Ascenion coached the team around Issels through the founding process and received an equity stake in return for its services.

### Dualis: New "artificial heart"

Dualis was founded in late 2006 as a spin-out from the German Aerospace Center (DLR) to further develop and market a new heart-assist device that may, for the first time, provide long-term support for critically ill heart patients. Cardiovascular disease is the leading cause of death in the Western world and many patients could benefit from a heart transplant. Limited organ availability, however, means that only about 5% of these can receive a transplantation.

"We want to provide new treatment options for the remaining 95% of patients," Andreas Achterberg, CFO of Dualis, says. Dualis' system which consists of a fully implantable mechanical pump and a wireless energy transfer system does not replace the natural heart but rather helps a diseased heart to pump blood through the body.

Due to the specific design of the pump, it is the first device of its kind to solve problems of blood-clotting or haemolysis. Moreover, it allows free movement of the patient and avoids the risk of infection because there is no extracorporeal pump or transcutaneous wire. The small, wireless control and energy supply unit can simply be worn on the belt.



### AmVac: Better prevention of widespread diseases



In late 2007, the Swiss-based company AmVac AG licensed a family of synthetic lipopeptides called MALP-2 from HZI that hold strong potential as vaccine adjuvants. As part of that deal, Ascenion obtained an equity stake in the company. The goal of AmVac is to provide new therapeutic and prophylactic vaccines in indications with high unmet medical needs. Some specific treatments might be particularly valuable for the treatment of babies, the elderly and patients with weak immune systems. With already two advanced projects in gynecology and urology indications and two versatile technology platforms for the creation of highly effective, yet safe vaccines, AmVac aims to become a leading player in the vaccine market.

### GO-Bio award: More specific medicines in cardiovascular disease



Nine projects out of 85 applications were selected for the GO-Bio award – a support program of the Germany Ministry of Education and Research (BMBF) – at the end of last year. Among the winners was the team lead by Enno Klußmann at the Leibniz-Institut für Molekulare Pharmakologie (FMP) in Berlin, with its innovative approach to using

specific protein-protein interactions as therapeutic targets. His work focuses on specific anchoring proteins, called AKAPs, and their role in regulating cellular processes.

By navigating key signalling molecules such as protein kinases to distinct areas within cells, AKAPs control cellular activities in a highly specific manner. "Traditional therapeutic approaches target certain classes of signalling molecules, a group of protein kinases, for instance, and thereby affect whole cell functions that depend on them in one way or another," Klußmann explains. "By targeting AKAP-dependent protein-protein interactions, we can rather precisely modulate individual activities mediated by defined signalling proteins."

Medicines developed on the basis of this concept could, therefore, combine higher efficacy with fewer side-effects. In collaboration with the FMP's screening unit, first AKAP-targeting agents have been identified that modulate activities of cultured heart muscle cells.

Together with Ascenion, the team developed a detailed project plan for the further maturation and subsequent commercialization of the approach. They intend to use the one million Euros that are now available from GO-Bio to establish proof-of-concept in relevant animal models. If this is successful, there is an option to receive further funds under the GO-Bio program to prepare the foundation of a new company.

## Turning Science into Business Opportunities

### "Mistaken" antibodies help diagnose cardiovascular disease

It has been known for years that autoantibodies – antibodies that mistakenly target own cells – play a pivotal role in the development of autoimmune diseases and chronic inflammation. Their involvement in cardiovascular diseases or other conditions, however, has long been ignored in the scientific community. Not so by Gerd Wallukat, group leader at the Max Delbrück Center for Molecular Medicine (MDC), and his team. Back in the 1980s, he first described autoantibodies against G-protein-coupled receptors in the sera of patients with cardiovascular diseases. Today, there is strong evidence that antibodies against this class of cell receptors contribute to the onset, progression and maintenance of manifold diseases. Chronic heart muscle disease (dilated cardiomyopathy, DCM) provides an example: About 70% of DCM patients show autoantibodies targeting the so-called beta1-AR receptor which is present on the surface of heart muscle cells.

"By binding to the receptor, the autoantibodies presumably impair the function of heart muscle cells," Wallukat explains. Moreover, in a clinical collaboration project, it was shown that removal of these autoantibodies by specific immune adsorption procedures (apheresis) led to improved cardiac function in DCM patients. This outcome not only supports the pathogenic role of autoantibodies in cardiovascular diseases, but has also led to the idea of using them for the development of new diagnostic tools or therapeutic concepts. A first license agreement for the development of new methods for the diagnosis or monitoring of certain cardiovascular diseases was closed at the end of last year with Ortho Clinical Diagnostics (OCD), a Johnson & Johnson Company. Autoantibody targets and applications in the fields of kidney transplant rejection, malignant hypertension and Raynaud's Syndrome are still available for licensing.

Together with Ascenion, MDC has built a substantial patent estate around Wallukat's work covering a range of well-characterized autoantibody targets on various G-protein-coupled receptors. These receptors function as "molecular switches" controlling the transmission of signals into cells. They decide whether certain cellular functions will be stimulated or tampered with in response to extracellular stimuli such as hormones, neurotransmitters or proteins. The receptor of the stress hormone adrenalin, for instance, belongs to this class of receptors.



**Germany's Next Top Technologies**  
**May 8, 2008**  
**Munich, Germany**

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BioVaria is organized by Ascenion GmbH and its partners EMBLEM Technology Transfer GmbH, National Genome Research Network, Fraunhofer VLS, PROvendis GmbH, MediGate GmbH, ipal GmbH and DKFZ.

**BioVaria**  
 München 2008

BioVaria, the nation's first dedicated biopharmaceutical showcasing event presenting 50 undiscovered, licensable technologies in the fields of cancer, infectious diseases, metabolism, autoimmune or neurodegenerative disorders and other disease areas. Learn more and register at:

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## Fostering Networks

### Going east: Impressions from Kyoto and Beijing



#### Changes in attitude

"The IP landscape in Asia has come a long way from the days when patents were primarily regarded as obstacles to copying what was already available in the marketplace," says Christian Stein, having just returned from two major events in Asia: the Science and Technology Forum (STS) in Japan, and the 11th Healthcare Industry Forum (HIF) in China. "There seems to be a clearer awareness of the benefits of IP among Chinese companies and their focus is clearly shifting towards innovation." Also, China is emerging as a highly relevant source and licensor of IP. For instance, Stein noted a strong demand for new technologies for the manufacturing of biologicals that could reduce the cost of goods and thus facilitate the nationwide distribution of urgently needed chemicals and medicines, e.g. influenza vaccines.

#### Towards global IP standards

The prime goal of IP protection – to serve the innovation process and bring public benefits – was a core theme throughout both events. Ambitious as it is, delegates agreed that there is a lot of work to be done, both on a national and international level. Improved harmonization of IP rights and rules for less-wealthy nations to gain access to IP-protected healthcare products provide just two examples of the many aspects that were intensely debated. "A further issue is that most universities across the globe are still lacking a professional technology transfer set-up", Stein says. One result of his visit to Asia is that Ascenion will assist Chinese universities in building up qualified technology transfer offices. The first workshops are planned for this year.

#### Biotech-NetWorkshop: Looking behind the scenes



In February this year, around 30 life-science entrepreneurs and almost as many experienced managers from the biopharmaceutical industry came together at Ringberg Castle for the 2nd Biotech-NetWorkshop jointly organized by Ascenion and Max Planck Innovation. The mixture of people, the varied program combining panel discussions and workshops with social in- and out-door activities and – last but not least – the unique spirit of the location provided for a stimulating, interactive atmosphere. Partnering, financing and management topics were intensely debated and participants gained valuable insights into strategic as well as practical aspects of management. "The information I've gathered is most helpful," one entrepreneur commented, "and I understand much more about the key issues in preparing, founding and building up a new venture."

#### Meet us at the forthcoming events:

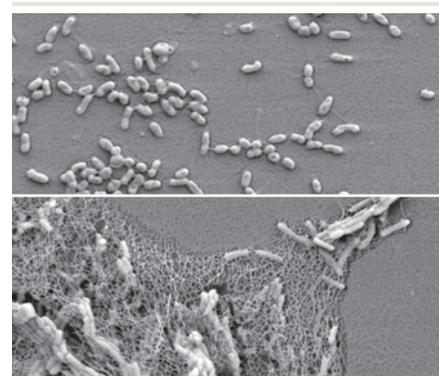
- BioVaria, May 8, 2008 – Munich, Germany
- ASTP Annual Meeting, May 29-30, 2008 – Bergen, Norway
- BIO, June 17-20, 2008 – San Diego, CA USA
- BioEurope, November 17-19, 2008 – Mannheim/Heidelberg, Germany

## News in Brief

### Green packaging

IP concerning a strain of polymer-producing bacteria owned by the HZI was selected for Deutsche Bank's and Clou Partners' patent fund "PatentPortfolio I". The microbes are a mutant form of naturally occurring marine bacteria that have a predilection for oil and produce so-called polyhydroxyalcanoate (PHA) polymers that are widely used for the production of biodegradable plastics.

"Polymer-producing bacteria as such have been known for years," Sabina Heim, Technology Manager with Ascenion, explains.



However, while bacteria normally store PHA polymers inside their cells for their own energy needs, HZI's mutant strain secretes the PHA molecules so that they can be easily harvested. This feature, together with an outstanding productivity, makes the technology highly attractive commercially. "With the HZI technology, we can set up a cost-effective, biological process for PHA production, for the first time," Heim continues. As part of the deal, mediated by Ascenion, PatentPortfolio I will fund the development of an optimized production process by HZI researchers over the next two years. In addition, HZI receives upfront payments as well as royalties on future revenues.

### Material business



Ascenion has again closed a number of material transfer agreements on behalf of its partners, who are increasingly recognised as attractive sources of specific, well-characterized antibodies and animal models. For detailed information see our full list of [antibodies](#) or [animal models](#) at [www.ascenion.de](http://www.ascenion.de).

## Spider silk helps neurons grow



Researchers of Hanover Medical School (MHH) have found that spider silk provides an ideal support for the regrowth of nerve cells when used in vivo as a bridge between nerves that were ruptured through an accident. "We see strong potential for multiple applications in human medicine," Ralf Cordes, Ascenion's technology manager at the MHH comments. "Over the longer-term, three-dimensional scaffolds made of spider silk could also help repair or replace larger portions of diseased tissues." Ascenion has therefore extended patent protection for the approach and is currently working with the inventors to attract funding for the further development of the technology through the preclinical stage as a basis for subsequent commercialization.

## Antibody therapy "made in Germany"

Removab<sup>®</sup> is now under review for market approval with the European Medicines Agency (EMA). In the event of a positive decision, the trifunctional anti-cancer antibody would be the first therapeutic antibody arising from German research to reach the market. It was created by TRION Pharma, a spin-out from the Helmholtz Zentrum München, and co-developed with Fresenius Biotech.

## New computed tomography (CT) system

Researchers at the Helmholtz Zentrum München, together with the University of Oregon, USA have developed a new image reconstruction system for computed tomo-

graphy that produces greater image quality at a lower radiation dose compared with standard systems. With the help of Ascenion a licensing agreement has been closed with YXLON International Group Holding GmbH, who will use and market the new system exclusively for commercial applications in material testing. The system also holds strong potential in the field of medical diagnostics. It could cut costs considerably while maintaining image quality at roughly half the current radiation exposure for patients.

## Anti-cancer compound hits market

In October 2007, Ixempra<sup>®</sup>, a semi-synthetic analogue of epothilone B, gained FDA approval for the treatment of advanced breast cancer when certain other medicines have failed or are no longer effective. The compound is based on epothilone technology that was licensed by Bristol-Myers Squibb from the HZI in the late 1990s.

## Vaccines against diabetes & multiple sclerosis

As part of a collaborative network, MDC researchers Kirsten Falk, Olaf Röttschke and their team received funding under the BMBF's initiative "Innovative Therapieverfahren auf molekularer und zellulärer Basis". Their idea is to create a novel vaccination approach exploiting the ability of malaria pathogen *Plasmodium falciparum* to hide from human immune recognition. By connecting its tolerance-inducing proteins to antigens that trigger undesirable immu-



ne reactions, the scientists hope to put the immune system back on track. "Basically, we aim to restore tolerance in cases where the body's own tissues become subject to immunological attack," Röttschke explains. This is the case in all autoimmune diseases including type 1 diabetes and multiple sclerosis. For the latter condition, the team intends to establish proof-of-concept in relevant animal models by end of the funding period in three years time.

Ascenion supported them in preparing their application with a particular focus on IP-relevant issues and strategies for commercial exploitation of research results.

## Going west

Two spin-outs from the Helmholtz Zentrum Munich, Genomatix Software GmbH and Activaero GmbH, established a US presence in 2007 in order to promote their increasing portfolio of products and services in a truly transatlantic manner.

## Editorial

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## Contact us

**Munich:** T +49 89 318814-0  
info@ascenion.de  
**Berlin:** T +49 30 9406 230 -1/-4  
berlin@ascenion.de  
**Braunschweig:** T +49 531 6181 2090  
braunschweig@ascenion.de  
**Hamburg:** T +49 40 22611 278  
habeck@ascenion.de  
**Hanover:** T +49 511 5328 921  
cordes@ascenion.de  
**Neuherberg:** T +49 89 3187 2850  
scheek@ascenion.de

[www.ascenion.de](http://www.ascenion.de)

## Latest Technology Offers

- Thuggacines for the treatment of tuberculosis [TO 02-00214](#)
- Antibiotic drug candidate from myxobacteria [TO 02-00236](#)
- Mutant mice lacking touch-evoked neuropathic pain [TO 03-00249](#)
- Antibiotic salts suitable for implant coating [TO 10-00028](#)
- Substances for treatment of trypanosomiasis [TO 13-00020](#)
- Diagnostic marker in Acute Lymphoblastic Leukemia (ALL) [TO 15-00004](#)
- Novel treatment option of hair loss [TO 16-00001](#)
- Target for fertility control in humans [TO 03-00220](#)