Technology transfer for academic research
A company of the LifeScience Foundation

ascenion

Annual Review 2019

New impetus for start-ups

Life Sciences into Business

Ascenion's Team

Together with our partners in science and industry, we do everything required to transfer excellent research into application. We support each and every step involved in knowledge and technology transfer, from the identification of promising projects to their translation and commercialization.

Promoting start-ups is a particular focus of our activities and expertise. Prospective entrepreneurs receive individual coaching, practical support and valuable introductions to potential business partners and investors.

Our team comprises over 30 members of staff at seven locations, with headquarters in Munich. We are interdisciplinary, international and industry experienced. Many of us have a biological sciences background and experience in start-ups, mid-sized companies or global concerns.

We are
» Technology managers, project developers and industry liaison managers
» Lawyers and expert negotiators
» Start-up coaches and equity managers

Simplifying the start-up process

Ascenion has already accompanied over 100 start-up projects. We have invested a lot of time, know-how and passion – and learnt so much in the process. Scientists who are keen to found a company can therefore benefit from our considerable experience: particularly as we are now observing two trends in the start-up scene that encourage us and concern us, respectively.

On the one hand, start-ups in Germany are gaining momentum. We are seeing more spin-offs with impressive teams that are advancing excellent projects and gaining significant financing. Start-ups are becoming an important vehicle for knowledge and technology transfer – on a par with licensing agreements. This is also reflected by the source of proceeds that we generate for our partner institutes: for the third year running, profits from equity transactions make up about half of the proceeds flowing to the research institutes and universities with which we work.

On the other hand, it is becoming increasingly difficult to reconcile the interests of the various parties involved in the start-up process, particularly regarding the amount of equity in their start-ups publicly funded research institutes should receive. This results in protracted negotiations that cost a huge amount of time and often leave scorched earth behind them. We are concerned by this trend, because start-ups need the rapid resolution of both scientific and business issues. In order to accelerate the founding process and make start-ups strong and effective, we urgently need a consensus on appropriate licensing and equity conditions that is supported by all parties involved: institutes, entrepreneurs, technology transfer organizations and policy makers.

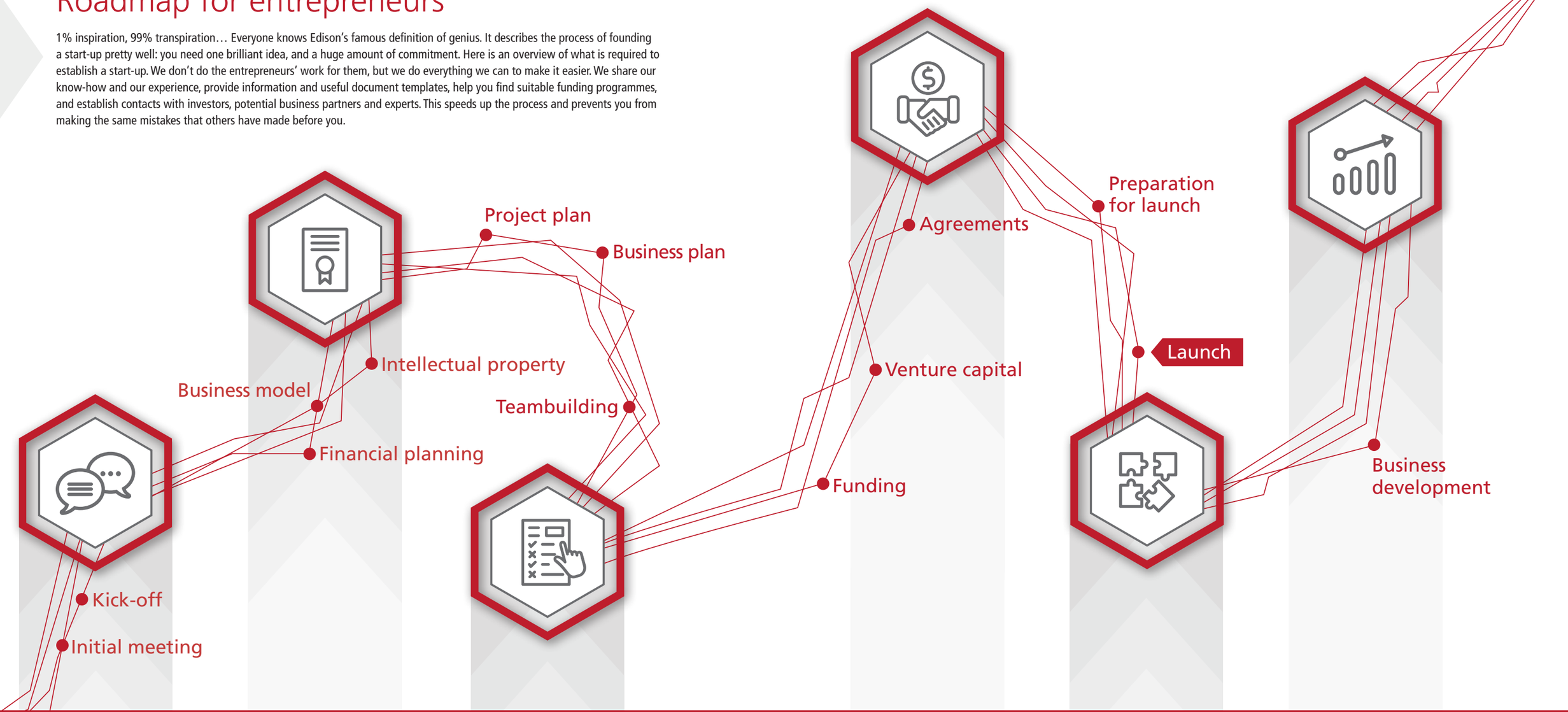
The LifeScience Foundation has developed a framework *(for details, see page 16)* that has already been signed by more than a dozen research institutes and universities, including institutes that are not endowing members of the foundation. If, together, we can further develop this draft and put it on a broader footing, it would do much to support start-up culture in Germany. The start-up process would become simpler and faster – and society would benefit on two fronts. First, because useful products are more likely to reach the market, and second, because in the event of commercial success, a fair share of revenue would go to publicly funded German institutes to finance further innovative research.

We look forward to a constructive dialogue!

Dr Christian A. Stein
CEO
Ascenion GmbH

Roadmap for entrepreneurs

1% inspiration, 99% transpiration… Everyone knows Edison's famous definition of genius. It describes the process of founding a start-up pretty well: you need one brilliant idea, and a huge amount of commitment. Here is an overview of what is required to establish a start-up. We don't do the entrepreneurs' work for them, but we do everything we can to make it easier. We share our know-how and our experience, provide information and useful document templates, help you find suitable funding programmes, and establish contacts with investors, potential business partners and experts. This speeds up the process and prevents you from making the same mistakes that others have made before you.



START

- Evaluate start-up project
- Define scope and expectation

ANALYSIS

- Develop and validate business idea
- Prepare financial model
- Evaluate patents

PREPARATION

- Specify project development
- Create business documents and marketing materials
- Build team

FINANCING

- Use available funding and funding instruments
- Gain investors
- Close licensing and equity agreements

SET-UP

- Define processes and policies
- Support foundation of start-up
- Manage IP

GROWTH

- Build business
- Gain (additional) partners, investors, experts
- Plan trade sale, IPO

PROVIREX: Curing HIV

Teams led by Prof. Joachim Hauber at the Heinrich Pette Institute (HPI) – Leibniz Institute for Experimental Virology and Prof. Frank Buchholz* at the Technische Universität Dresden have developed a completely new approach to the therapy of HIV-1 infection. With the help of the designer recombinase Brec1 – which acts like a pair of 'molecular scissors' – they aim to remove the virus from infected cells rather than just keeping it in check, as with current forms of treatment.

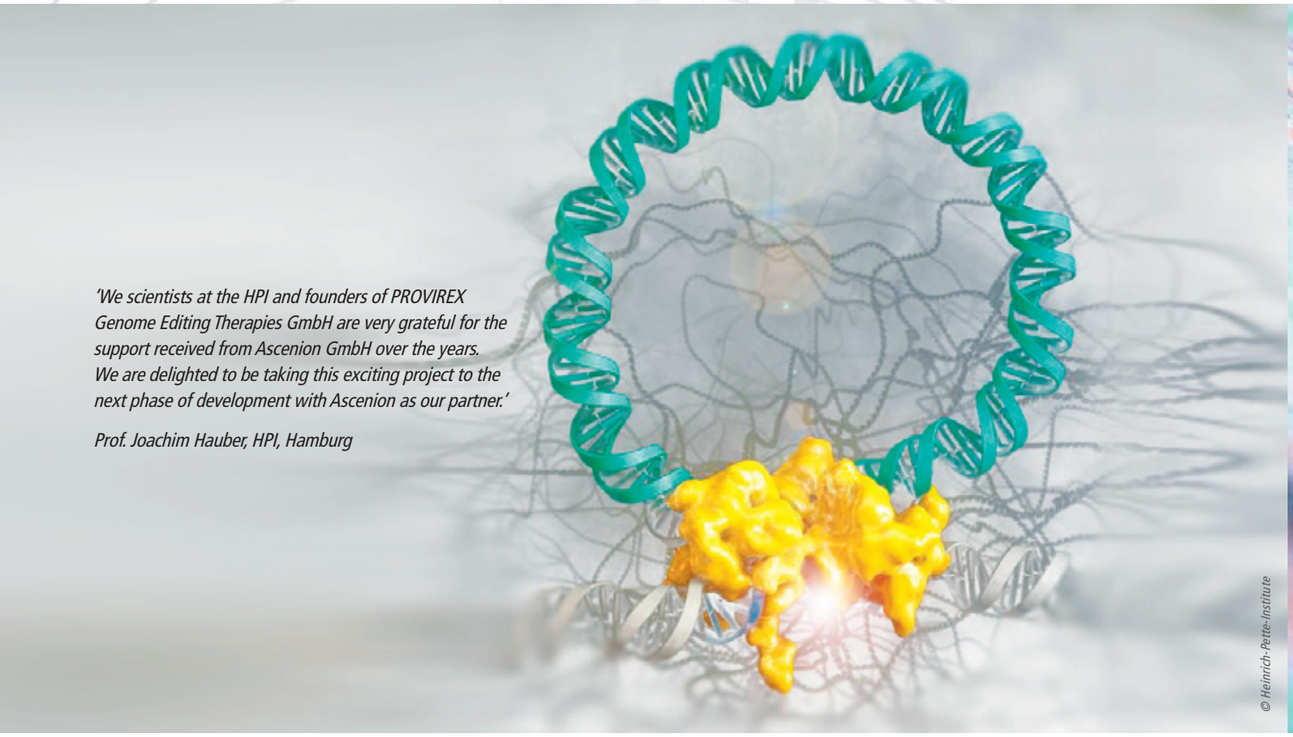
Thanks to the scientists' exceptional and long-standing commitment, together with public and private funding for the project, it has been possible to retain and further develop this innovative concept in Germany. Initial clinical trials will be conducted at the Medical Center Hamburg-Eppendorf (UKE).
Funding for the translation and clinical development of the approach were provided by the German Federal Ministry of Education and Research (BMBF) following a joint application by the UKE and the HPI. Furthermore, the HPI is being financially supported during the project by the Hamburg Authority for Science, Research and Gender Equality, and the ForTra gGmbH für Forschungstransfer of the Else Kröner-Fresenius Foundation. A further key project partner is the German biotech company Miltenyi Biotec, who are contributing important materials and processes.

Ascenion has accompanied the scientists for years through all the ups and downs, secured the IP, supported the negotiation of agreements and mediated constructively between the partners throughout. Both Ascenion and the Innovationsstarter Fonds Hamburg hold equity in PROVIREX.

*previously at the Max Planck Institute of Molecular Cell Biology and Genetics

'We scientists at the HPI and founders of PROVIREX Genome Editing Therapies GmbH are very grateful for the support received from Ascenion GmbH over the years. We are delighted to be taking this exciting project to the next phase of development with Ascenion as our partner.'

Prof. Joachim Hauber, HPI, Hamburg



© Heinrich-Pette-Institute

T-knife: Destroying cancer cells

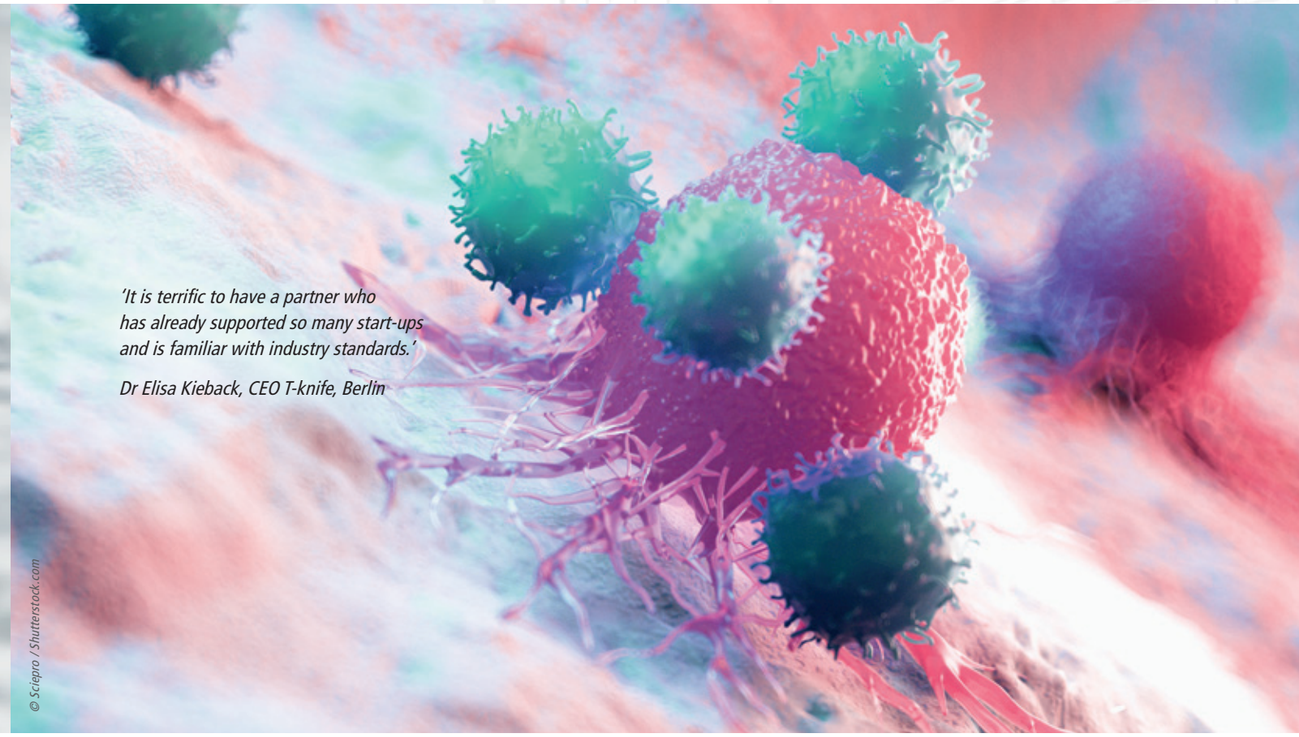
For over 15 years, Prof. Thomas Blankenstein and his teams at the Max Delbrück Center for Molecular Medicine (MDC) in the Helmholtz Association and at the Berlin Charité have been pursuing the goal of using T cells in cancer therapy. Their vision is a promising one, as T cells are particularly effective 'killer cells' of the immune system.

T cells distinguish between 'foreign' and 'self', i.e. they recognize cells with foreign – viral or bacterial – antigens and destroy them, while ignoring normal cells of the body (tolerance). The latter often include cancer cells which, while they may display unusual patterns of expression compared with healthy cells, typically do not carry any foreign antigens. The team at the MDC has achieved a breakthrough on the crucial question of how human immune tolerance mechanisms can be circumvented and cancer cells made susceptible to T cells. They have established a mouse model with a broad repertoire of human T-cell receptors (TCRs), in which they can stimulate the production of specific human TCRs against cancer cells through immunization with cancer-associated antigens. In this way, the MDC scientists and their colleagues at the Charité have generated a TCR specific for the tumour-associated antigen MAGE-A1. Using so-called adoptive T-cell therapy, this receptor can be smuggled *ex vivo* into the patient's T cells, which are then re-administered to them as a cell product. A Phase I clinical trial at the Charité was launched in spring 2020.

Ascenion, together with its technology transfer colleagues at the MDC, has accompanied the start-up project from the outset, progressively expanding the IP basis, extending freedom to operate, and supporting the acquisition of funding. Furthermore, Ascenion, in consultation with the MDC and the Charité, has led the negotiation of licensing, cooperation and equity agreements with T-knife.

'It is terrific to have a partner who has already supported so many start-ups and is familiar with industry standards.'

Dr Elisa Kieback, CEO T-knife, Berlin



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New participations

WBC Drug Delivery Technologies
The beginning of 2019 saw the launch of WBC, a spin-off from the Helmholtz Centre for Infection Research (HZI) and its branch, the Helmholtz Institute for Pharmaceutical Research (HIPS). The start-up is developing a novel delivery technology based on a key patent from the HZI whereby drugs can be transported through eukaryotic cell membranes to their target location.

PROVIREX
The Hamburg start-up PROVIREX, founded in October 2019, is developing a new approach to curing HIV infection.
Read more on page 6.

Financing

HepaRegeniX
HepaRegeniX in Tübingen acquired EUR 11 million in a Series B financing round at the end of 2019. The company is using the funding to advance a novel drug candidate for liver disease to clinical trials. Their goal is to restore the natural regenerative capacity of the liver.

Equity portfolio end of 2019

amcure, Berlin Cures, biomax, Cardior, consentris, HepaRegeniX, inSCREENex, Isodetect, iTheraMedical, medigene, MedTherm, Omeicos, photonion, Protectimmun, Provirex, SPERO Therapeutics, tknife, Tube Pharma, vectura

Clinical milestones

Omeicos
In April 2019 the company commenced a Phase II study of OMT-28 for the treatment of atrial fibrillation, which is due to be completed in summer 2020. Omeicos' OMT-28 targets a natural cell-protective pathway to stabilize cardiac rhythm.

Berlin Cures
A Phase IIa study of the DNA aptamer BC007 in cardiac failure has been underway since April 2019. The drug neutralizes a certain group of antibodies involved in causing the illness.

Cardior
August 2019 saw the commencement of the first clinical trial of CDR132L in cardiac insufficiency. Cardior's approach is the first to target a microRNA that plays a significant role in the pathological growth of heart muscle.

Exits

Inamed
In November 2019, Inamed GmbH in Munich was acquired by the NUVISAN Group, an international contract research organization and pharmaceutical service provider. Ascenion's oldest portfolio company has hence found an ideal partner with which to continue its 20-year success story. The Inamed team, which will be completely retained in the long term, extends NUVISAN's expertise with specific know-how in the area of respiratory and rare diseases.

WBC Drug Delivery Technologies
Launched only at the beginning of 2019, WBC was acquired in September 2019 by Klaria Pharma Holding AB. The drug-delivery technologies of the two companies complement each other perfectly, and when combined can allow the effective administration of drugs – including antibiotics, vaccines and peptides – via the mucosal route, i.e. without injection. Klaria Pharma Holding AB is listed on the First North market of the Stockholm stock exchange.

Zellkraftwerk
In May 2019 the multiplex cytometry specialist Zellkraftwerk was acquired by Canopy BiosciencesTM LLC. The merger results in a multi-omics company offering an attractive service portfolio in the area of phenotypic and genotypic analysis. Canopy also obtained financing at the time of the acquisition, securing the basis for extending the company's portfolio and its continued growth. The location of Zellkraftwerk and its management at the Hannover Medical School will be retained.

2019 IN FIGURES

LIFESCIENCE FOUNDATION

EUR 2.16 m from Ascenion's revenues distributed to the Foundation

EUR 1.7 m made available as grants for projects at endowing institutes

PARTNERS IN SCIENCE

25 research institutes, universities and university hospitals

10 of which are endowing members of the LifeScience Foundation

TRANSLATION

40 technologies supported in the project development phase

EUR 10.98 m in funding acquired for translation

LICENCES & COOPERATIONS

36 revenue-generating agreements closed with industry partners

140 further agreements relating to commercial exploitation supported

EUR 4.49 m in revenue for our partner institutes through agreements supported by us: including licences, options and sales of materials

> 1,500 active contacts to industry and investors

PROTECTING IDEAS

107 invention disclosures assessed

48 patent applications managed

820 patent families and research materials managed in total

START-UPS

23 start-up projects accompanied by us

3 exits/equity transactions

EUR 11 m in financing acquired by 1 portfolio company

PRODUCT PROGRESS

4 clinical milestones

- Phase I clinical trial of oligonucleotide CDR132L in cardiac insufficiency begins
- Phase II clinical trial of drug candidate OMT-28 in atrial fibrillation begins
- Phase II clinical trial of the antibiotic BTZ-043 in tuberculosis begins
- Phase II clinical trial of an aptamer in cardiac insufficiency begins

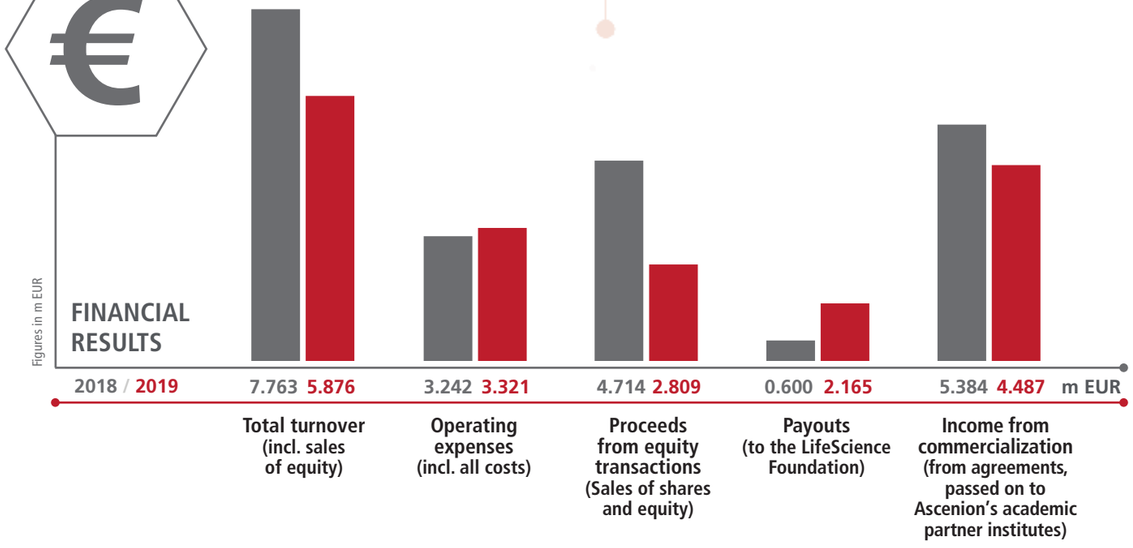
TRAINING

15 training courses held for scientists on topics in knowledge and technology transfer

Certification

Since 2019, Ascenion is certified for its quality management in accordance with the European standard DIN EN ISO 9001:2015. The certification comprises the areas of consulting, evaluation and support for start-ups in life-science technology transfer, and also equity management.
'This is a clear signal to our partners. We will continue to improve and maintain the transparency and quality of our services at a high level,' comments Dr Christian A. Stein, CEO of Ascenion.

FINANCIAL RESULTS

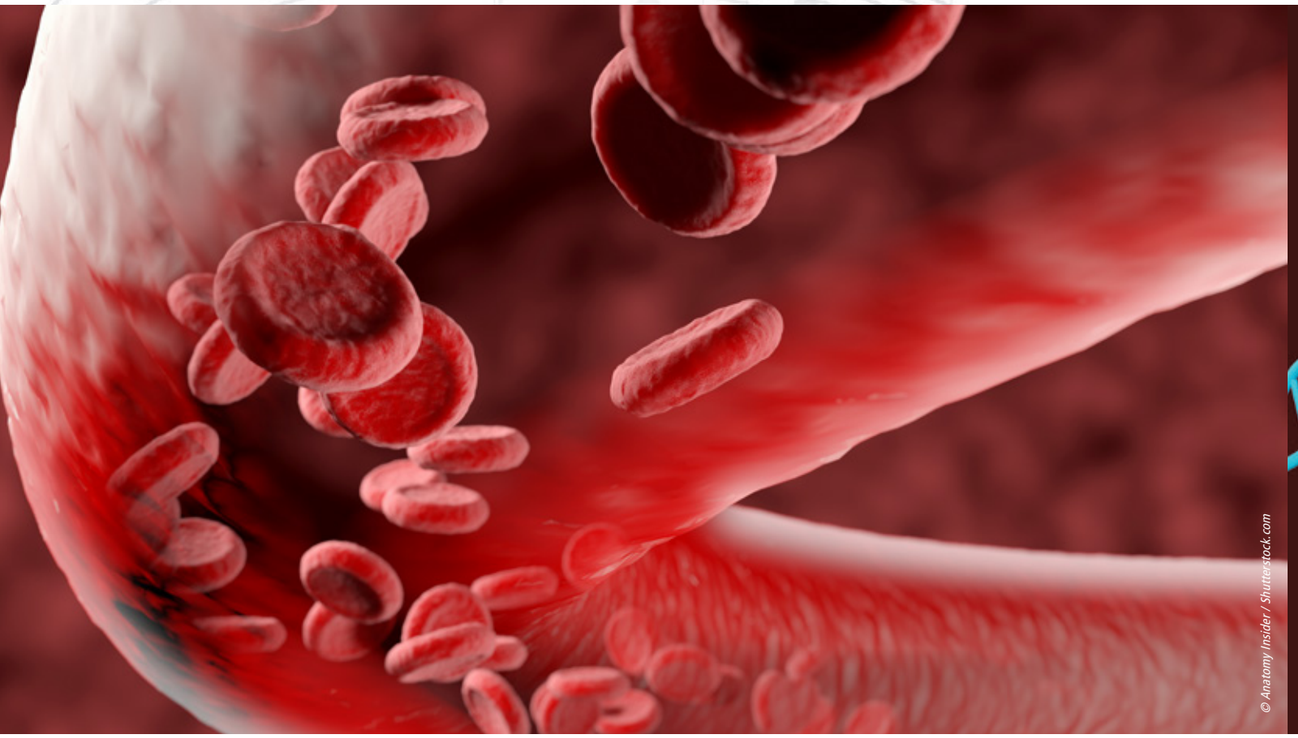


TRANSLATION
HANNOVER MEDICAL SCHOOL

A natural approach for blood vessels

Dr Thomas Aper, Prof. Mathias Wilhelmi and their team at the Department of Cardiothoracic, Transplant and Vascular Surgery (Director: Prof. Axel Haverich) at the Hannover Medical School (MHH) have developed a new approach to producing natural vascular prostheses. Using a high-speed rotation method, the blood clotting protein fibrin is first compacted and then formed into stable tubes of any desired diameter and length. The prostheses have similar biomechanical properties to natural blood vessels and can be stored at room temperature for up to six months. They can therefore be stockpiled and taken 'off the shelf' as and when required for bypass operations. Findings in model systems show that the prostheses are rapidly colonized with endothelial cells in the body, and are gradually converted to neoarteries. If results obtained from ongoing studies are confirmed, these natural vascular prostheses could avoid the need for transplantation of blood vessels from other parts of the body in the long term, or replace arteries made of synthetic materials that can trigger rejection reactions. In Germany, this would benefit up to 50,000 patients a year in cardiac surgery alone.

Ascenion has been working closely with the clinicians for several years. Together, they have been able to secure patent protection for the prosthesis production process and have acquired EUR 1 million for translation through VIP+, the validation funding programme of the German Federal Ministry of Education and Research. This should allow the project to advance to the start of clinical trials within around three years.



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LICENSING DEAL
HELMHOLTZ ZENTRUM MÜNCHEN

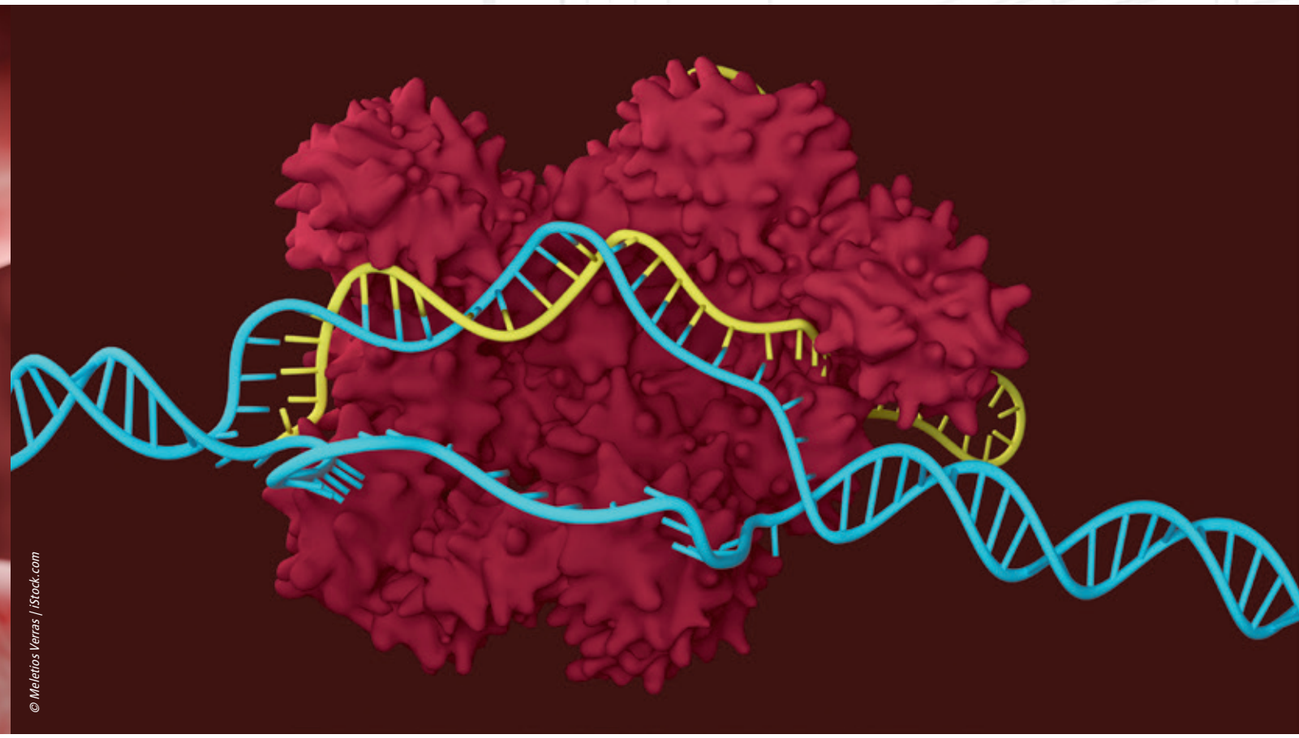
Innovative gene editing tool

Poseida, Demeetra and Hera BioLabs have recently launched a new tool for the targeted alteration of genes that offers an attractive alternative to the widely used CRISPR-Cas9 method. Their system, *Cas-CLOVER™*, employs the endonuclease Clo51, discovered and characterized by Dr Ralf Kühn* at the Institute of Developmental Genetics of the Helmholtz Zentrum München. The Helmholtz Zentrum München has patented this technology in collaboration with Ascenion to create a solid basis for its commercialization.

The three companies have acquired exclusive licences for Clo51 and, by fusing the enzyme to inactive Cas9, have created a system that is just as efficient as CRISPR-Cas9, but more precise, as no off-target activity has been observed. This confers a significant advantage, particularly for the development of gene therapies.

The method will be made broadly available by the companies: Poseida develops innovative approaches to cellular immunotherapy and gene therapy, Demeetra supports applications in industrial biotechnology and agriculture, and Hera BioLabs provides services in drug discovery and pre-clinical research. In addition, third parties may acquire licences to use the *Cas-CLOVER™* technology as a research tool.

*at the Max Delbrück Center for Molecular Medicine (MDC) since 2014.



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Platform for life-science deals and start-ups

BioVaria is our international event that brings inventors and entrepreneurs together with potential licensees and investors. Innovative minds from academic research and the European start-up scene find the forum and the network they need to advance their ideas into applications.

BioVaria Highlights 2019

66 TECHNOLOGIES

15 TECHNOLOGY TRANSFER PARTNERS

>250 PARTICIPANTS

53 RESEARCH INSTITUTES & UNIVERSITIES

27 TECHNOLOGY PITCHES PLUS **66** POSTERS

17 START-UPS

2 WINNERS OF THE BIOVARIA STARTUP PITCH & PARTNER AWARDS: **ISD IMMUNOTECH** AND **MINDPAX.ME**

BIOVARIA

Using existing technologies and developing new ones

Nearly all Ascenion's partner institutes are engaged in the fight against COVID-19. Many new projects have been launched, and existing ones have been re-evaluated and given a new focus. The latter tactic will hopefully allow better control of the pandemic in the short and medium term, until specific vaccines and therapies are available.

COVID-19-relevant technologies from our portfolio

Ascenion has selected seven technologies with relevance to COVID-19 and discussed them with decision makers from industry in an interactive web seminar. The technologies include tools, assays and neutralizing antibodies:

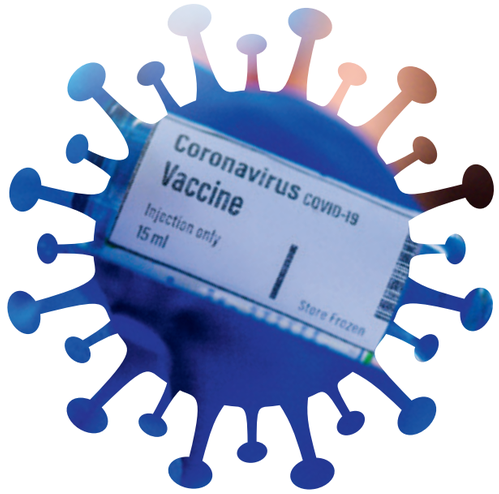
- Therapeutic neutralizing antibodies for treatment of COVID-19 infection
- Novel labyrinthopeptins as anti-viral agents
- Cystobactamides – novel antibacterials against gram-negative pathogens
- Cyclic di-Nucleotides as adjuvants
- TRACR Detect - novel platform technology for RNA detection based on CRISPR/Cas technology
- Lateral flow immunoassay with covalently clustered particles for enhanced sensitivity
- Research tools for COVID-19

The resonance was extremely positive, and Ascenion is now planning further web seminars to present selected technologies relevant to various current topics to potential industry partners.

VPM1002 vaccine revisited

Vakzine Projekt Management GmbH (VPM), successfully sold to the Serum Institute of India last year, has begun a large-scale Phase III SARS-CoV-2 study with its VPM1002 vaccine that was developed for tuberculosis.* In model systems, the vaccine also protects from respiratory virus infections, presumably via unspecific activation of the immune system. In this way, VPM1002 may reduce the risk of severe disease in SARS-CoV-2 infection and help to bridge the gap until a specific vaccine is available. The study has enrolled older people and healthcare workers.

*see VPM's press release 'Hope for the elderly in the corona pandemic – First participants receive VPM1002 in a late-stage phase III clinical trial in Germany' of June 23, 2020.



What's the right amount of equity?

Together with several research institutes, the LifeScience Foundation for the Promotion of Science and Research has defined a framework for dealing with start-ups in order to create transparency and accelerate the founding process.

Start-ups will be actively encouraged and supported

Here the goal of transferring inventions into applications for the benefit of society is paramount, not the support of individuals. An institute can decide on other forms of utilization, if these appear to be more promising.

Shareholdings of 10% to 20% are appropriate

Combined with licensing conditions that are market conform and optimized for start-ups, dilutable minority shareholdings create fair and legally sound starting conditions. They comply with international best practice.

Research institutes and universities with equity in start-ups will enable professional investment management

Research institutes must undertake to fulfil their responsibilities as shareholders, including being able to act quickly and competently in the event of a further financing round or sale. This task may also be assigned to a service provider. There is no evidence to suggest that the participation of institutes reduces or limits the founding, financing or development of start-ups.

Ascenion is a 100% subsidiary of the LifeScience Foundation and distributes surpluses from its business operations and proceeds from equity transactions to the Foundation, which in turn makes them available to its endowing institutes in the form of research grants. This structure is unique in Germany, and has proved its worth to the endowing institutes.

EUR 1.7 million in grants provided by the Foundation for 3 projects in 2019

11 endowing research institutes in the Foundation as of 2019

LifeScience Stiftung

Protection from infectious diseases

The LifeScience Foundation granted the Helmholtz Centre for Infection Research (HZI) around EUR 1 million in research funding in 2019. This will be used by the HZI over a four-year period to fund projects offering new ways to protect the population against infectious diseases that have a good chance of being implemented. The 10 most promising projects were selected in a competition by external experts. They focus on three areas:

Antimicrobial resistance

Key resistance strategies must be better understood as an important prerequisite for the development of new anti-infectives and diagnostics for early detection.

Chronic viral infections

The focus is on cytomegalovirus (CMV), for which there is still no vaccine. Target structures will be identified and adoptive T-cell therapies for prophylaxis and treatment investigated.

Epidemiological basis

Solutions to improve public heath will be sought, including research into lifestyle factors associated with the incidence of acute infections.

The selected projects will be carried out by postgraduate students who are particularly interested in developing their translational competence.

The Foundation's funds originate to a large extent from the proceeds of Ascenion's equity transactions.

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Connecting science and industry

We have continuously supported more than 25 academic institutions in 2019, as well as many other individual projects. Our network in industry and capital investment includes numerous decision makers all over the world with whom we maintain personal contact, often over many years.

HELMHOLTZ ASSOCIATION

- DZNE, German Center for Neurodegenerative Diseases
- **HZDR, Helmholtz-Zentrum Dresden-Rossendorf**
- **HZI, Helmholtz Centre for Infection Research**
- **Helmholtz Zentrum München, German Research Center for Environmental Health**
- **MDC, Max Delbrück Center for Molecular Medicine in the Helmholtz Association**

LEIBNIZ ASSOCIATION

- ATB, Leibniz Institute for Agricultural Engineering and Bioeconomy
- **DIfE, German Institute of Human Nutrition**
- **DPZ, German Primate Center**
- FLI, Fritz Lipmann Institute - Leibniz Institute on Aging
- **FZB, Research Center Borstel - Leibniz Lung Center**
- **HKI, Hans Knoell Institute - Leibniz Institute for Natural Product Research and Infection Biology**
- HPI, Heinrich Pette Institute - Leibniz Institute for Experimental Virology and Immunology
- LIN, Leibniz Institute for Neurobiology

UNIVERSITIES, UNIVERSITY HOSPITALS AND FURTHER PARTNER INSTITUTES

- CAU, Kiel University
- **Charité - Universitätsmedizin Berlin**
- **MHH, Hannover Medical School**
- MUI, Medical University of Innsbruck
- EKFS, Else Kröner-Fresenius-Stiftung
- iba, Institute for Bioprocessing and Analytical Measurement Techniques
- IMB, Institute of Molecular Biology
- IMBA, Institute of Molecular Biotechnology
- LIFE & BRAIN
- MGC, Mouse Genetics Cologne Foundation
- TWINCORE, Centre for Experimental and Clinical Infection Research
- UMG, University Medical Center Göttingen

Endowing institutes of the LifeScience Foundation are highlighted.

Business and investors

Ascenion boasts a comprehensive worldwide network of industry representatives and capital investors in relevant sectors. Long-term personal contacts form the basis for the successful initiation of cooperation and licensing agreements.

Knowledge and technology transfer

As accredited coaches, consultants, trainers and experts, Ascenion's employees are contributing continuously to the development of the technology transfer landscape. They are involved in training programmes – often in a voluntary capacity – establishing professional standards and the promotion of technology transfer at all levels: regional, national and international.

In 2019 Ascenion was active in over 18 initiatives and associations, such as:

- ASTP, A World of Knowledge Transfer
- Alliance of Technology Transfer Professionals (ATTP)
- Association of University Technology Managers® (AUTM), USA
- BayStartUP
- BioDeutschland
- BioFIT
- DECHEMA
- Forum MedTech Pharma
- Horizon 2020-Projects: ESOTRAC + UTILE
- IDEA Summit
- Innoderm
- Knowledge Transfer Ireland
- Licensing Executives Society (LES)
- Life Science Inkubator
- Life Science Nord
- TransferAllianz
- TTS Global Initiative
- Vienna Business Agency

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