Technology transfer for academic research
A company of the LifeScience Foundation

ascenion

ANNUAL REPORT 2015

Life Sciences into Business

Advancing good ideas

Since 2001, Ascenion has been helping public research institutes and university hospitals to advance products and services that can change lives: new cancer therapies for example, or diagnostics and environmentally friendly technologies.

We work closely with our partners to
- identify and patent promising ideas,
- develop them until they become attractive to investors and industry partners, and
- commercialize them through licensing agreements, cooperations or spin-offs.

As a 100% subsidiary of the LifeScience Foundation for the Promotion of Science and Research, we act in the interests of researchers, their institutes and the community.

We are a 30-strong international team of technology managers, analysts, lawyers and project developers and are at home in academia and industry:
- **20** with a background in the biological and natural sciences,
- **8** with experience in the international biopharmaceutical industry,
- **3** lawyers.

Overview 2015

It's exactly what drives us: the approval, after decades of work, of a drug that offers patients a new and effective therapy option. In this case, BLINCYTO® (Blinatumomab), a cancer therapy from the US company Amgen, approved in the EU in November 2015 for a particularly aggressive form of leukaemia.

More than 30 years of research and development – initially, among others, at the Helmholtz Association's Max Delbrück Center for Molecular Medicine (MDC), then at the start-up Micromet, later at Amgen – are the foundation for this success. A clever patenting strategy and professionally negotiated contracts also ensured that the MDC benefited financially. This is a superb example of successful technology transfer. It demonstrates what can be achieved when research institutes, technology transfer and industry make a long-term investment to reach a common goal.

Many of our other partners have, with our help, reached an impressive number of technology transfer milestones: in the USA, a further drug involving an MDC patent was approved: VONVENDI from Baxalta (now Shire) for the treatment of bleeding disorders.

All in all, Ascenion has supported technology transfer at 28 research institutes and university hospitals. For these, Ascenion has negotiated a total of **148 contracts**, of which **40 are revenue-earning licence or cooperation agreements.** The relevant projects are as varied as our partners, and span innovative approaches to gene therapy, as well as diagnostics, technology platforms and potential therapeutic agents against diseases such as tuberculosis and other infectious diseases.

Project development has – following the trend of recent years – become an important focus of our activities. We have worked hand in hand with our partners to raise their projects to a higher level of development, including start-ups from the Helmholtz Centre for Infection Research (HZI) and the Hannover Medical School (MHH). In addition, we have helped our partners to make optimal use of funding programmes and translational tools. Thus we helped the MDC to acquire **funding of EUR 4.5 million** from the German Federal Ministry of Education and Research (BMBF), and for the HZI we were able to initiate a **translational project** with the Lead Discovery Center, thanks also to support from the Helmholtz Validation Fund.

Considerable progress was also made in 2015 in the areas of **start-ups and equity management.** Ascenion acquired equity in **3 start-ups** and, within the scope of a licensing agreement, **equity in an established company. Four of Ascenion's portfolio companies** acquired financing totalling **EUR 15.3 million**, over a quarter of this coming from the Spinnovator programme. Furthermore, **2 companies were sold** and significant revenue was generated from milestone payments and the **sale of shares**.

Ascenion's partners gained a total income in 2015 of around **EUR 9.5 million from agreements** negotiated by Ascenion. In addition, Ascenion was able to distribute **EUR 1.2 million to the LifeScience Foundation**, mostly from sale of equity. This money will be made available as research funding to the Foundation's endowing institutes.

We thank all our partners – particularly the scientists – for their fantastic ideas, their commitment and perseverance. It is the many small steps over a long period of time that ultimately lead to success. BLINCYTO® serves as a huge motivation for what we do. But we also want to mention the many, less prominent intermediate successes we experienced in 2015. These include the commencement of a Phase II clinical study for image-guided surgery from SurgVision, the commencement of a further Phase II study of an improved tuberculosis vaccine, and the launch of a Phase I/II study of a new immunotherapy by Medigene in acute myeloid leukaemia.

Dr. Christian A. Stein, CEO

Ascenion’s partners in academia

Ascenion supported technology transfer at a total of 28 public research institutes and university hospitals in 2015. Of these, 10 are endowing institutes of the LifeScience Foundation for the Promotion of Science and Research. The focus of all our cooperations is on the life sciences.

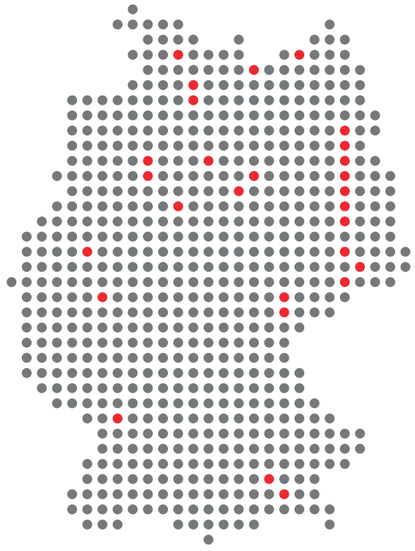
Over 5,000 scientists supported (long-term partners)

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-Gemeinschaft
- ATB, Leibniz Institute for Agricultural Engineering and Bioeconomy
- BNITM, Bernhard Nocht Institute for Tropical Medicine
- DIfE, German Institute of Human Nutrition
- DPZ, German Primate Center
- DRFZ, German Rheumatism Research Centre
- FLI, Fritz Lipmann Institute - Leibniz Institute on Aging
- FZB, Research Center Borstel – Leibniz Center for Medicine and Biosciences
- HKI, Hans Knoell Institute - Leibniz Institute for Natural Product Research and Infection Biology
- HPI, Heinrich Pette Institute for Experimental Virology and Immunology
- IFW, Leibniz Institute for Solid State and Materials Research Dresden
- IPF, Leibniz Institute for Polymer Research Dresden
- IPK, Leibniz Institute of Plant Genetics and Crop Plant Research
- LIKAT, Leibniz Institute for Catalysis
- LIN, Leibniz Institute for Neurobiology

Universities, university hospitals and others:
- Charité - Universitätsmedizin Berlin
- MHH, Hannover Medical School
- TWINCORE, Centre for Experimental and Clinical Infection Research
- BTO, Bergen Teknologioverføring (Norway)
- DZHK, German Center for Cardiovascular Disease
- LIFE & BRAIN
- MCG, Mouse Genetics Cologne Foundation
- University Medical Center Göttingen
- University of La Laguna (Tenerife)

Ascenion has also supported various institutions regarding specific issues, e.g.
- RWTH Aachen University
- Technische Universität Darmstadt
- University of Hradec Králové (Czech Republic)
- University of Rijeka (Croatia)
- University of Siegen



Ascenion’s partners in business and industry

At the end of 2015, Ascenion was managing around 360 active contracts for its partners. Contractual partners include global concerns, leading regional companies – for example in Asia, the USA or Scandinavia – innovative mid-sized companies, start-ups, venture capitalists, banks and investment funds. They value Ascenion as a professional partner and central provider of one of the biggest and highest quality life-science portfolios in Europe.

Over 1,500 active contacts in business

2015 in figures

IDENTIFY AND PROTECT

commercially promising research results

96 invention disclosures

38 patent applications

20 training courses for scientists to raise awareness of technology transfer

RESEARCH

28 public research institutes in the Helmholtz and Leibniz Associations, universities and university hospitals

DEVELOP

to a level interesting to industry and investors

EUR 12.8 m funding raised for partner institutes

50% approval rate for supported funding applications

4 start-up projects and several technology developments intensively supported

ECONOMIC BENEFITS

Together with our clients, we turned over a total volume of more than EUR 2 billion In therapeutics, diagnostics and other products.

The companies in which Ascenion held equity in 2015 employed a total of circa 200 staff.

APPLICATION

- EU approval of BLINCYTO® for the treatment of a specific form of leukaemia
- US approval of VONVENDI for the treatment of bleeding disorders
- Launch of Phase II clinical study of image-guided surgery
- Launch of Phase II clinical study of a vaccine against tuberculosis

COMMERCIALIZATION

via licensing, cooperations or start-ups

40 revenue-generating licensing and cooperation agreements negotiated, plus 108 additional contracts, e.g. material transfer agreements

3 new start-up shareholdings acquired

4 portfolio companies financed with a total of EUR 15.3 m (from various sources), EUR 3.6 m of which from the Spinnovator programme

3 portfolio companies and shareholdings sold

EUR 9.5 m in revenues for Ascenion's partners from agreements negotiated by Ascenion

EUR 1.2 m distributed to the LifeScience Foundation, around 2/3 from sale of equity and around 1/3 from surpluses from Ascenion's operating activities

EUR 444,000 in funding confirmed by the LifeScience Foundation for research projects at endowing institutes.

Rapid repair: VONVENDI for bleeding disorders

In December 2015, a new drug was approved in the USA for patients suffering from a rare form of von Willebrand disease. Due to an inherited defect, von Willebrand factor in these patients is altered to such a degree that massive and dangerous bleeding can occur. In healthy patients, von Willebrand factor ensures that blood platelets in the circulation are immediately recruited to repair blood vessels as soon as they are injured. The new drug, VONVENDI was developed by Baxalta (previously Baxter, now Shire) and is the first, and so far only, recombinant agent for the treatment of von Willebrand disease.

In clinical studies it demonstrated a 100% treatment success rate. VONVENDI is based on a substance patent belonging to the MDC. Several years ago scientists there examined active agents that could be used for the treatment of bleeding disorders, including von Willebrand factor. At that time, a substance patent was applied for and subsequently licensed to Baxter by the MDC with the help of Ascenion in 2010.

Identifying and protecting promising research results

The close and trusting cooperation with scientists and those responsible for technology transfer at our partner institutes form the basis of successful technology transfer. We take up ideas and projects that hold promise for useful applications as early as possible. Together, we review their potential, develop an appropriate patenting strategy and accompany the process. In the past year we evaluated 96 invention disclosures and accompanied 38 patent applications.

The complete portfolio managed by Ascenion currently comprises around 750 patent families and commercially attractive materials:

750 technologies and materials

War on metastases: amcure

In the past year, Ascenion intensively accompanied the spin-off amcure as part of the Spinnovator programme. This start-up from the Karlsruhe Institute of Technology (KIT) developed an active agent for the treatment of cancer. In model systems, the peptide is not only able to stop the growth of primary tumours, but also prevents the development of metastases. Should these observations be confirmed in cancer patients, this would represent a significant breakthrough in cancer therapy.

'More than 90% of cancer patients don't die from the primary tumour,' explains Ascenion's project manager, 'but from metastases.' In December 2015, the BMBF confirmed Spinnovator funding of EUR 1.9 million for amcure. In addition, a consortium of private investors confirmed they would be providing an equivalent sum. Together, these funds enable the commencement of clinical studies in 2016.

Developing projects for the market

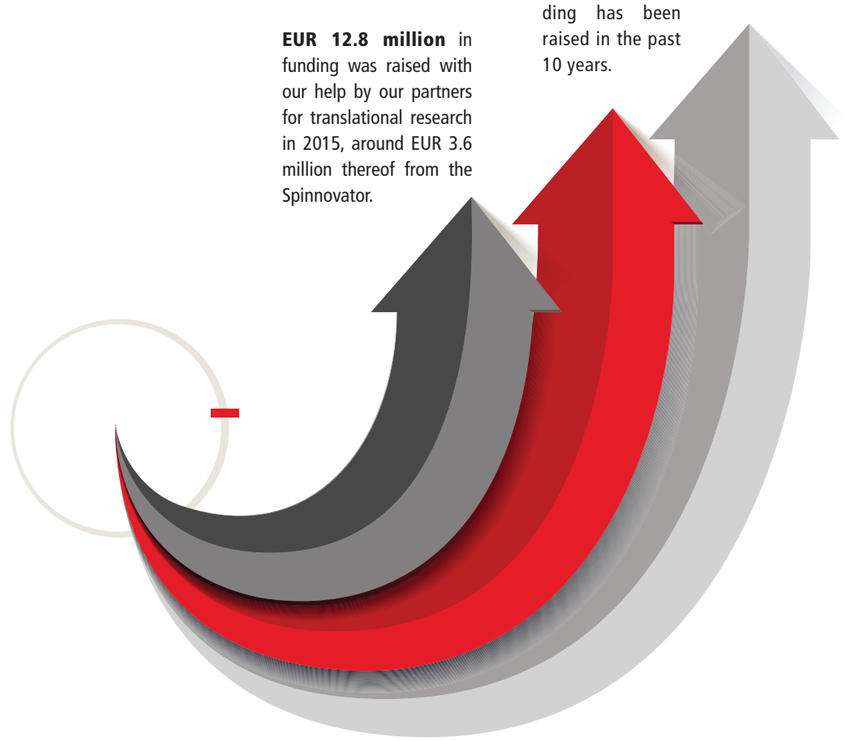
Through professional project development, Ascenion closes the gap between academic research and industrial development. In close cooperation with our partner institutes and international experts, we draw up detailed development plans for selected projects and advance them systematically. We focus all activities and collaborators on the development goal and dovetail project development with the commercial shaping of the project. This results in an asset that is highly attractive to investors and industry representatives, and that can be directly transferred into a start-up or licensing partnership.

Ascenion also supports the financing of project development. For this we make use of numerous existing funding programmes, as well as our own instruments that we have developed and realised together with private and public investors, such as the Spinnovator.

EUR 12.8 million in funding was raised with our help by our partners for translational research in 2015, around EUR 3.6 million thereof from the Spinnovator.

Around **EUR 41 million** in funding has been raised in the past 10 years.

The approval rate for supported funding applications in 2015 is **50%**.



Finding partners and structuring partnerships

We find the right partner for each project and negotiate contracts that support our common goals – in other words we lower hurdles, raise the chances of successful application, accelerate progress – and the academic inventors and their institutes benefit from an appropriate share in the commercial success.

For this reason, we are in permanent contact with industry and investors – all over the world. We also act for international inventor consortia and develop contractual structures that combine several forms of cooperation and compensation, including coverage of staff and material costs, company shares, upfront and milestone payments, and licensing fees.

40 revenue-generating licence and cooperation agreements negotiated for our partners in 2015.

We have held over **125** one-on-one meetings with representatives of the biopharmaceutical industry in 2015 at **7** international events* in 5 countries and had over **500** interactions with industry, at which we presented technologies from our partner institutes and discussed possible partnerships.

* Plus many individual talks during BioVaria and the Innovation Days

EUR **9.5** million in 2015 alone, generated by licence and material agreements negotiated and partly initiated by us for our partners.

No place to hide: BLINCYTO® for cancer

Patients suffering from a rare form of acute lymphoblastic leukaemia (ALL) now have a new treatment option: BLINCYTO® (Blinatumomab), an antibody derivative that activates the body's own immune system specifically against the cancer cells. It helps immune cells to recognize and destroy cancer cells that previously evaded an immune response through a clever camouflage strategy. The drug was approved in the EU in November 2015, and is the first therapeutic advance for those affected in over 20 years.

The product is partly based on intellectual property arising at the Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC). It was initially developed by the Munich start-up Micromet, which was later acquired by Amgen. Ascenion negotiated the licence agreement between Micromet and the MDC that was closed shortly thereafter.

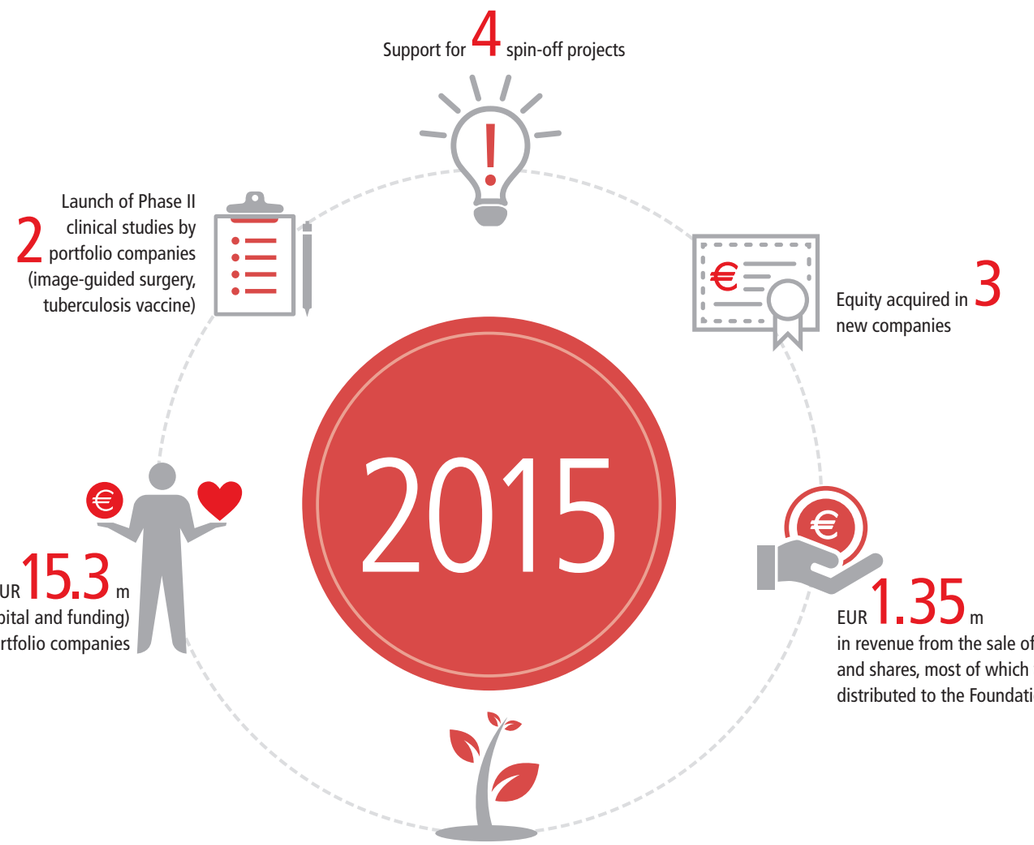
A vaccine for all: VPM1002 against tuberculosis

July 2015 saw the start of a Phase II clinical study in South Africa – a tuberculosis hot spot. For the first time, infants exposed to HIV received the new vaccine VPM1002, which originated at the Max Planck Institute for Infection Biology and is being jointly developed with the Vakzine Projekt Management GmbH (VPM) and the Serum Institute of India (SII). The results of previous studies have consistently shown that VPM1002 is significantly more effective and safer than the conventional BCG vaccine that has been in use for around 100 years.

The vaccine offers new hope for infants with congenital immunodeficiency, but also for adults the world over. According to the WHO, more than 9 million people become infected with tuberculosis per year, and over 4,000 die from the disease every day.
In 2008, Ascenion acquired 70% of shares in VPM, which was spun off from the Helmholtz Centre for Infection Research, and continues to advise the company on numerous strategic and IP-relevant issues. For example, Ascenion actively supported the licencing agreement with the developing partner SII in 2013.

Supporting spin-offs and growth

Ascenion has already advised and supported over 90 spin-off projects for its partners and acquired equity in 42 companies in the process. According to each project and its requirements, we provide support through intensive pre-launch project development, help with business and financial planning, coach the team, recruit experts, secure funding and approach investors. We normally also negotiate shareholder and licensing agreements, monitor company growth and manage equity. We continue to advise the company after its foundation, should the company founders wish.



Equity in a total of 21 spin-offs
- **13** product development
- **2** software / big data
- **4** services / CRO
- **2** product development / services

Improved therapy for diabetes in children: Fr1da

Ascenion's parent company, the LifeScience Foundation for the Promotion of Science and Research, has provided funding of nearly EUR 0.5 million for the Fr1da study at the Institute of Diabetes Research, Helmholtz Zentrum München.

Scientists and physicians hope to improve the screening and optimal treatment of type 1 diabetes in children. Using only a few drops of blood, a rapid test can diagnose the disease before symptoms occur. This allows the affected family to learn how to avoid critical metabolic imbalances in their child. In Germany alone, around 30,000 children are affected by the disease, a further 2,000 acquiring it each year.

The trial is a cooperation project between several institutes and associations and is being supported by a number of sponsors. Apart from screening, the trial will also evaluate innovative approaches to diabetes therapy being developed at the Helmholtz Zentrum München.

Source: Helmholtz Zentrum München

LifeScience Stiftung increasing added value

In 2001 four institutes of the Helmholtz Association developed a new model for professionalizing their technology transfer. They established the LifeScience Foundation for the Promotion of Science and Research, together with its 100% subsidiary, Ascenion. A key fundamental idea was then – and still is today – that making centrally established technology transfer expertise and experience available to all interested research institutes as required is economical and expedient. Furthermore, the foundation model provides the possibility of reinvesting the proceeds of technology transfer back into research in the most extensive and flexible way possible. Hence Ascenion distributes a large part of its income from sale of equity and operating activities to the Foundation: a total of EUR 9.5 million since its foundation. The endowing institutes are mostly free to decide when and for which projects they wish to take advantage of this project-specific funding.

In 2015 the LifeScience Foundation had

10 founding and endowing institutes,
4 institutes in the Helmholtz Association,
6 institutes in the Leibniz Association and
the Hannover Medical School (MHH),

6 new projects at 5 institutes with confirmed funding of around EUR 444,000,

EUR **1.2** million in payouts from Ascenion
around 2/3 from sale of equity and around 1/3
from surpluses from Ascenion's operating activities.

BioVaria marketplace for innovative life-science projects

In cooperation with other technology transfer organizations, Ascenion organized the 8th BioVaria in 2015. The event is already a fixed date in the calendars of many investors and decision makers in the international biopharmaceutical industry. They take the opportunity to get to know a broad spectrum of commercially attractive technologies and selected spin-offs on one single day, and to meet key figures from European research and technology transfer. The common goal is to forge partnerships for the further development of innovative projects.

BioVaria 2015 in figures:

180 participants in total
60 from industry

16 technology transfer organizations and
50 research institutes from
10 European countries

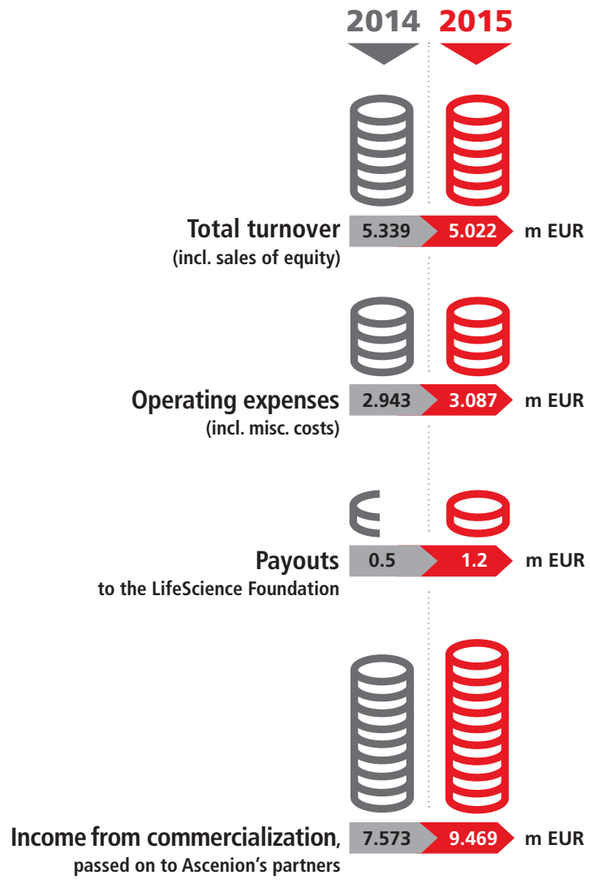
Spin-off Panel with **7** start-ups from
4 European countries

Numerous individual discussions

58 technologies: potential diagnostics and therapeutics, as well as platform technologies,
20 of which as short presentations

Financial results in 2014 und 2015

Ascenion supports its partners along the whole value chain: from scouting to project development and commercialization. These services are remunerated through a mixture of fees and success-related bonuses. In the case of spin-offs, Ascenion also usually acquires shares in the newly founded company.



Ascenion's partners profit financially at several levels:

- They receive revenues from contracts negotiated by Ascenion. In 2015 this was nearly EUR 10 million.
- As endowing members, they have access to funding from the LifeScience Foundation. Ascenion distributes funds to the Foundation – primarily income from sale of equity, plus surpluses from operating activities. In 2015 this came to over EUR 1 million additionally.

Here the 'critical mass' – in other words the large number of partners and inventions – is crucial to the total financial success. Only then can risk be spread effectively: many early-stage projects must be supported in order to achieve a few significant commercial successes.

Ascenion's structure

The LifeScience Foundation is the sole shareholder of Ascenion GmbH. Important business decisions are made in close cooperation between Ascenion's CEO and the Foundation's board members, Nicolaus Steenken and Dr Ronald Mertz.

The endowing institutes are not affiliated with the Foundation under corporate law. They are represented by their board members or CEOs in the Foundation's council ("Stiftungsrat"), and thereby participate in important decisions, e.g. the use of the foundation's assets.

Ascenion is economically independent. Its business activities are supervised by the advisory board.

The board members are Dr Manfred Baier, Dr Timm-H. Jessen and Dr Joachim Rothe.

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