ascenion

Technology transfer for academic research A company of the LifeScience Foundation

Annual Review

Life Sciences into Business

Ascenion's Team

Ascenion is an independent knowledge and technology transfer company that supports more than 30 European partner institutes with a life-science focus: research institutes, universities, university hospitals and associated institutions. We are committed to transferring excellent research into useful applications for the benefit of society. Together with our partners, we have launched many start-ups and products from which millions of people are now benefitting.

Supporting start-ups is a major focus of our activities, and has been given additional impetus over the past year by advances in digital health.

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 and project developers
- » Lawyers and expert negotiators
- » Start-up coaches and equity managers
- » Analysts and industry liaison managers



Digital health comes of age



We have sadly become all too familiar with exponential growth curves over the past two years. A comparable dynamic in the field of digital health, however, fills us with optimism. After a slow development phase, the practical relevance of digital health is suddenly visible: Al-supported algorithms can recognize skin cancer more reliably than experts, and telemedicine allows patients to consult

their doctor even in the midst of a pandemic. You can find many other examples here in this report. Our pipeline is bursting and the potential is considerable.

Among our partner institutes alone, seven start-ups were launched last year, four of these with the help of the Berlin Institute of Health (BIH) Digital Health Accelerator programme. It is an excellent example of how research institutes can support the translation of promising ideas and technologies into useful medical products. We greatly appreciate this fruitful cooperation.

As is usually the case in knowledge and technology transfer, there is a time lag between positive developments like these and the resulting financial success. This year we recorded a decrease in turnover, but expect an increase in

revenue over the coming years, driven by income from our rapidly expanding investment activities. The majority of this revenue will be distributed by the LifeScience Foundation to our endowing institutes. These funds can be used by the institutes as desired – including for the translation of further business ideas. This provides a sustainable, financially sound basis for supporting spin-offs from public research institutes, independently from public-sector funding.

My special thanks go to our staff and partners in science and industry who, despite all the restrictions, have gone the extra mile this year to maintain the relationships that are so crucial to knowledge and technology transfer.

I look forward to the continued collaboration with our partners, and as much live contact as possible in the coming months!

Dr Christian A. Stein CEO Ascenion GmbH

▷ FOCUS DIGITAL HEALTH

Founding a digital health company

'All key players in our healthcare system have by now realized that digital health can solve many challenges in healthcare provision: industry, government, clinicians, healthcare workers, scientists and investors.'

Klaus Nitschke, Berlin Institute of Health @ Charité

We are seeing an increasing number of products on the market that demonstrate the benefits of digital health for patients. Telemedicine is now a reality, not least as a result of the coronavirus pandemic. The same applies to AI-enabled diagnostics and wearables, such as smart watches, that record vital sign data and can monitor fitness, well-being

and health. In the future, we can expect AI-assisted prognoses, individually tailored artificial joints and heart valves from 3D printers, and virtual reality solutions that allow surgeons to practice complex operations - just to name a few developing trends.

PATIENT BENEFITS

- » Improved access to medical care
- » Fewer errors and more precise results in diagnostics
- » More effective, personalized disease therapies
- » More successful prevention and aftercare
- » More patient autonomy when coping with illness and health risks
- » Faster and more efficient drug development
- » Simplification of procedures in general practice, hospitals and public health authorities

'In Germany we're very good at putting the ball on the penalty spot, but we don't score enough goals. We have to do better.'

Klaus Nitschke, Berlin Institute of Health @ Charité

It will be interesting to see who's going to win the game. Germany has excellent scientists and technologies. But other countries are way ahead of us when it comes to translation. On the one hand, we need to lower bureaucratic hurdles; on the other, we need more venture capital and more entrepreneurs. The market is global, highly competitive, and dominated by large corporations.

It's therefore hard for entrepreneurs to get a foothold – but it is possible. Excellence, professionalism and rapid product development are what count. This is why programmes such as the Berlin Institute of Health Digital Health Accelerator (BIH DHA) are so valuable. Alongside funding, the programme offers the necessary know-how for rapidly transforming digital health ideas into validated, marketable products and getting start-ups up and running.

Tips for entrepreneurs

Together with Klaus Nitschke, BIH DHA Co-Initiator and Advisor we have put together a few tips for scientists interested in founding:

Protecting your IP and publishing your results are not mutually exclusive Yes, you can have both: the publications that are important for your academic career and the IP protection required for commercialization. You just have to go about it the right way. As soon as you are even vaguely considering transferring your idea into commercial application, contact your technology transfer office immediately. We'll respond right away.

Open-source software and public data sources are possible sticking points Usage rights for software and data are complex, and two aspects are important with regard to commercial use. First, one should ascertain whether commercial use of the data and codes of interest - including all component elements - is actually permitted. Some open-source licences exclude commercial use. Second, it's important to develop a proprietary core for your digital health project. Even in cases where patent registration is neither straightforward nor sensible, underlying IP is important for investors and industry partners. Once again: talk to us as soon as possible.

Decide if you 'only' need money, or if know-how and/or IP is also important to you For the 'money only' option, you can use public funding programmes for translation. With these, you retain full control of your start-up project. If you're after money and support form mentors and experts who can advise you regarding product and business development, markets and legal matters, choose a programme such as the BIH DHA, if available. This will increase your chances of success. In return, you give up a small share of your company. The profits accruing from this share go to support further start-up projects, creating a financially sustainable funding model.

Being an entrepreneur and pursuing a medical or academic career are not mutually exclusive Most scientists and physicians didn't choose their careers by chance. It's possible to pursue your start-up project without giving up your vocation. For example, you could take up an advisory position as major shareholder. Your technology transfer office/institute and Ascenion can help you to build a suitable team for your company, but some input from you will be essential to the project's success.

Example BIH DHA: Excellent support for entrepreneurs from the Charité, MDC and BIH If you work at the Charité - Universitätsmedizin Berlin, the Max Delbrück Center for Molecular Medicine (MDC) or the Berlin Institute of Health (BIH), have a closer look at what the BIH's Digital Health Accelerator (BIH DHA) has to offer. It accompanies you through a structured process of iterative product development, supported by:

- » Funding (incl. pro-rata protected time off from clinical duties)
- » Coaching/mentoring by distinguished national and international experts
- » Access to networks (talent, development partners, industry, investors)
- » Interdisciplinary BIH DHA team
- » Co-working space
- » Start-up founding

Support is divided into two phases:

- » DHA Stage 1: from idea to prototype (6 months)
- » DHA Stage 2: from prototype to product up to market launch (up to 18+ months)

▷ FOCUS DIGITAL HEALTH

mTOMADY: Healthcare provision in Africa

More than a billion people have no access to medical care, in many cases due to financial obstacles. They have no health insurance, no savings, often not even a bank account.

Two physicians at the Charité, Dr. Julius Emmrich and Dr. Samuel Knauß, together with co-founder Elsa Rajemison and her mTOMADY team, have come up with an ingenious solution: a digital wallet that works on the simplest of mobile phones, even without an internet connection. Users can set up a health savings account on the platform, take out health insurance or pay for medical treatment. This can save lives. For example, it prevents situations in which accident victims can't receive emergency care, or acutely ill patients don't seek medical help, because they don't have enough cash in their pockets to pay for it.

The system is currently in use in Madagascar, where it has gained over 70 healthcare providers and the Ministry of Health as partners. It will be introduced in Ghana and Uganda this year.

mTOMADY is a spin-off from the Charité and the BIH. The BIH DHA supported the project with know-how and starting capital of EUR 1 million.

x-Cardiac: Early warning system for intensive care units

After major surgery it's not unusual for patients in intensive care units to develop complications. If clinical staff could identify at-risk patients early on, it would allow them to react more promptly and save lives. To this end, Prof. Alexander Meyer, physician and computer scientist at the German Heart Center Berlin (DHZB), has developed an algorithm that collates data from various monitoring instruments in modern intensive care units and evaluates them intelligently to enable complications to be recognized before they become critical.

The software has been trained with the help of anonymized data from more than 50,000 patients and is being tested in the intensive care units of the DHZB during normal operation since April 2018.



In July 2021, the start-up was certified as a medical device manufacturer in the EU and also received approval for its first product – 'x-c-bleeding' – for the prediction of postoperative bleeding. A second product 'x-c-renal-injury' for acute renal failure is to follow. There are many more conceivable applications.

x-Cardiac is a spin-off from the Charité and the Berlin Institute of Health (BIH), and has been supported by Ascenion, the BIH Digital Health Accelerator and the DHZB, among others.



▷FOCUS DIGITAL HEALTH

SORMAS: Controlling epidemics

Over recent months we have all experienced at first hand the dangers posed by highly infectious diseases. Only a few years ago, this was primarily considered to be a problem in underdeveloped, low-income regions. In 2014, with the aim of saving lives in these regions, Prof. Gérard Krause from the Helmholtz Centre for Infection Research, started to develop a modular software that allowed outbreaks to be recognized early, their progression to be monitored, and health care resources to be deployed where they were needed. Together with a number of partners, he has developed this concept into a platform called SORMAS (Surveillance Outbreak Response Management and Analysis System) that is currently deployed in many regions of Africa and Europe in the management of 37 infectious diseases, including Ebola, malaria, cholera, measles – and now COVID-19.

SORMAS links specific epidemiological expertise to diverse data collection and processing systems. To manage the coronavirus pandemic in Germany, for example, it links data from German public health offices with the monitoring network at the Robert-Koch Institute and electronic symptom diaries of people who have tested positive. This not only simplifies many procedures at public health offices, but also supports cooperation between different government departments. The platform is available to each public health office in compliance with data protection laws, and is operated from a dedicated virtual server at the German Federal Information Technology Centre.

AI does it better: Image analysis in medical diagnostics

Pathologists and clinicians take a lot of time to thoroughly analyse complex images such as tissue sections or X-rays – and they still make mistakes. Even experienced practitioners. Two start-ups from the Charité and BIH have developed AI-based solutions for better diagnostics. Both are supported by Ascenion and the BIH DHA.

Aignostics: Precision diagnostics for pathology

Cancer, infections, autoimmune and other diseases cause visible changes in patients' tissues. Analysing these changes has been the cornerstone of clinical diagnostics for decades. The AI-platform from Aignostics, developed by Prof. Frederik Klauschen, Prof. Klaus-Robert Müller and their colleagues, is able to recognize known disease-associated characteristics in standardized form to a high degree of precision, increasing throughput while lowering error rates.

But this is not all: the platform helps to identify new markers that predict whether or not a patient will respond to a particular therapy – for example during a clinical trial. The AI-based analysis not only reveals associations between complex tissue images and clinical outcomes, but also identifies the pixels in these images critical for determining this correlation. Based on this information, pathologists can identify markers of prognostic value for the therapeutic approach under investigation.

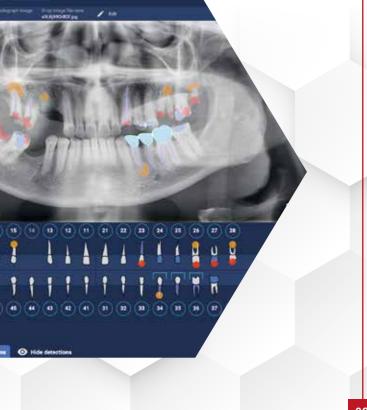
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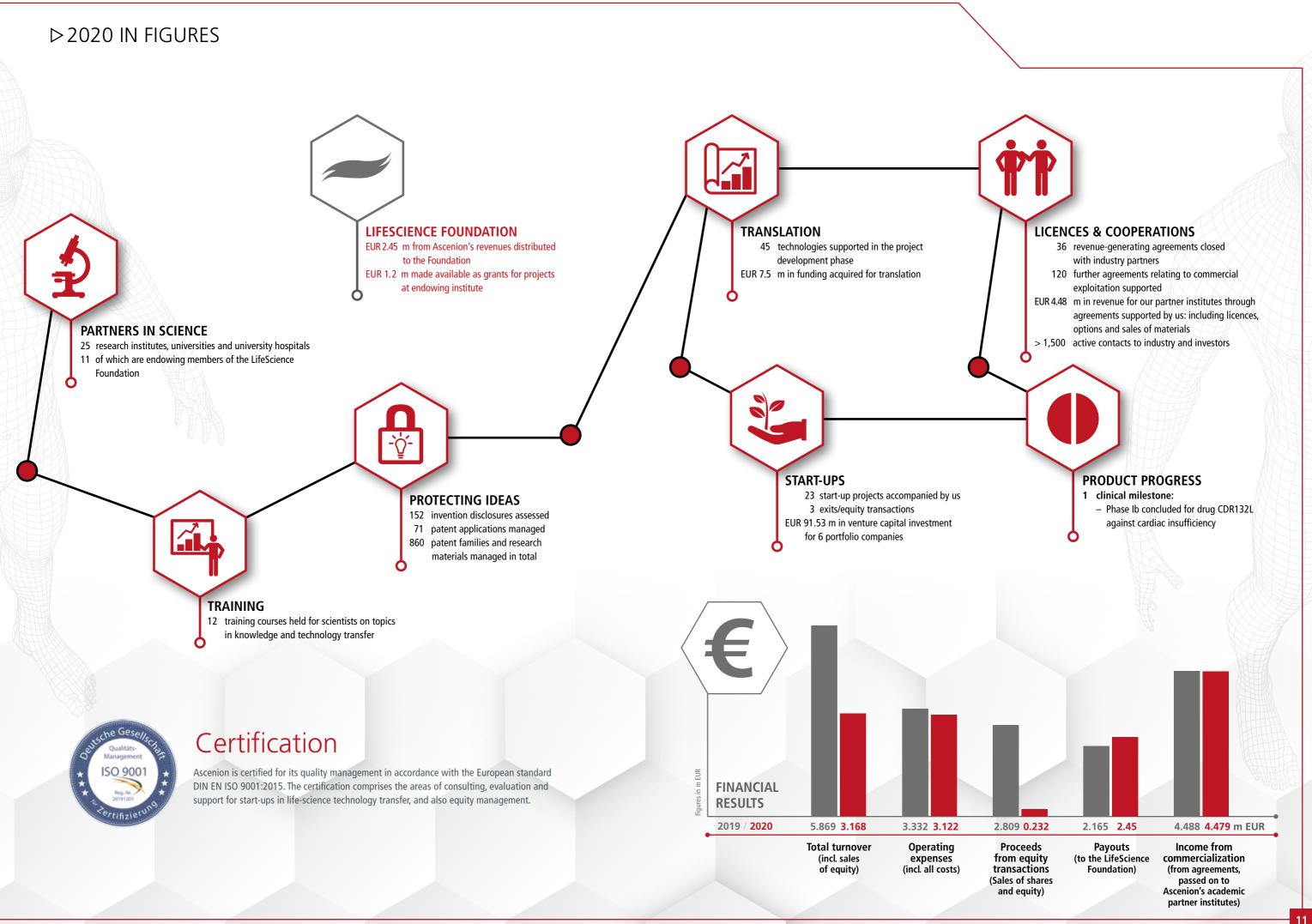
dentalXrai:

Better decisions in dentistry

X-ray images are used in dental diagnostics to detect caries, infections, implants and root fillings. Differentiating between these is not always easy – even for experienced practitioners. Prof. Falk Schwendicke and his team had developed an AI-based platform that can help. Dentists and companies specializing in dental health can simply upload their X-rays for immediate analysis. The results are precise and available in a form that is compatible with software used in dental surgeries. The time saved can be used more efficiently for patient consultation and treatments.

With the help of a vast dental data set which not only includes X-ray images, but also clinical and socio-demographic data from the Charité and further clinical partners all over the world, the underlying model has - and continues to be - optimized.





▷ START-UP MILESTONES 2020

7 new participations

Molecular diagnostics for better therapy decisions in skin disease



Aignostics (Charité, BIH) Al-supported precision diagnostics for pathology



dentalXrai (Charité, BIH) AI-based analysis of X-ray images in dentistry



mTOMADY (Charité, BIH) Digital platform for financial inclusion in healthcare

Dermagnostix (Helmholtz Zentrum München)



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ROSCUE

x-cardiac

MTOMADY

Porous (Charité) Diagnosis of cortical bone health using 3D ultrasound

Roscue (Helmholtz Zentrum München) New therapies based on ferroptosis: protecting tissues from reperfusion injury after circulatory disorders

x-Cardiac (Charité, BIH, DZHB) Early warning system for intensive care units: recognizing complications before they become critical

Financing

Six companies in Ascenion's 2020 portfolio have acquired a total of EUR 91.53 million in capital. The following financing rounds have been published:



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T-knife, a spin-off from the MDC and the Charité acquired Series A financing of EUR 66 million in April 2020. It's core business is the innovative HuTCR platform for developing new cancer therapies.

Aignostics, a spin-off from the Charité and the BIH, obtained seed financing of EUR 5 million in August 2020 in order to further develop its AI-based diagnostic solutions for pathology.

Product progress

In November 2020, Cardior concluded a Phase Ib study of the drug CDR132L against cardiac insufficiency. The company is the first to target a microRNA that plays an important role in the pathological growth of heart muscle cells.

In addition, Amcure, Berlin Cures and Medigene all had candidate drugs in clinical trials in 2020.

Exits / Investment business

In April 2020, Formula Pharmaceuticals, a partner of the Max Delbrück Center for Molecular Medicine (MDC), merged with cell therapy specialist Colmmune. The surviving company, Colmmune, will continue the cooperation with the MDC.

In September 2020, the US diagnostics specialist Bruker Corporation acquired Canopy Biosciences[™], LLC, which the year before itself acquired Zellkraftwerk, a spin-off from the Hannover Medical School.

In December 2020, the Austrian venture capital firm Horizonte Venture Management acquired Ascenion's oldest existing portfolio company, Biomax Informatics AG. The company started life as one of the first bioinformatics pioneers, growing from a supplier of specialized genome notation software to a provider of integrated knowledge management solutions for the life sciences. Ascenion sold all its shares in Biomax as part of the acquisition.

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⊳COLLABORATION

Immune cells against pulmonary infection

Macrophages play an important role in cellular immunity, and are responsible for the destruction of pathogenic viruses and, above all, bacteria. Scientists have had the vision of producing macrophages and other therapeutically useful cells on a large scale to treat infectious diseases for over 15 years. This would allow infections to be targeted that cannot be cured with existing therapies. Researchers at the Hannover Medical School (MHH) – Prof. Dr Nico Lachmann, Dr Mania Ackermann and Dr Robert Zweigerdt – have taken a major step forward in achieving this goal. Their approach makes use of so-called 'induced pluripotent stem cells' (iPS cells) that are derived from human somatic cells and can then be reprogrammed into any human cell type. The MHH team has developed a technology for differentiating iPS cells into macrophages in special bioreactors, and producing them in any required quantity.

With Ascenion's support, the MHH has closed a cooperation and exclusive licensing agreement with Novo Nordisk. Together, the partners hope to advance the approach into clinical application.



⊳LICENSING

Sleeping Beauty for efficient and stable gene transfer

What seemed a few years ago to be science fiction is now reality: cell and gene therapy play an important role in the treatment of diseases such as cancer. However, firstgeneration gene therapy approaches are based on viral gene transfer systems, which can lead to critical side effects in some cases. They are also complicated and expensive to produce, which limits their suitability for routine use in large groups of patients.

The 'Sleeping-Beauty' transposon system developed at the Max Delbrück Center for Molecular Medicine (MDC) by Dr Zsuzsanna Izsvák and Prof. Dr Zoltán Ivics (now at the Paul-Ehrlich-Institut) offers an attractive alternative. Transposons are 'jumping genes': DNA elements that can change their position in the genome. These non-viral gene vectors are cheaper to produce and simpler to use than viral gene



transfer systems, and have been shown to be considerably more effective in many studies conducted in various model systems. The first clinical trial of the most recent – and most effective – member of the Sleeping Beauty generation (SB100X) begins in 2021.

Ascenion has been working closely with the inventors for many years to secure IP and commercialize the system. Demand is rising rapidly. The team has supported numerous licencing agreements for various applications of SB100X:

- Cell and gene therapy, in particular adoptive (CAR) T cell therapies
- Production of recombinant proteins, such as antibodies
- R&D tool for simple and rapid production of stable genetically modified cells

▷COVID-19-RELATED PROJECTS

Many of our partners are contributing in one way or another to combating the pandemic. Here is a small selection of some of these projects:

Inhalable antiseptic against SARS-CoV-2

People with early COVID-19 symptoms and a positive test result could in the future be able to reduce their viral load and activate their immune system with an inhalation therapy, or even a nasal spray. The active substance is N-chlorotaurine (NCT), a natural antiseptic that Prof. Waldemar Gottardi together with Prof. Markus Nagl and his team at the Medical University of Innsbruck (MUI) have been investigating for a long time, and with which they have initial clinical experience. A clinical trial in patients with SARS-CoV-2 is in preparation. Ascenion supported MUI and the inventors in the finalization of a license agreement with a pharmaceutical company.

Passive immunization with neutralizing antibodies

Some people cannot be vaccinated because their immune system is compromised or overloaded. Others are not yet vaccinated and need instant protection because they have come into contact with an infected individual. Both can benefit from so-called passive immunization - the administration of specific antibodies. These can prevent coronavirus from entering cells and replicating. Prof. Harald Prüß and his team from the Helmholtz Innovation Lab BaoBab at the German Center for Neurodegenerative Diseases (DZNE) and the Charité have isolated antibodies from the blood of individuals who have recovered from COVID-19 and developed and validated suitable candidates. The work is being conducted in cooperation with Miltenyi Biotec.

Multiplex analysis in COVID-19 diagnosis

PCR and LAMP-Seq tests indicate whether SARS-Cov-2 is present, but don't provide any further details. The new LEOPARD procedure, developed at the Helmholtz Institute for RNA-based Infection Research (HIRI) and the Julius-Maximilians-Universität (JMU) Würzburg, can do more. Prof. Chase Beisel and his team use the CRISPR-Cas9-System to aid diagnosis in an imaginative way, allowing an almost unlimited number of markers to be analysed in one test. This makes it possible, for example, to test simultaneously which virus variants are present. Ascenion supported patent protection of the method as well as the acquisition of funding and the structuring of collaborations for further development.

Research tools & assays

Successful research into infection processes and the development of diagnostics and therapies relies on the availability of suitable tools. Prof. Stefan Pöhlmann and his team at the German Primate Center (DPZ) offer special plasmids, antibodies and cell lines. Ascenion supported the DPZ in commercializing them with interested companies. Other institutions, e.g. the Institute of Molecular Biotechnology (IMBA) und TWINCORE, have developed specific assays.

High-throughput diagnosis of COVID-19

Next-generation sequencing (NGS) allows large amounts of genetic information to be analysed in a short time. A Viennese team lead by Dr Ulrich Elling at the Institute of Molecular Biotechnology (IMBA) and Dr Luisa Cochella at the Research Institute of Molecular Pharmacology (IMP) has developed this method for the sensitive high-through put diagnosis of COVID-19. Depending on the information required, it is possible to differentiate between COVID-19 and other respiratory diseases, or to determine SARS-CoV-2 variants. The method, which deliberately does not require any limited equipment or reagents, is ideal for monitoring vulnerable groups of people, for example in healthcare, care homes or educational establishments. It is already in use in Austria, and, with support from Ascenion, was recently licenced for the Chinese market. It can readily be adapted to other purposes (e.g. future pandemics).

Life Science Stiftung

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.

11 endowing research institutes in the Foundation as of 2020

EUR 1.2 million in grants provided by the Foundation in 2020 for 5 projects, plus one top-up grant for an existing project

DPZ:

Understanding the control of finger and hand movements The Foundation has funded the purchase of a multidisciplinary surgical microscope at the German Primate Center (DPZ). It is required for studies concerning the cortical control of finger and hand movements. DPZ scientists hope for a better understanding of how these movements are coordinated in the primate brain, and to use this knowledge to develop real-time decoding algorithms. The research is central to the rehabilitation of patients with paralysis and the development of neuroprosthetics.

HKI:

Identifying useful natural products in the microbial cosmos

The Leibniz Institute for Natural Product Research and Infection Biology – Hans Knöll Institute (HKI) is using Foundation funding to further develop its high-throughput microfluidic platform. This allows numerous microorganisms – up to 9 million single cells per hour – to be isolated from their natural environment, cultivated in minute picolitre droplets and analysed for useful natural products in an ultra-high-throughput screening process. The platform can be used, for example, to identify new antibiotics.



FZB:

Understanding difference in the progression of tuberculosis

The Research Center Borstel – Leibniz Lung Center (FZB) has received a Foundation grant to investigate the roll of cytokine IL-10 produced by B cells in the development of tuberculosis. The results are contributing to a better understanding of individual and sex-specific differences in tuberculosis. In the long term, this knowledge can lead to the development of new vaccination strategies and host-directed therapy approaches that are optimally tailored to individual patients.

HZI:

A nanoscopic view of infection processes

At the Helmholtz Centre for Infection Research (HZI), the Foundation is supporting research into virus–cell interactions at the molecular level. Only a few viral and cellular proteins are involved in contact between viruses and their host cells. Their interaction governs the initiation and progression of each viral infection. HZI scientists are using modern microscopy techniques to visualize viral and cellular nanostructures during an infection, shining a light on the basic processes of viral infection.

▷ SCIENCE PARTNERS

Connecting science and industry

We have continuously supported more than 25 academic institutions in 2020, 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, Leibniz Institute for Experimental Virology
- LIN, Leibniz Institute for Neurobiology

Endowing institutes of the LifeScience Foundation are highlighted.

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

▷INDUSTRY PARTNERS

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.

Global concerns Regional innovation leaders Medium-sized companies Incubators Pharmaceuticals Food Start-ups Environmental technology IT Diagnostics Medical technology Banks Venture capitalists CROS Foundations Biotechnology Family Offices

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 2020 Ascenion was active in over 22 initiatives, associations and joint projects, 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
- Fokus Transfer the portal for knowledge and technology transfer
- GO-Bio initial (Ascenion)
- Horizon 2020-Projects: ESOTRAC + UTILE
- ITN consortium 'AIDD' (HMGU)
- ITN consortium 'SMABEYOND' (MHH)

- Forum MedTech Pharma
- 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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Imprint:

This report is published annually by Ascenion: Ascenion GmbH, Herzogstrasse 64, 80803 München, Germany Represented by: Dr Christian A. Stein (CEO) Register Court: Amtsgericht München HRB 118236 VAT Identification Number: DE 812299325