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**Press Release**

Frank Fleschner
PR Manager
Phone +49 89 949-20421
Frank.Fleschner@messe-muenchen.de

# Trend Report

## Where personalized medicine is already effective

**In modern medicine, personalized treatment strategies are becoming increasingly important. Their objective: better therapies through medical services tailored to the individual. With specific methods of molecular genetics, diseases can be better controlled, as well as prevented. Tangible successes are already evident in HIV and cancer. However, a decisive factor for treatment success is individual patient characterization and appropriate pre-testing in order to determine which drugs are suitable for a particular patient and which are not. According to vfa (Verband der forschenden Pharma-Unternehmen – the German association of research-based pharmaceutical companies), some 67 drugs are currently being used in a "personalized" manner in Germany. And the number increases every year.**

### Innovation potentials and investments

"Personalized medicine is the medicine of the future," says Dr. Richard Mitreiter, Head of Department at the German Aerospace Center (DLR), Project Management Health for the Federal Ministry of Education and Research (BMBF). The ongoing rapid technological development in life sciences, biomedicine and information technology has opened up fascinating perspectives for the development of novel treatment approaches that are optimized for individuals and specific patient groups. "The challenge of the coming decade is to develop sustainable solutions for clinical practice and marketable product innovations from the many-faceted results of research. This also includes finding suitable models for reimbursement in the healthcare system and developing the regulatory framework further," explains Mitreiter. "**Since 2013**, the Federal Ministry of Education and Research – the BMBF – has invested **some 360 million euros** from project funding and significant amounts from institutional funding into personalized medicine, and will continue to support this."

### Diagnosis and therapy in tandem

"Personalized medicine has advanced rapidly in recent years. The prerequisite for this was the mapping and decoding of the genome," asserts Dr. Martin Walger, Managing Director of the German Diagnostics Industry Association (VDGH). The

decoding of the human genome and the resulting possibilities of modern genetic diagnostics have significantly accelerated this trend. Standardized therapy concepts have so far often been aimed at overall patient groups, without taking into account the health status of each individual and his or her physical condition, and without differentiation according to age and sex. Accordingly, drugs and therapies for identical diseases would show differing degrees of efficiency, ranging from highly efficient to completely ineffective. Hence, today's medical research focuses on the development of new types of individual-oriented diagnostic procedures and innovative drugs for bespoke treatment approaches.

Oncological patients in particular benefit from the fact that companion diagnostics provide important information before and during treatment: This information enables a tailored therapy approach and shows whether a drug is or is not suitable and effective. "Molecular genetic methods such as next-generation sequencing (NGS) technologies can now be used to create comprehensive tumor profiles or even entire genome sequencings in a short time," explains Walger. For this reason, individualized or "personalized" treatment methods are already being **successfully used today in diagnostics and therapy for breast and colon cancer**. In the case of colorectal cancer, for example, a genetic test on a tissue sample from the tumor can now be used to determine exactly which drugs are suitable for a particular patient, and which are not. Personalized therapies also yield treatment successes in the case of **HIV-induced immunodeficiency and certain infectious diseases such as hepatitis**. Modern diagnostics not only provides the pretests necessary for successful application of personalized medicine, but also enables increasingly better differential diagnosis. Today, six genotypes of hepatitis C viruses can already be distinguished in the laboratory.

**Use in oncology**

Personalized medicine has had its greatest successes so far in oncology, where personalization is of particular importance for efficient treatment. Cancer cells arise through mutations. However, not all cancers are the same. In tumor tissues from different patients with the same type of cancer, the mutations found are yet not necessarily the same. However, whether certain therapies are effective or not depends on the mutations. Immunoglobulins such as the monoclonal antibodies cetuximab (trade name Erbitux; Eli Lilly, Bristol-Myers Squibb, Merck) or panitumumab (trade name Vectibix; Amgen) can be effective in advanced colorectal cancer only if the KRAS gene has not mutated yet. A genetic test can now be used to determine by taking a tissue sample from the tumor whether or not the drugs are effective for the particular patient. Thanks to tissue diagnostics, tumors and metastases can be precisely identified in oncology, which enables more precise monitoring and opens up prospects for tailored treatment.

Knowledge of the genetic data enables earlier and more precise diagnosis, more effective prevention, and optimized treatment. Here it is important to elucidate and understand the processes in the body. In this way, the mechanisms of action of relevant drugs can be specifically determined in order to develop tailor-made therapies. Successes with personalized therapy approaches have been achieved in breast, colon and lung cancer, as well as in rare malignant tumor diseases such as mantle cell lymphoma.

Breast cancer patients whose tumor cells overexpress the special growth factor receptor HER2 can be treated with anti-HER2 therapy (trade names Herceptin, Perjeta; Roche) based on the active ingredients trastuzumab or pertuzumab. Certain **lung cancers** can also be treated with targeted drugs. For example, in some non-small cell lung tumors, the active ingredient erlotinib (trade name Tarceva; Roche) can be used to inhibit the EGFR gene, which shows specific mutations in lung cancer. The ALK mutation that is frequently found in non-small cell lung cancer can likewise be treated with the targeted drug alectinib (trade name Alecensa; Roche).

**The battle against Parkinson's and Alzheimer's diseases**

In addition to the wide application range of personalized medicine in personalized cancer therapy, personalized diagnosis is also used **against Parkinson's and Alzheimer's diseases, as well as in the field of intestinal microbiology and personalized hearing support**.

The therapeutic options for Parkinson's disease address the causal chain in order to detect causally involved molecular defects on the one hand, and to study pathological α-synuclein species and their propagation on the other. α-synuclein (encoded by the SNCA gene) is a transport protein in the brain that regulates the release of dopamine. Mutations in the SNCA gene are responsible for certain inheritable forms of Parkinson's disease. The drugs available today can only protect the dopaminergic nerve cells from damage and thus halt the progression of the disease. Hopes are pinned on research into the antioxidant coenzyme Q10, which may be of particular benefit to patients with impaired mitochondrial function.

Research into new anti-Alzheimer drugs also enjoys high priority in the pharmaceutical industry. However, the success rate is sobering. Nevertheless, the important finding has been made that treatment with drugs for slowing down or prevention must be started very early. This has become possible because both β-amyloid and tau fibrils, two different protein compounds characteristic of Alzheimer's disease, can now be detected using non-invasive imaging techniques. These two protein deposits disturb communication in and between the nerve cells to such an extent that the nerve cells die. This is because Alzheimer's disease alters degra-

dation of the amyloid precursor protein found in the organism. The β-amyloid proteins thus produced in the course of the disease accumulate as toxic oligomers and lump together to form insoluble deposits between the nerve cells. These so-called β-amyloid plaques, also known as Alzheimer plaques, can then no longer be broken down by the body.

The tau protein in turn helps to form microtubules in healthy cells and is thus responsible for the stability and nutrient supply of the cells. In Alzheimer's disease, the tau protein is chemically altered so that it is deposited in the form of fibers, the so-called tau fibrils. As a result, the diseased nerve cells lose their shape and function until they decay. Drugs with active ingredients such as aducanumab (Biogen), solanezumab (Eli Lilly) or gantenerumab (Roche), which are designed to prevent and reduce formation of plaques, are in the test phase and await marketing authorization. Therapeutic active vaccines to be administered concomitantly with the actual treatment are also in the trial phase in the fight against Alzheimer's disease.

**Predicting strokes**

"**Predictive stroke modeling** enables person-related prediction of strokes, since it integrates multidisciplinary sources such as genomics, biochemistry, social issues, lifestyle, sex, or the working environment," explains VDGH Managing Director Walger. "One recent achievement is the liquid-biopsy method." The latter enables detection of circulating tumor cells or tumor DNA in the blood. This requires highly sensitive detection methods such as advanced polymerase chain reaction (PCR) and next-generation sequencing (NGS) technologies. "In the next few years, liquid biopsies are likely to become more and more important alongside conventional biopsies, i.e. sampling of tissue and its histopathological examination, also because they are less invasive for the patient," says Walger. Liquid biopsies can be used for early detection of tumors in screening, for therapy monitoring, or for estimating an individual risk of metastasis.

**Bioanalysis as stimulator**

Pivotal for these medical successes are high-resolution analysis as well as biotechnological and chemical research. Biotechnological advances in particular are important for novel developments in the drug discovery field of pharmaceutical research and point-of-care diagnostics.

Efficient development of highly effective substances is possible only in high-tech laboratories with powerful automated analysis systems and high-throughput sequencing. Analytical technology is an important source of impulses for the tailor-made development of active substances. Target-oriented studies of drug interac-

tions and target binding of active ingredients would not be possible without automated procedures such as high-throughput screening and biotechnological methods.

Modern analysis and molecular genetics methods make it possible to elucidate genetic and biological processes, demystify molecular structures and switch points, and understand the mechanisms of gene expression in order to successfully apply targeted individualized, tailor-made therapeutic concepts. A key role is played by disease-specific biomarkers that provide scientists with meaningful information about the type, molecular cause, and status of the disease. “The diagnostics industry is cooperating closely with the pharmaceutical industry on research into biomarkers and the development of corresponding tests, which are a prerequisite for personalized medicine,” adds VDGH Managing Director Walger. As a result, targeted therapies can be initiated for various types of cancer, such as breast, colon or lung cancer, and for HIV, significantly increasing the success of treatment.

Personalized gene therapies, regenerative medicine, tissue engineering and bioprinting likewise open up new paths in tissue and organ research. Functional organ structures from so-called biofabrication for intelligent therapies are based on the use of tailor-made biomaterials such as functional peptides, and allow novel individual treatment methods. It is thus possible to grow certain cell cultures and tissue structures in culture and nutrient media for use as implants in orthopedic, plastic and cardiovascular surgery. Human in-vitro models based on human cells, in particular from the human liver, are already being developed by Hepacult.

**The potential of personalized medicine**

The member surveys of the VDGH show that personalized medicine has gained importance for more and more companies in the in-vitro diagnostics (IVD) industry. While in 2016 there were about 27 percent of the IVD companies surveyed active in this field, the share had grown to more than 61 percent by 2019, and the trend is still upwards.

“Researchers predict that in the future most types of cancer will be diagnosable at an early stage thanks to genetic blood tests,” says Walger. “A prerequisite for this is development of validated biomarkers with high sensitivity in order to be able to detect the disease in the pre-symptomatic stage. This is one of the tasks and challenges the life science and diagnostics industries are working on. On the therapeutic side, developments in immunoncology, cell therapy and gene therapy are decisive fields in which a great deal is already happening today and will be even more so in the next five to eight years.”

According to the VDGH, progress has been made in recent years in the reimbursement of companion diagnostics by statutory health insurance. “If use of a medicinal product requires prior testing, a remuneration figure for the test procedure must be agreed upon in due time. This automatism promotes implementation of personalized medicine outside the inpatient setting,” explains Walger.

**Digitization and data management are a key to success**

Computer-aided drug design and next-generation ultra-high-throughput methods generate gigantic amounts of data very quickly. Here, digitization creates the necessary basis for meaningful evaluations and efficient data management for biobanks, peptide libraries, or patient data. Further successes in personalized medicine will crucially depend on digitization. Innovative and fast technologies that enable ever more precise diagnostics in ever shorter times generate enormous quantities of data that need to be stored, analyzed and intelligently merged. “With each data set, the understanding of diseases improves, patterns can be recognized, and indications for new treatment strategies can be derived. This means an enormous transfer effort. Intelligent information and data management – and this also includes the possibility of using data from care reality – are the prerequisite for this,” according to Walger.

**Next-generation technologies at analytica**

Next-generation technologies from biological and genetic research, diagnostics and analysis are the pacemakers for Personalized Medicine. **The latest trends from these areas will be presented to the experts at analytica 2020.** The trade fair comprehensively presents cutting-edge technologies and future-oriented methods. To discuss their experiences, international experts and the global players meet in Munich, where the know-how of the industry and the latest state of the art will be exemplified.

The user is presented with well-structured and comprehensive practical system solutions, which allow shorter analysis and test times as well as better interpretation possibilities of the measurement results and central availability of meaningful data to be achieved. New diagnostic possibilities and individual therapies are possible only through novel molecular genetic methods, as presented at analytica. Effective and precise diagnostics is ultimately the crucial prerequisite for more treatment successes in personalized medicine.