BioRN

OUR STRATEGY FOR THE FUTURE

BioRN

Life Science Cluster Rhein-Neckar

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Executive Summary

Recent advances in biotechnology and medical biology provide many novel options for treating diseases. While much of the scientific progress emerges from academic research, large biotech and pharma companies have the fundamental expertise and funding options necessary for the actual transfer of scientific results to application. At the same time, a decrease in drug development productivity and rising healthcare costs put enormous pressure on both the pharmaceutical industry and healthcare systems in general.

The Rhine-Main-Neckar region around Heidelberg is home to both academic excellence and strong industrial players in very close geographic proximity. As such the region is an outstanding example of a biomedical cluster, and - because of the rich ecosystem covering the entire value creation chain and a dedicated cluster management - has seen a constant rise since the foundation of the BioRN Network more than 25 years ago.

With the vision to make life science matter and innovation happen, and following a set of guiding principles, BioRN strives to become one of the leading European life science clusters.

For this end, a clear strategy is devised through analysis of the ecosystem, and with input from all stakeholders. Existing strengths are used to generate opportunities, and to neutralize threats and weaknesses, a key component being the unique combination of global pharma and leading academic institutions in the region. This combination is used as a lever to support the transfer of basic research toward medicines and products, in particular by de-risking the development process and company formation, as well as by attracting investment. In addition, at the interface between industry, academia and government, BioRN is contributing to the development of a new lead industry Baden-Württemberg, with the aim to advance the cluster as a whole.

In line with current trends and needs the strategy is regularly updated and its goals are reached by the conception and implementation of activities within the following four fields of action:

1. Networking & Stakeholder Engagement
2. Promotion & Visibility
3. Cross-organizational Functions
4. Translational Support & Growth

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1. An Analysis of the Current State

Research and Innovation in the Life Sciences

The advent of personalized medicine and a host of novel therapeutic modalities - born from tremendous advances in biotechnology and an ever-increasing understanding of human biology - promises groundbreaking new opportunities for curing formerly untreatable diseases. Much of this progress is driven by academic research and young start-up companies as drivers of unconventional approaches. The most notable example for this trend is the recent development and approval of a COVID-19 vaccine within less than a year and as a first ever medicine based on mRNA technology, which was pioneered in academic labs and developed by the German SME BioNTech.

"The old pharma model had to change, forcing big biotech and pharma companies to revisit their business models"

At the same time health care expenditure is rising on average 4% each year [1], not only because of aging populations but also because the share of novel and personalized, expensive therapeutic modalitiesis is growing. For instance, the percentage of biologics, i.e. therapeutic antibodies and peptides, approved by the FDA grew from on average 10% in the late 1990's to 28% in 2021[2].

This seemingly favorable environment for biotech and pharma companies is countered by an apparently unstoppable trend of increasing costs for each new medicine reaching the market, with estimates ranging up to 4.5 billion US dollars [3] per medicine.

The reasons for this development are manifold: Fine-tuning of molecular stratification of patient populations leading to smaller market shares for any single drug; clinical trial success rates as low as 5% [4]; higher development and manufacturing costs for advanced medicinal therapeutic products (AMTPs), such as gene and cell therapies, which many times are personalized and therefore targeting smaller patient populations; and complicated, novel regulations pharmaceutical companies have to comply with. These trends might potentially result in placing an enormous financial burden on healthcare systems, which in turn makes payers and providers wary of adopting novel medicines into practice, resulting in further decreasing revenues. In addition, there is a wave of expiring patents on former blockbuster drugs.

The old pharma model had to change, forcing big biotech and pharma companies to revisit their business models. As both academic research institutes and small companies

[1] Statistisches Bundesamt https://www.destatis.de/
[2] https://doi.org/10.1038/d41573-022-00001-9
[3] https://doi.org/10.1007/s40273-021-01065-y
[4] https://doi:10.1093/biostatistics/kxx069

emerged as very powerful innovation engines, they were predestined to play an important role in the transformation of the pharmaceutical industry. At the same time, these organization would benefit most from the input of global corporations in terms of financing, product development expertise, distribution and marketing.

"Support the ingenuity and pioneering spirit of thousands of scientists and entrepreneurs early on"

In recent years, big companies started to increasingly outsource their R&D efforts, and what is more, they started to rely to a growing extent on external innovation to feed their drug candidate pipelines. For that end such global companies are continuously developing and testing new (open) innovation models to fill their pipelines and increase the chances of success. They come in a variety of flavors, amongst others e.g. industry-hosted incubators or accelerators, diverse types of early stage partnerships or grant programs with academia, or the establishment of strategic ventures funds.

The strategy behind all these programs is the same: to build on and support the ingenuity and pioneering spirit of thousands of scientists and entrepreneurs early on, and to subsequently help them to decrease the high inherent risks of the complex biology their ventures are based upon. They can do this with their financial possibilities, and their expertise in both drug development and commercial roll-out, which helps academic research projects and smaller companies exactly where they need it most. However, the "valley of death", the famous gap in between academic research and industry readiness both in terms of financing and expertise, persists and is an ever-present concern for any kind of successful commercialization of projects born out of an academic environment.

1. An Analysis of the Current State

The Rhein-Main-Neckar Region

The region around Heidelberg at the border between Baden-Württemberg, Rhineland-Palatinate and Hesse, and connected by the rivers Rhein, Main and Neckar traditionally holds an excellent academic reputation. This reputation is based on the oldest German University, the Ruperto Carola, which was founded in 1386 in Heidelberg and still is for the third time in a row one of eleven German "Excellence" universities. Together with the German Cancer Research Center (DKFZ), the European Molecular Biology Laboratory (EMBL), and the Max Planck Institute for Medical Research the different institutes of Heidelberg University and the University Clinic form an extremely dense nucleus of biomedical research, almost 9000 scientists [5] doing their science in walking distance. In the surrounding region further centers of academic excellence are situated: the universities of Frankfurt, Freiburg, Mainz and Tübingen, the Karlsruhe Institute of Technology (KIT) and several Fraunhofer Institutes. This academic excellence with a focus on the life sciences falls together with a strong regional presence of global healthcare corporations. AbbVie, Boehringer Ingelheim, Merck, Roche and Sanofi all have important R&D sites or even their global headquarters in the Rhein-Main-Neckar region, others like Bayer, Cytiva, Evotec, GlaxoSmithKline and Johnson & Johnson have strong ties to the region. This combination was honored in 1996 when the cluster won a national competition to become one of three German bioregions supported by the federal government. The associated funding and additional money flowing to the region after being awarded the "Leading Edge Cluster" label in 2008 – in total about 70 million Euros matched by industry partners- led to a steep rise and the region becoming one of Germany's largest biomedical research cluster. The creation of start-ups and economic value were at the core of the "BioRegio" cluster back then and still are a core driver for BioRN today. By now the sector in the region around Heidelberg employs almost 10,000 people in about 70 companies and has a yearly revenue of over 2 billion Euros [6]. Research and hospital care are especially strong in oncology and immunology. In total, hospitals in Heidelberg alone treat more than 180,000 patients per year [7], whereas on the technological side personalized medicine, novel therapeutics, imaging and novel molecular biology

"This academic excellence with a focus on the life sciences falls together with a strong regional presence of global healthcare corporations"

[5] City of Heidelberg (Anlage 01 zur Drucksache 0206/2021/IV)

[6] Biopro (extrapolation from Gesundheitsindustrie Branchenreport 2021)

[7] City of Heidelberg (Statistisches Jahrbuch 2020)

technologies, the “omics”, are emphasized. Overall, Heidelberg attracted 34 Nobel Prizes, 78 ERC grants, and boasts an impressive average number of over 6,000 scientific publications per year [8]. What is more, a clear sign of the region’s commercial potential is a total output of more than 1,500 patents [8]. Recently, the role model and strength of the former core around Heidelberg has sparked interest from other German and European regions, drawing many additional research institutes and companies from the entire biomedical value creation chain to an ever-growing cluster.

In spite of this promising trend in recent years, several issues threaten the further development of the cluster. Some are associated with its recent growth. For example, the practical integration - in the form of concrete collaborations - of new players into the network becomes more challenging, likewise, an overall dispersion and increasingly complex situation leads to a limited knowledge of processes and initiatives even among otherwise well-connected stakeholders. Other issues are rather grounded on structural problems of both cultural and legislative nature. As academic achievements tend to be more highly valued than commercial success in such a traditional academic environment, the pool of entrepreneurs trying to transfer their research into application and start a business is limited. In addition, there is relatively little private money available for venture capital backing of young companies.

In order to support the growth of the life science industry and build a thriving, world-class life science environment, such issues must be addressed by the cluster.


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[8] Institute reports, BioRN analysis

2. A Strategy for the Future

BioRN is the innovation cluster of the Rhein-Main-Neckar region around Heidelberg, one of Germany's strongest biotech hubs. An innovation cluster is more than a mere agglomeration of individual organizations. It is based on the constant interaction between academia, industry and government for the production, transfer and application of knowledge. This approach refers to a spiral model of innovation, called triple-helix model, and enables highest rates of innovation. Indeed, such clusters, regardless of the sector, show higher productivity, higher wages, higher growth and employment rates in comparison to other regions.

BioRN establishes initiatives to bridge the regional innovation stakeholders and to nurture and extend connections between members. It also fosters connections to other regions of innovation worldwide and stands for the promotion and visibility of the life science region at the national and international level. BioRN acts as a neutral player, supporting cross-organizational programs and initiatives that advance the life science region as a whole. At the interface between academia and industry, BioRN provides translation support, especially by leveraging the unique combination of global pharma and leading academic institutions in the region. It now employs a clear strategy to maintain the current position and even further improve conditions by leveraging cluster-specific advantages as a basis for a future life science cluster of excellence.

Mission and Vision

Our mission is to develop the region into a world-leading life science cluster attracting international investments and top global talent.

Our vision is to make life science matter and innovation happen.

Guiding Principles

We are a team and have a common vision. Together we have the strength to make a difference and develop the Rhine-Main-Neckar region into a world-leading life science cluster.

We have integrity. Integrity is the core for our cluster work – as trusted and professional partners we take confidentiality very seriously.

We love innovation. We embrace and support scientific and technological innovation; they are the drivers of our work.

We are driven. We combine passion, excellence, and commitment to bring our projects to perfection.

We are respectful. We live the values of diversity, equity, and inclusion in our work, our projects and within our network.

We act economically. We use our resources responsibly.

We are a community. We foster partnerships and collaborative efforts, to meet the individual needs in our cluster community.

Strategy Development and Review

To define goals for the development of the cluster and to outline a clear path towards achieving these goals, BioRN regularly analyzes the framework conditions of the life science industry in general and the cluster itself to update its strategy and activities. An existing strategy is continually challenged through a classical bottom-up approach, evaluating our stakeholders' input throughout the year:

a. the BioRN boards as representatives of all regional innovation stakeholders are intimately involved in defining which new initiatives, activities and topics should be actively pursued by BioRN to fine-tune the current strategy.

b. a yearly member survey provides feedback from the member base both on general trends as well as potentially missing or changed services the cluster provides to its members.

c. a regularly updated SWOT analysis (see Figure 1) of the region's life science ecosystem is an additional tool for strategy building against which the aims of single activities can be tested.

d. the BioRN operational team collects input from the cluster participants in a continuous process and holds a yearly team workshop to evaluate this input and needs.

e. Every five years the existing strategy is formally challenged in a dedicated workshop format by members of the BioRN Boards. Learnings from these processes are used to define the next 5-year strategy.

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Figure 1: SWOT Analysis
Analysing of specific Strengths, Weaknesses, Opportunities and Threats of the region's life science ecosystem.

SWOT Analysis

Strengths

Unique combination of scientific, academic excellence, two large and closely linked university clinics, and the active presence of several global pharmaceutical companies in the region

The favorable economic situation in Baden-Württemberg allows easier access to larger infrastructural projects and highly skilled employees

Weaknesses

Lack of entrepreneurial spirit and valueing traditional academic success over economic achievements leading to unsatisfactory transfer of academic research

Lack of a critical mass of young, innovative companies

Risk aversion limits the supply of venture capital necessary for the development of new companies

Threats

Lack of unity, due to a large and highly complex ecosystem, leading to inefficiency, a perceived lack of critical mass and resentment

Loss of political support as a consequence of fragmentation of regional stakeholders and insufficient interest representation

Leveraging on the cluster's strengths to create opportunities

Opportunities

Both matching science with industry as well as bridging the "valley of death" in terms of funding and expertise counter the lack of enterpreneurial spirit and the limited number of innovative companies, taken together resulting in an increased academic and commercial output

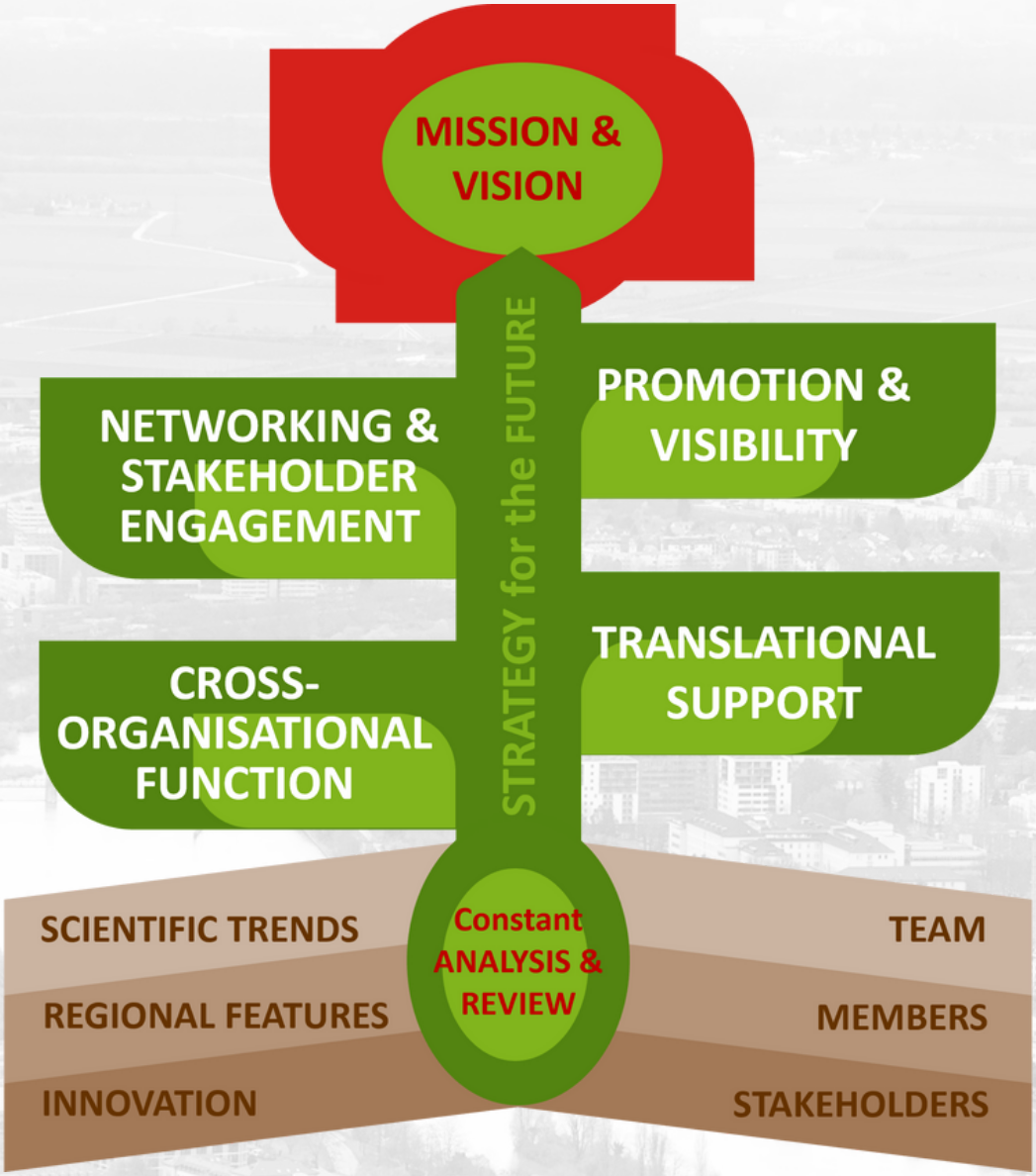
Internationalization is a pre-condition for growth and attractiveness for both people and capital. Internationalisation means: entering new markets, foreign companies coming to the region and adapting international best practice models to the region's specifics

Harmonization of processes and ongoing initiatives fights regional dispersion, helps internal and external actors to navigate the ecosystem, and strengthens ties to policy makers

Opportunities counter and neutralize weaknesses and threats, that might stall the further development of the cluster

Making Life Science matter ... and Innovation happen!

With the vision to make life science matter and innovation happen, and following a set of guiding principles, BioRN strives to become one of the leading European life science clusters.



In line with current trends and needs the strategy is regularly updated and its goals are reached by the conception and implementation of activities within four fields of action.

3. Activities to Meet the Future

Based on the tools and procedures described above, and taking into consideration input from all stakeholders, BioRN has devised four fields of action. Each field of action consists of a set of activities and services, which – in combination or alone – are designed to use strengths to make opportunities become a reality and at the same time neutralize weaknesses and threats.

NETWORKING & STAKEHOLDER ENGAGEMENT

We bridge members regionally and towards other innovative ecosystems worldwide. Nurturing and extending connections among regional innovation stakeholders is at the core of BioRN's activities. Activities and services within this pillar support the harmonization of initiatives and processes and strengthen connections between industry and academia. They also counteract any potential lack of unity and the potential consequent loss of political support. Events in particular increase the region's visibility and by presenting lighthouse stories and opportunities might help to overcome some of the region's weaknesses associated with risk aversion and lack of entrepreneurship.

- Decision makers from the network's innovation stakeholders are represented in the **BioRN Executive Board**, the **Strategic Advisory Board** and the **Scientific Advisory Board**. The close relationship of boards and management team also ensures a seamless transmission of trends and issues from basis to management and allows a fast-track reality check of newly devised initiatives and services.

- Our established networking and event formats:

  - Since 2009, each year the **BioRN Annual Conference** has been a valuable source of top information, lively discussions, and networking opportunities with international experts from different fields of the life sciences. This flagship event helps to join all members of the network in one event.

  - The **BioRN Lounge** is a monthly networking event in an informal setting, centered around current science and industry trends, a platform to get to know diverse actors from the network.

  - The **BioRN Espresso** is a structured peer-to peer event, to exchange on general operational topics of high relevance for SMEs. The concept is to share hands-on experience and solutions to common challenges.

- Access to **international cluster networks** enables best practice exchange and facilitates connection to international partners, market entry and international public funding opportunities. Such connections also increase international visibility of the cluster as a whole.

PROMOTION & VISIBILITY

We stand for the promotion and visibility of the life science region at international and national level. Activities and services within this pillar broadly support the economic and scientific development of the regional life science ecosystem. They make cluster actors and their success stories visible for the national and international audience thereby positioning the region as an important biomedical hub, attracting talent and capital. They also help to achieve an equal distribution of information within the cluster, foster an entrepreneurial spirit by highlighting success stories, and support connections within the network.

- **Public relations** – Promotion and dissemination of news, activities and successes of all members and stakeholders simplifies access to knowledge of initiatives and opportunities for participation.

- **Proactive dialog with public (health) authorities** helps to secure political support and provides influence on policies in biotechnology and healthcare. Important focus areas are the improvement of technology transfer, capital investment in health and biotech, availability of lab space and general research infrastructure for the region, and the removal of bureaucratic hurdles for government grants and financing.

- Showcasing and representing the **local ecosystem and stakeholders** at national and international events and professional meetings, positioning the region as an important biomedical hub.

- **Thematic workshops** are held by mem-bers for members, and provide SMEs from the network with a forum to align on different technologies, technical topics and services. In addition, member companies can increase their visibility by promoting their expertise and products.

- **Attract high profile (international) events** – to the region to improve national and international visibility, attract global talent and capital.

CROSS-ORGANISATIONAL FUNCTION

BioRN has a unique position at the interface between academia and industry. We support inter-institutional initiatives to facilitate applied biosciences in the region. BioRN is a neutral partner without self-purpose or financial interests and will act without bias solely for the benefit of the region and its members. Activities and services within this pillar serve to harmonize and unify the region – also at the political level. They also help the cluster management to maintain close relationships with important stakeholders, and to remain up-to-date on all life science related topics including the abilities of members and stakeholders.

- Coordination of inter-institutional **funding applications** and **funded projects**, offering long standing experience with national and international funding schemes, as well as project management expertise.
- Coordination of **inter-institutional events** offering long standing experience with event management and a good knowledge of practical logistics.
- **Central point of contact** for external enquiries regarding life science topics. A fast and efficient direction of interested parties towards the right contact person within the region, positions the region as an easily accessible cluster, with positive corollary effects in terms of visibility and attractivity.
- Support of the new **"Innovation Campus Rhein Neckar"** and the development of a new lead industry for health in the German State of Baden-Württemberg.
- Support in identification of **potential partners** from SMEs, industry and academia. This helps to forge new partnerships for the cluster's stakeholders and comprises also the efficient matching of academic and early industry projects with partners from international corporates (see Translation Support). This enforces BioRN's position as interface between academia and industry and increases the regions attractivity for such international corporates.

TRANSLATIONAL SUPPORT

We provide translation support, especially by leveraging the unique combination of global pharma and leading academic institutions in the region. We manage different programs to support the development of research (academic) ideas through clinical and product development until commercialization. Translational programs to be supported by BioRN are selected by the BioRN Boards based on regional specific needs and their ability to de-risk the company formation and development process. Activities and services within this pillar foster entrepreneurship in academia by matching academic researchers with industry experts and help to bridge gaps in funding and expertise in the development and commercial roll-out of life science products. They also strengthen the economic growth of the region in general.

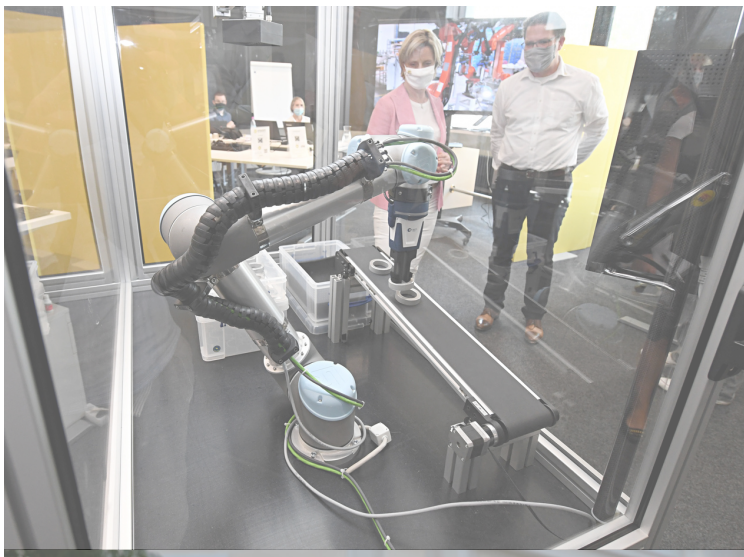
- A new working group, **BioRN Investment**, is taking up impulses from the network and the BioRN Boards to revisit the topic of insufficient risk investment capital for life science start-ups after the seed phase. The working group will identify weaknesses in the existing financial ecosystem, look at various existing funds/financing models (including public funding schemes), and will develop a suitable model for the region.

- Custom-fit search and care-free matchmaking to enable innovation. The **BioRN Scout partnering program** joins major regional and European networks to effectively match healthcare innovation seekers with innovators. Through its scouting program BioRN positions itself as a regional hub for Southwestern Germany and beyond towards international large corporates. It enhances the visibility of innovative academic projects and smaller companies from the regions, thereby facilitating the transfer of research towards application.

- **EIT Health Catapult** is a training and competition program to award the best business concepts from medtech, biotech, and digital health in the EU. Through this program BioRN is embedded in a large international network of startups, global healthcare companies and venture capital firms on which also the regional ecosystem can draw.

- **EIT Health Bridgehead** is enabling mature foreign start-ups to expand their business into our regional and national market. As a result, BioRN gains new networks and experience in issues of internationalization which in turn can be used to the regional stakeholders' benefit when they want to enter new markets. In addition, such foreign companies bring innovative solutions to the German market and many strive to establish subsidiaries in the region.

- With the government-funded project **BioInteRNational**, BioRN will pilot an internationalization support to be established as service to the cluster's SME that want to expand to foreign markets. Networks with relevant experts and stakeholders in target countries will be established, thereby expanding BioRN's international network and facilitating growth of regional companies.



BioRN Life Science Cluster Rhine Neckar

Im Neuenheimer Feld 582
69120 Heidelberg, Germany

info@biorn.org

www.biorn.org