

BIH

Frontiers in Translational Medicine – Scientific and Structural Challenges

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What is Translation?

"Translation is the Transfer of Basic Scientific Research Results into new Preventive, Diagnostic or Therapeutic Methods for the Application to Humans."

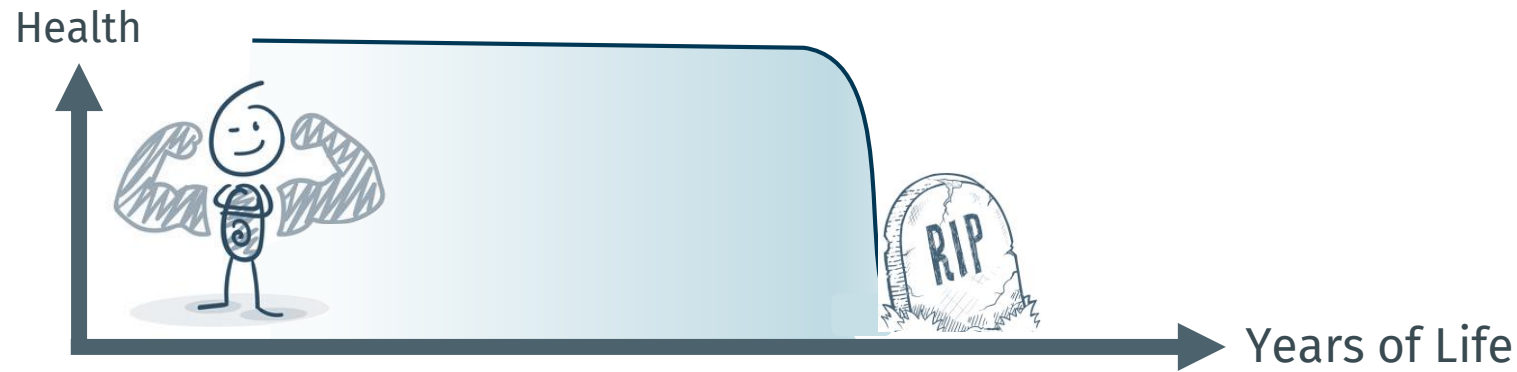
(DFG, Recommendations for the Promotion of Translational Research in University Medicine, 2019)



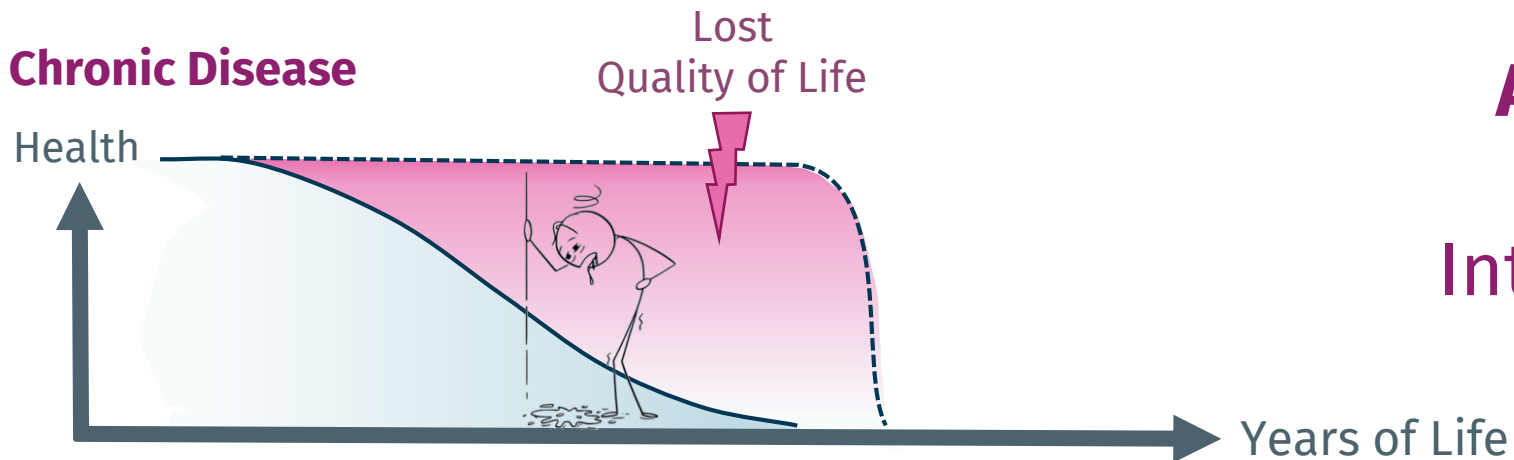
The image shows a screenshot of a Wikipedia article. At the top, there are navigation tabs for 'Article', 'Talk', 'Read', 'Edit', and 'View history', along with a search bar labeled 'Search Wikipedia'. The main heading is 'Translational medicine'. Below the heading, it says 'From Wikipedia, the free encyclopedia'. The text of the article defines translational medicine as an interdisciplinary branch of the biomedical field supported by three main pillars: benchside, bedside, and community. It states that the goal of translational medicine is to combine disciplines, resources, expertise, and techniques within these pillars to promote enhancements in prevention, diagnosis, and therapies. The text concludes by stating that translational medicine is a highly interdisciplinary field, the primary goal of which is to coalesce assets of various natures within the individual pillars in order to improve the global healthcare system significantly.

Medical Need: Why Do We Need Translation?

Desired Scenario

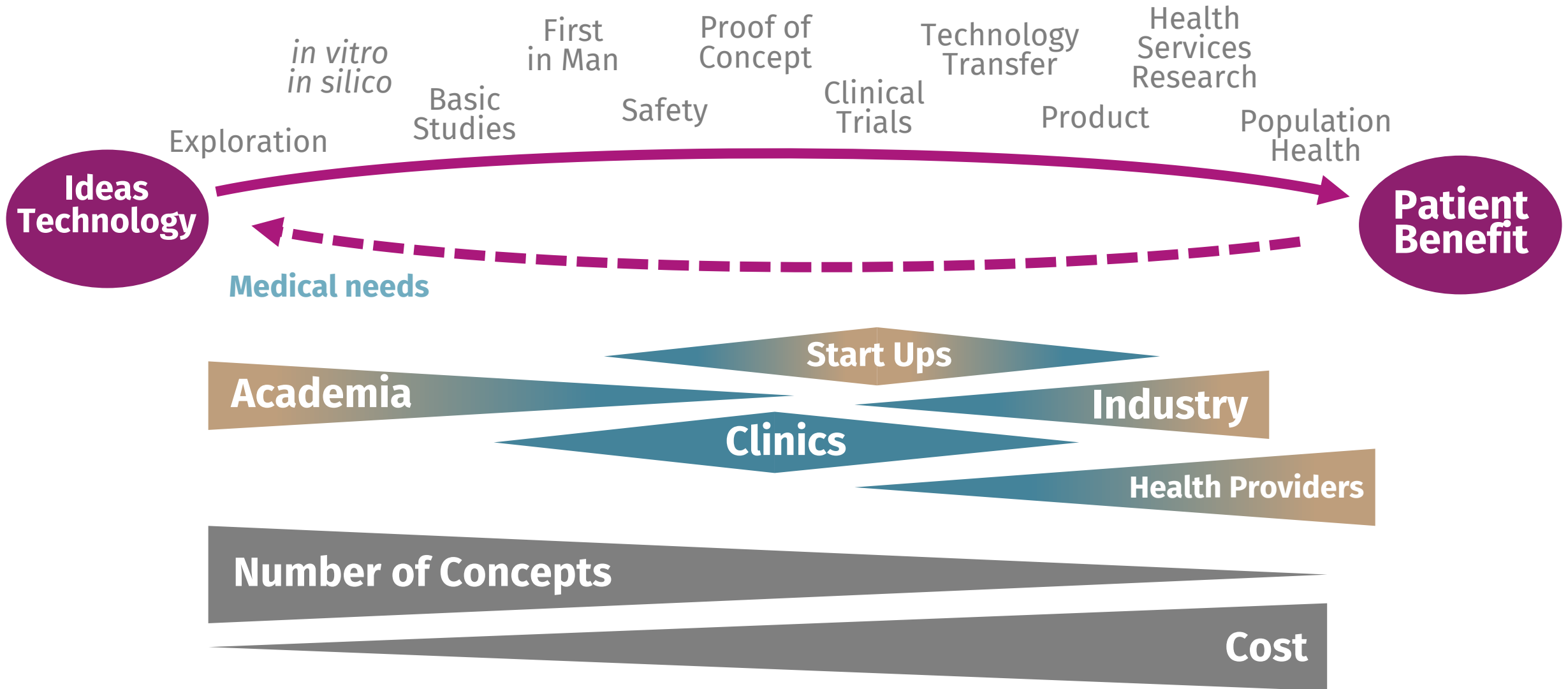


Chronic Disease



Aim of Translation:
Increase
Integral Quality of Life

The Translational Value Chain



Status of Translation


Too slow, too expensive

Erooms Law:

The cost of developing a new drug doubles approximately every nine years.

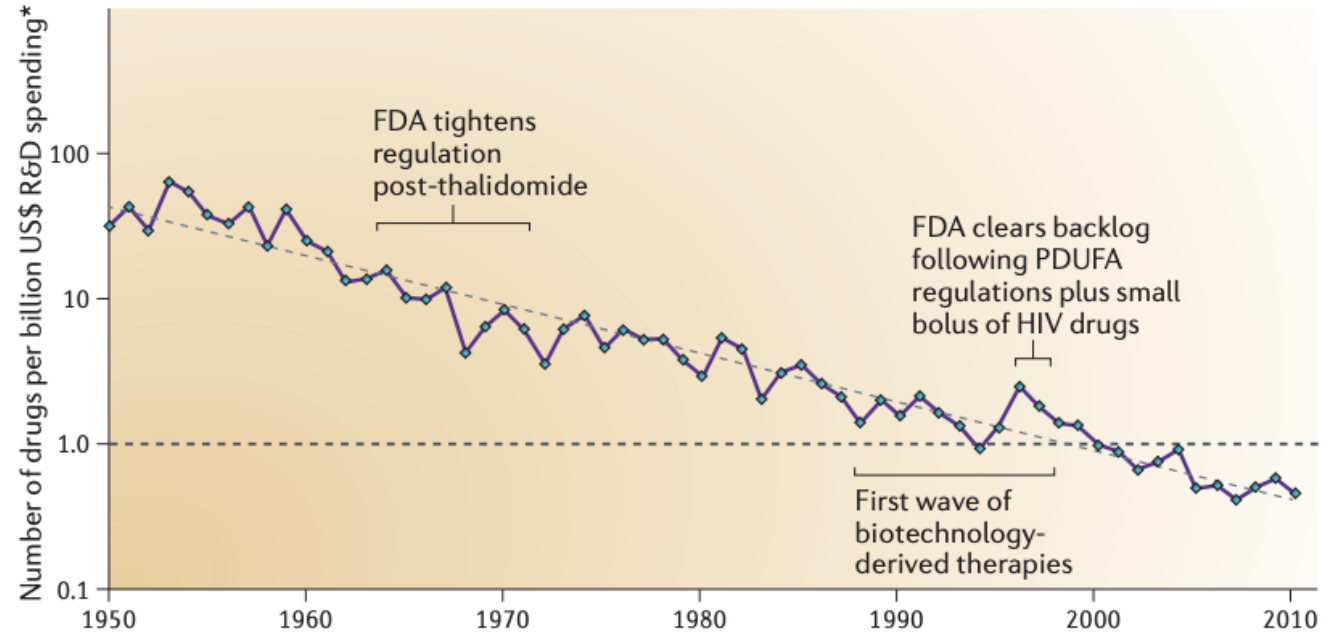
Opinion | Published: 01 March 2012

Diagnosing the decline in pharmaceutical R&D efficiency

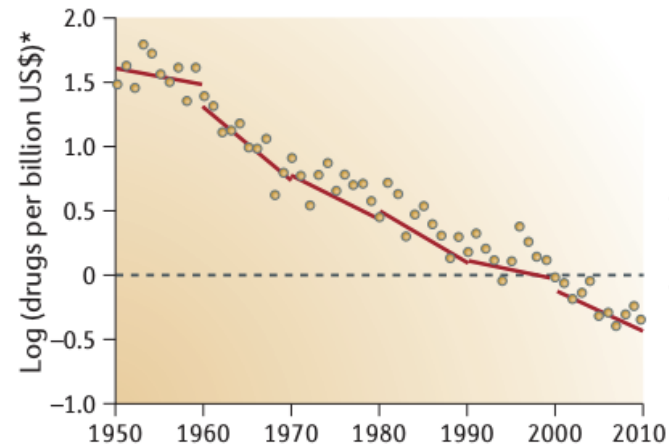
Jack W. Scannell , Alex Blanckley, Helen Boldon & Brian Warrington

Nature Reviews Drug Discovery **11**, 191–200 (2012) | [Cite this article](#)

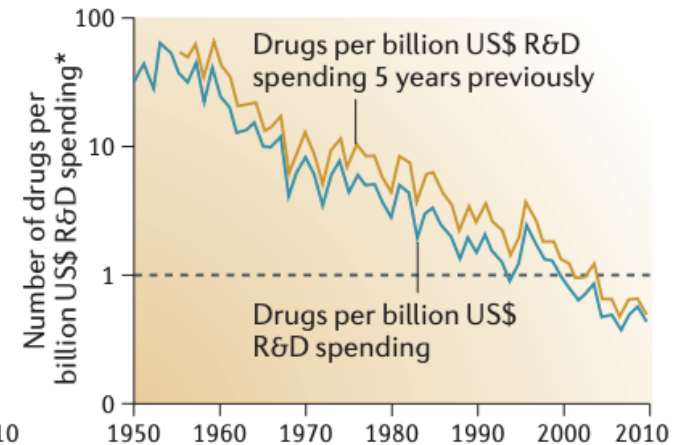
a Overall trend in R&D efficiency (inflation-adjusted)



b Rate of decline over 10-year periods



c Adjusting for 5-year delay in spending impact



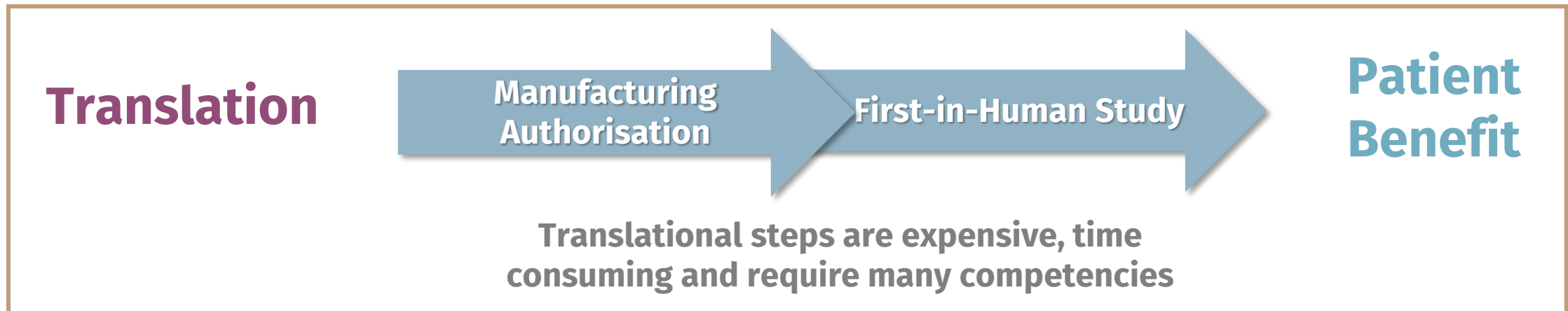
Causes

“Local Cultures”

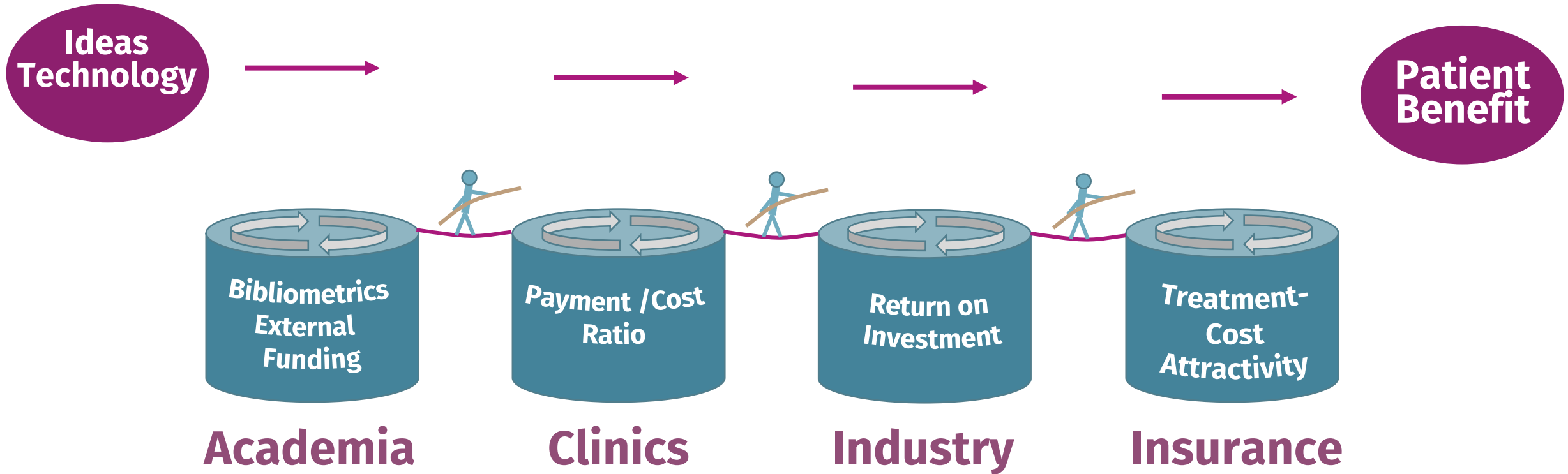


Causes

“Local Cultures”

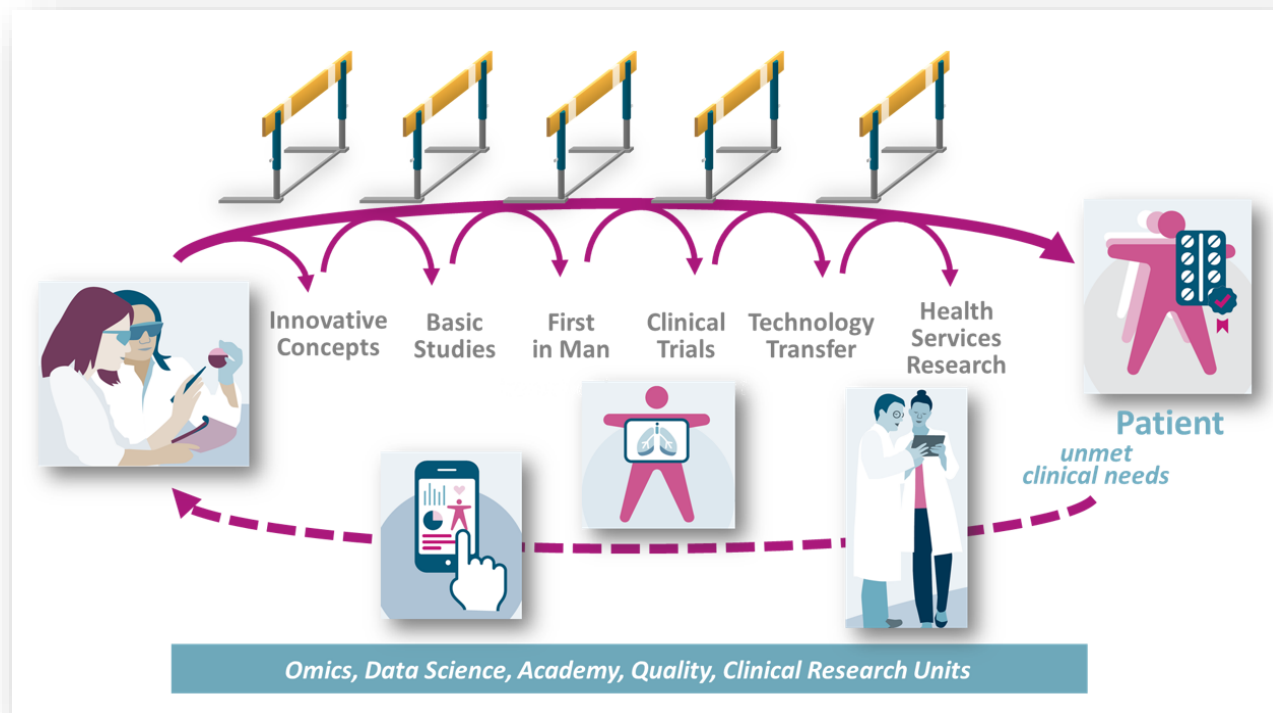


Causes “Happy Silos”

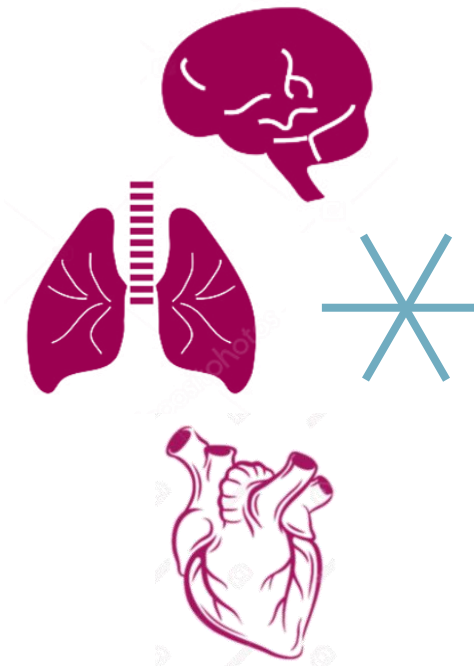


Causes

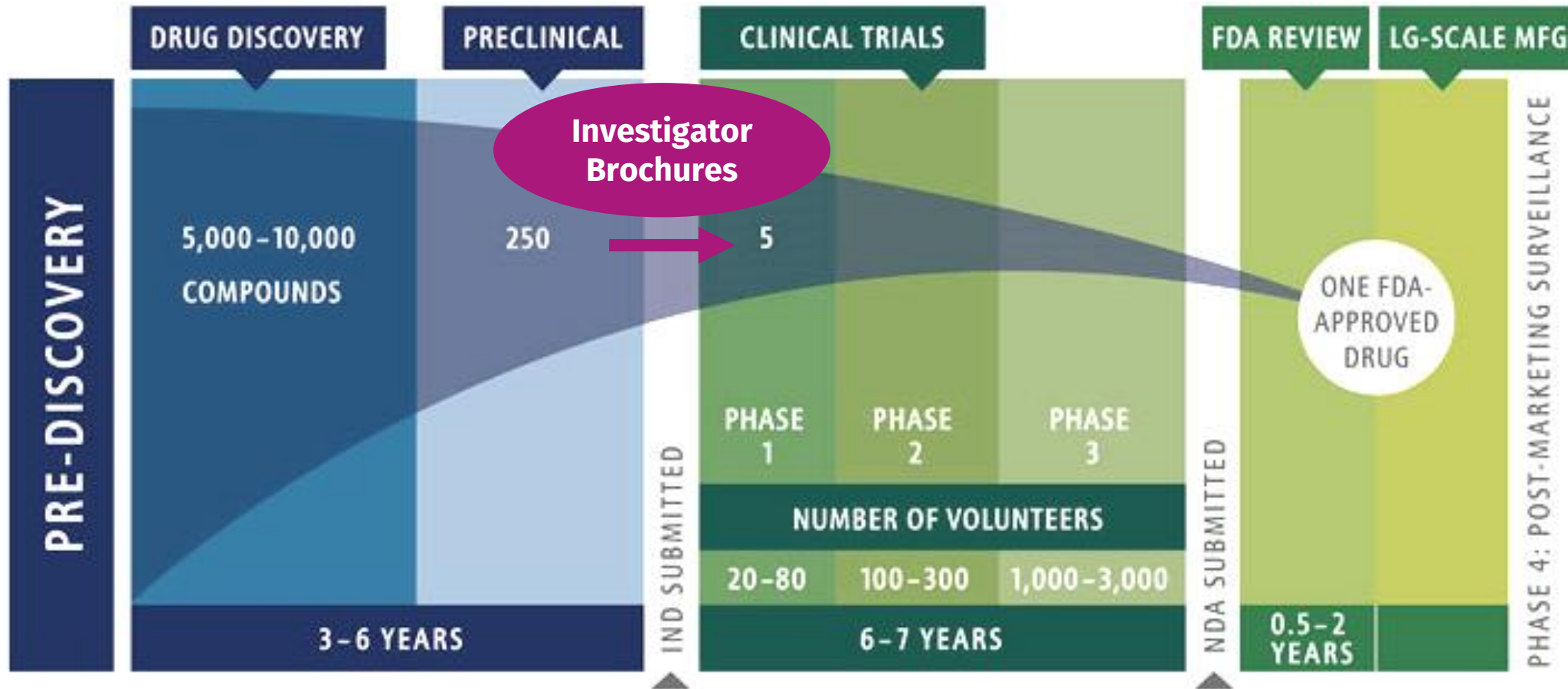
Not Sufficiently Addressed:
High Complexity of Translation



Overarching Disease Mechanisms



An Unexpected Hurdle in Drug Development



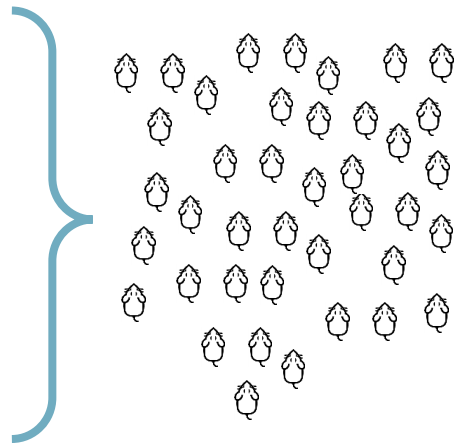
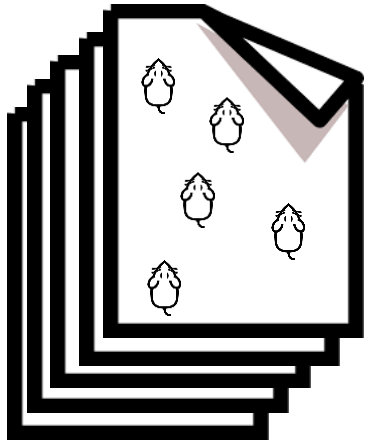
Cost

An Unexpected Hurdle in Drug Development

Preclinical Efficacy Studies in IBs

109 Investigator Brochures (IBs) for phase I/II trials

708 Pre-Clinical Efficacy Studies (PCES)



Reference to published reports: 11%

Practices to address validity threats

- Sample Size Calculation: 0%
- Blinded outcome assessment: 0%
- Randomization = 4%
- Sample size reported: 26%

Positive Outcome: 90%

No effect: 6%

Unclear: 4%



Lack of robustness in preclinical evidence

Chances

New Disruptive Technologies Meet Personalized Medicine

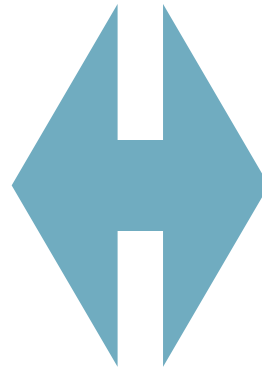
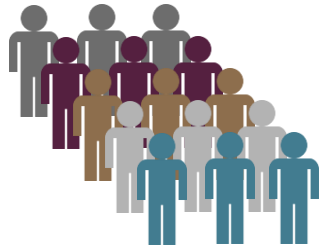
Precision Medicine



Optimized Therapy
for Individuals

instead of

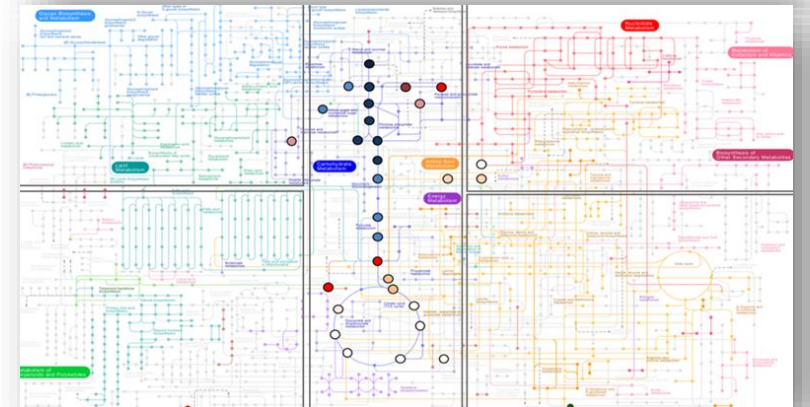
Blockbusters for
Everyone



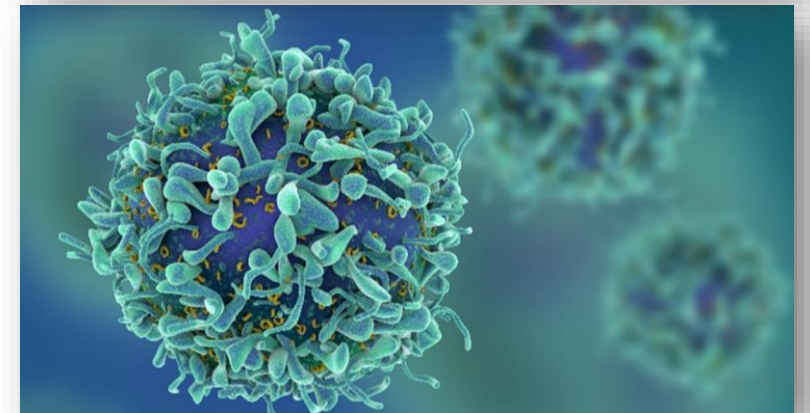
Digital Medicine



Omics

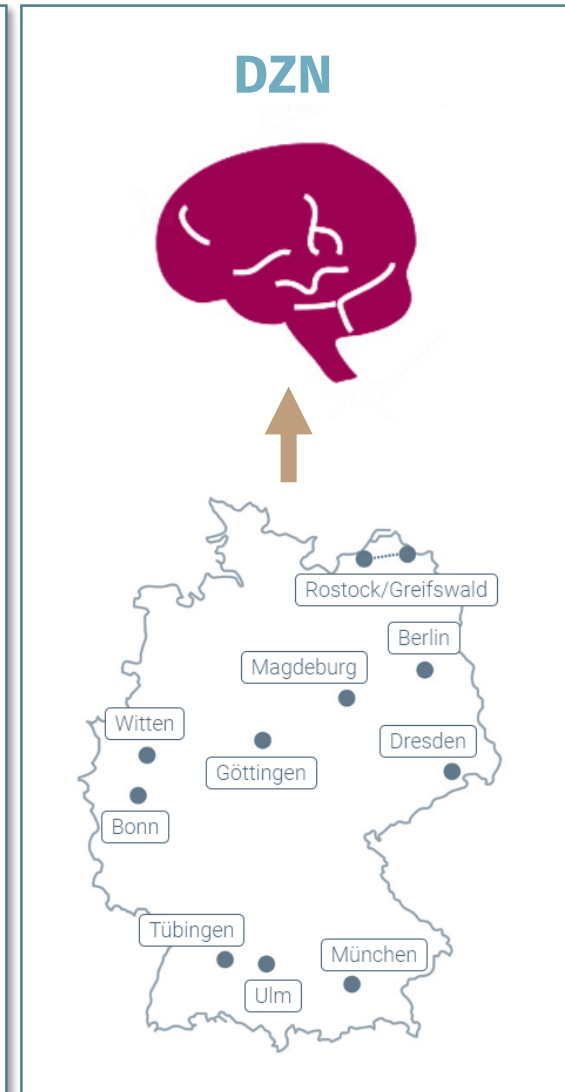
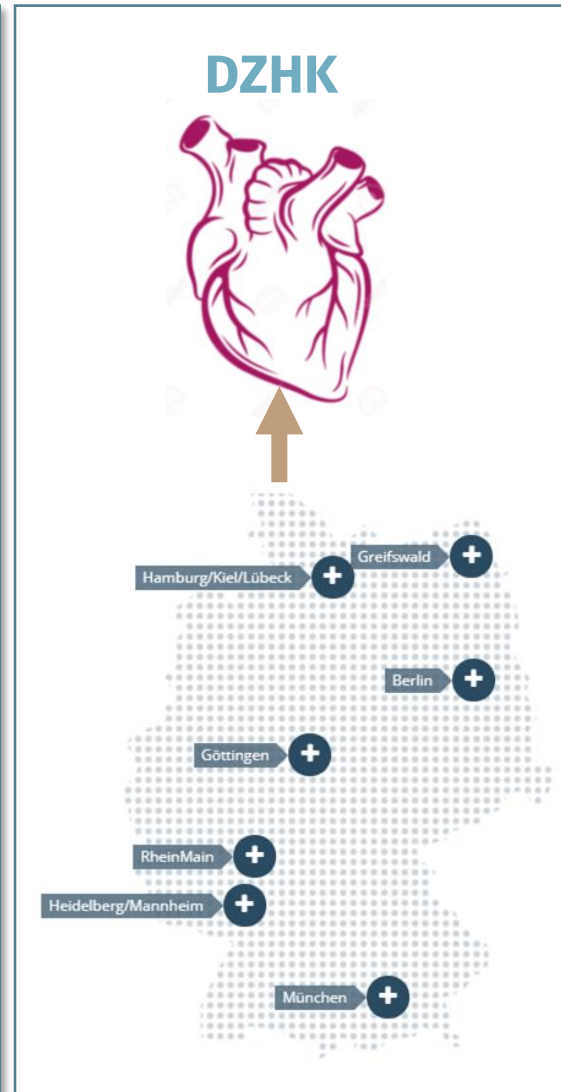
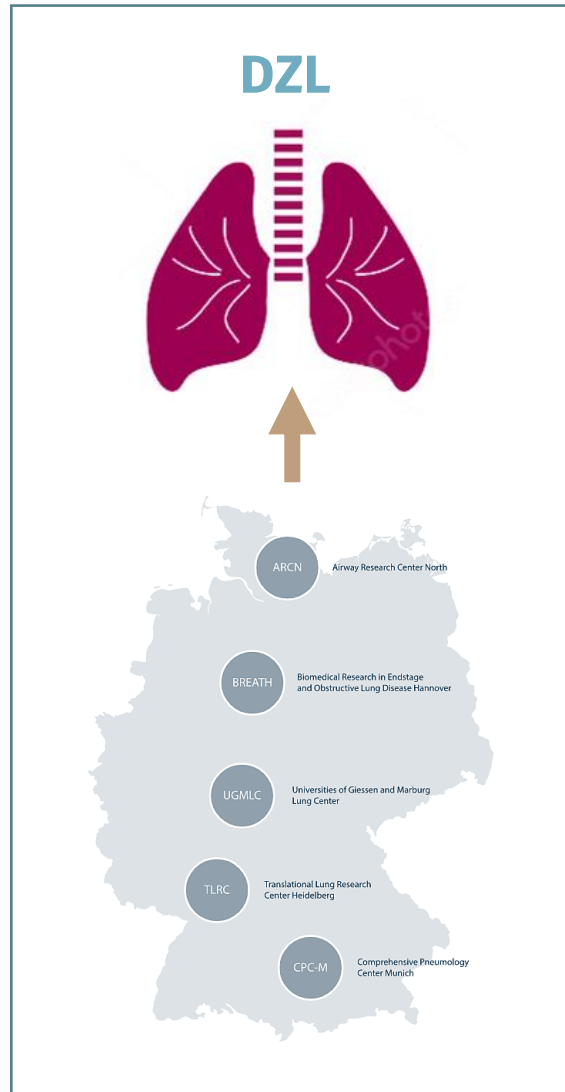


Cell Engineering



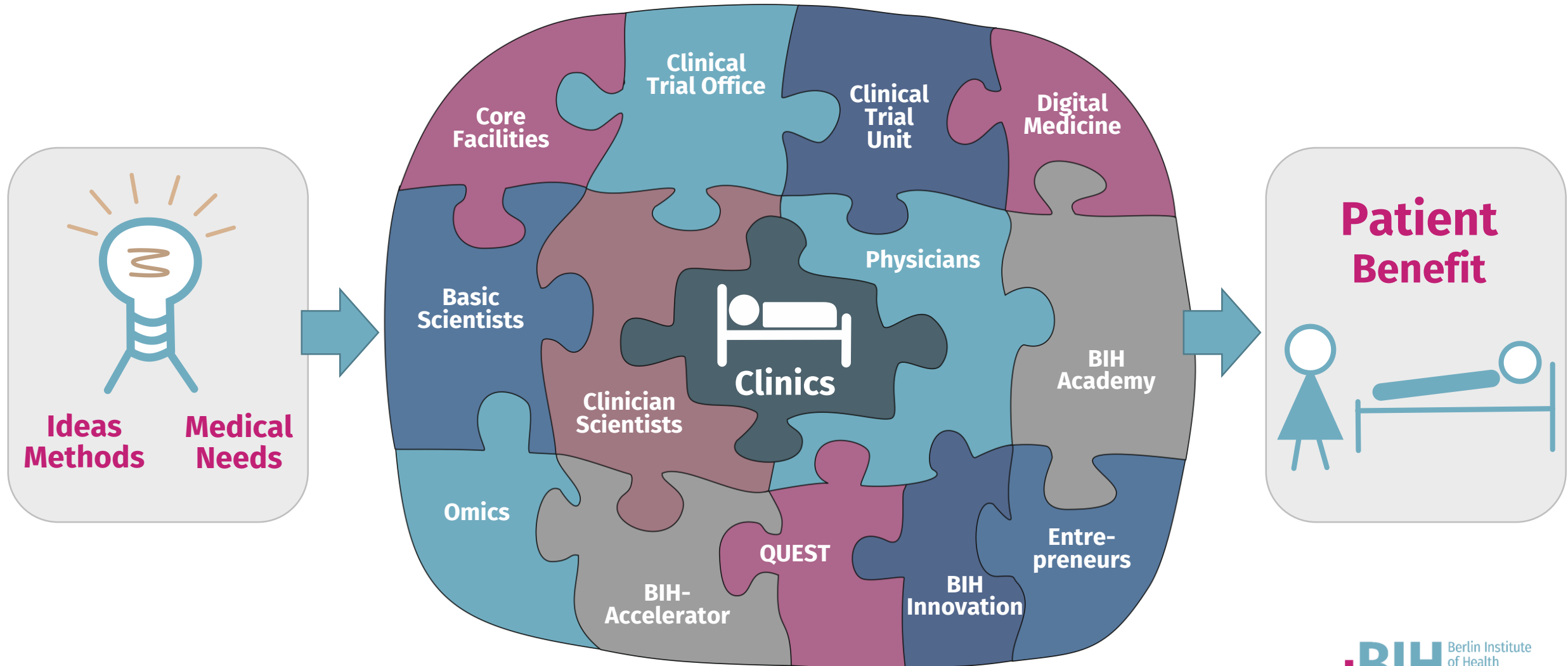
Approaches: DZG

- Best Experts from All Over Germany Focus on One Disease



BIH Approach

- *Systems Medicine in a Translational Ecosystem*



BIH: Core Principles

Full Circle

Building a comprehensive translational Value-Chain
From Bench to Clinical Reality ↔ Clinical Challenges to Bench

Campus

One place to bring actors, institutions, clinics and infrastructure together

Multisector

Community includes basic and clinical scientists, data scientists, technology expert, innovators, entrepreneurs and transfer experts

Partnering

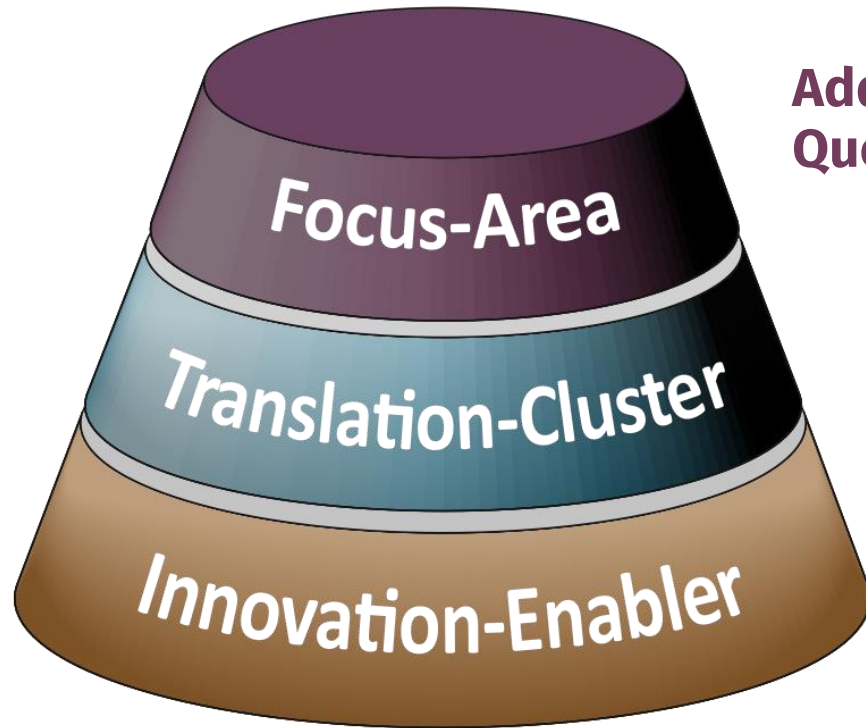
Cooperation with external partners from science an industry wherever needed

Value

New mechanisms to ensure quality, value and robustness of processes and results

BIH: Structure

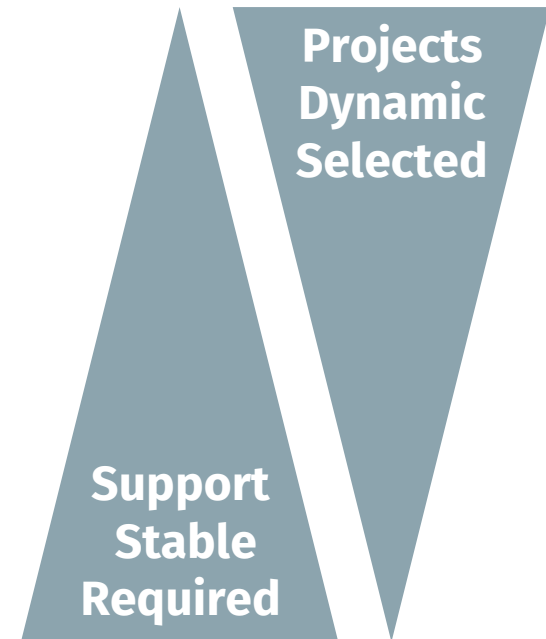
-Systems Medicine in a Translational Ecosystem-



Address Burning Questions

Match Experts with Disruptive Technology

Generate a Translational Mindset



Translational Ecosystem

Innovation-Enablers: Approaches and Incentives

BIH-Academy	<i>People</i>	Task Approach Incentives	Establish a faculty skilled in medical translation Support personal development and careers BIA - Career Support Initiatives
QUEST	<i>Quality</i>	Task Approach Incentives	Assure optimal use of material and human resources Define and assure value of research Value-Incentives (<i>VoM</i>)
BIH-Accelerator	<i>Support</i>	Task Approach Incentives	Increase speed and probability-of-success in translation Bridge gaps in the translational process Translation-Incentives (<i>ToM</i>)
BIH-Innovation	<i>Transfer</i>	Task Approach Incentives	Increase effectivity of innovation transfer Provide structures and support for effective transfer Innovation-Incentives (<i>IoM</i>)

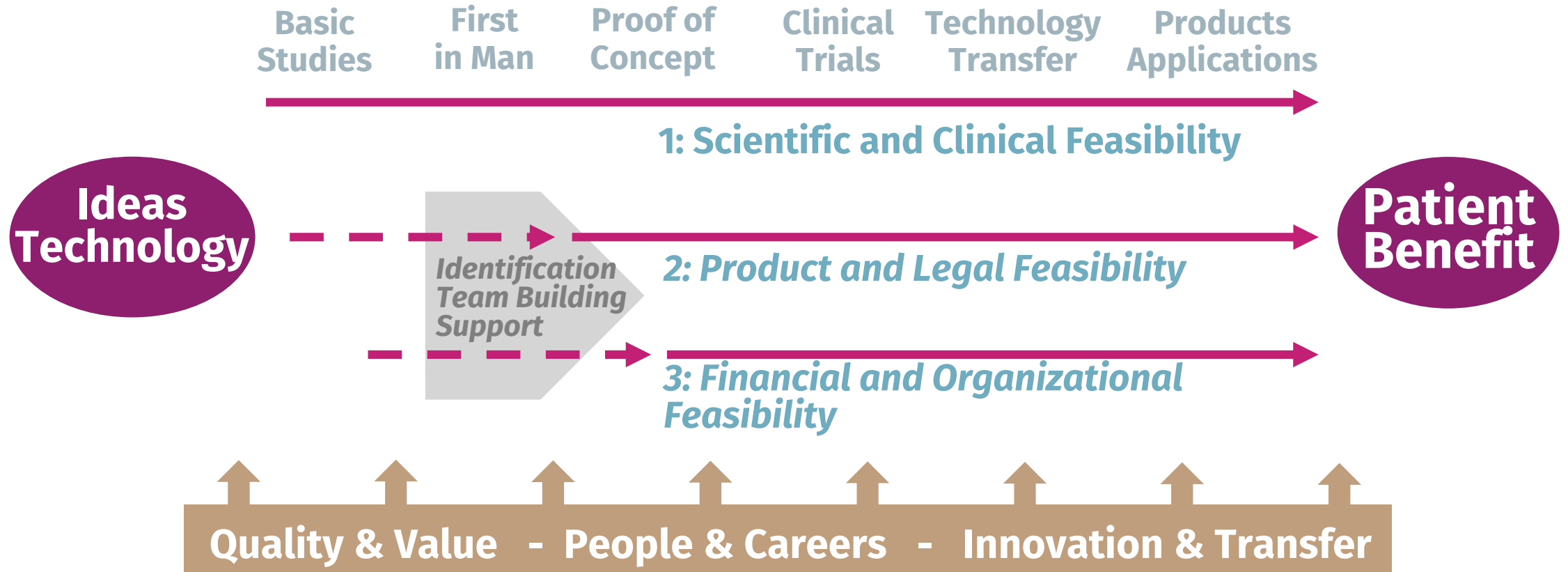
Translational Ecosystem

Innovation-Enablers: Addressing the Value Chain



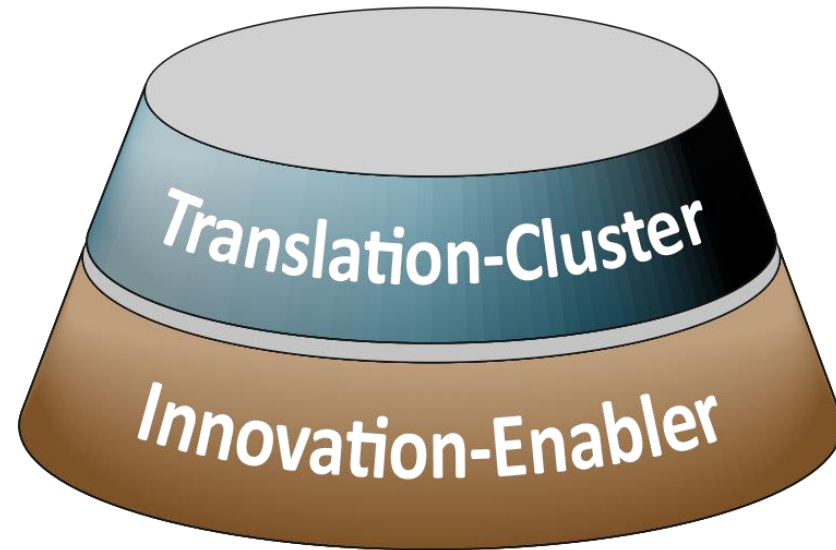
Translational Ecosystem

Innovation-Enablers: Addressing the Value Chain



Translational Ecosystem

Translation-Clusters: Technology and Faculty



Match Experts with
Disruptive Technology



Generate a
Translational Mindset

choose

*Areas With
Disruptive
Technological
Potential*

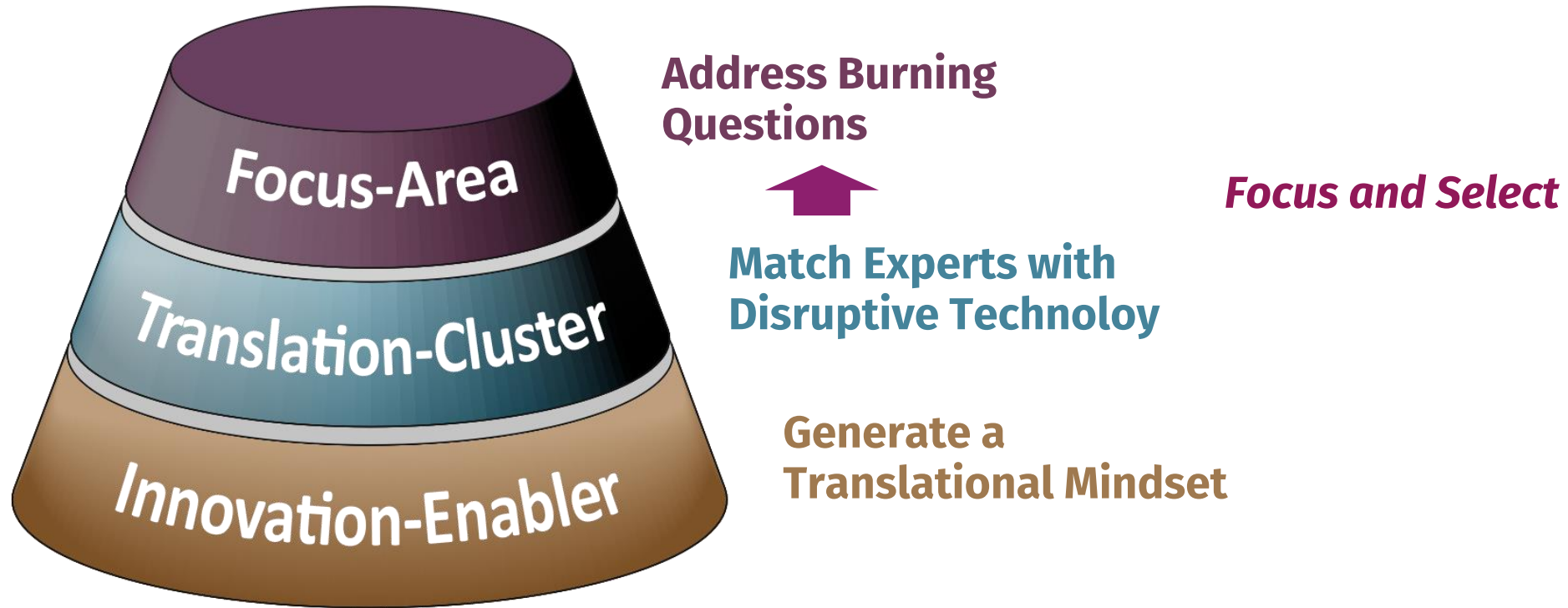
Translational Ecosystem

Translation-Clusters: Technology and Faculty

Clinical Studies		<i>Clinical Study Center Clinical Research Units</i>	<i>Medical Informatics Biostatistics BeLOVE</i>
Digital Medicine	Data	<i>High Performance Computing Health Data Platform</i>	<i>Artificial Intelligence Simulation / Digital Twins Big Data</i>
Omics	Information	<i>Next Generation Sequencing Mass Spectrometry Metabolomics</i>	<i>Biobanking Single Cell Approaches</i>
Cell Engineering	Targeted Cells	<i>Gene Editing Stem Cells ATMP / GMP</i>	<i>'Human on a Chip' Organoids</i>

Translational Ecosystem

Focus-Areas: Address Prominent Questions



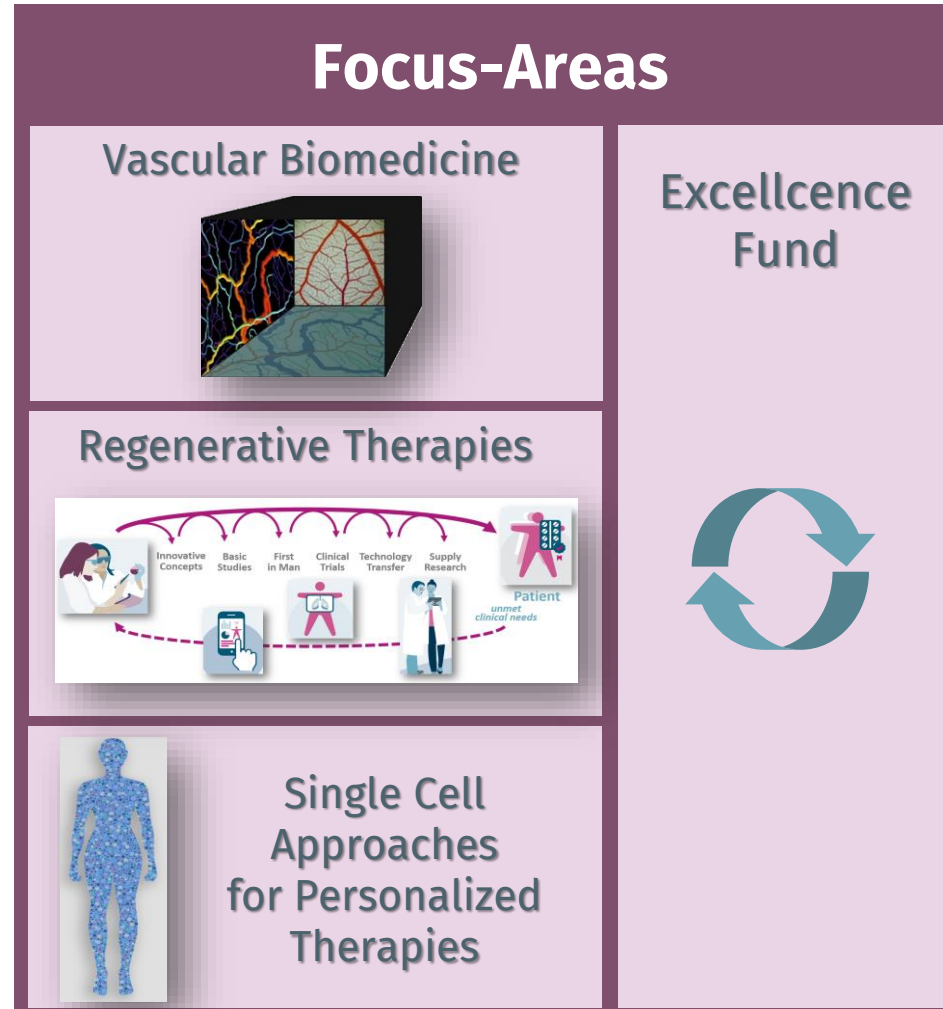
Translational Ecosystem

Focus-Areas: Address Burning Questions

Focus and Select

Criteria

- **Cross-Cutting**
- **High Potential for Major Translational Success**
- **Excellent Expertise and Competencies in the Translational Ecosystem**



Translational Ecosystem

Focus-Areas: Address Burning Questions

Vascular Biomedicine		(Micro-)vascular dysfunction is a cross-cutting patho-mechanism contributing to many diseases in all major organ systems
Single Cell Approaches	Flagship Project 'Life Time'	Cells of a given cell type exhibit individual properties and fates – analysing and addressing that offers fundamentally new medical options
Regenerative Therapies	Flagship Project 'RESTORE'	Advanced therapies and 'living drugs' will replace and supplement approaches to allow true regeneration
Excellence Fund		Dynamic mechanism to support initiatives with high translational potential

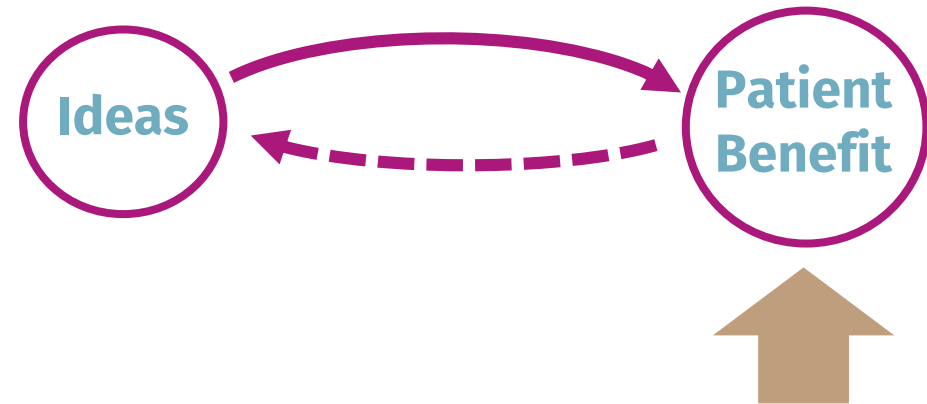
BIH: How Do We Measure the Fulfilment of Our Mission?

Mission: Research Turned Into Health

BIH is dedicated to improving the prediction of progressive diseases and developing advanced therapies for unmet medical needs in order to restore or maintain people's quality of life.

Primary KPI's

- Introduction of new preventive, diagnostic and therapeutic options into the clinic
- Products and launches
- Changes in guidelines
- Return of investments (licensing, selling)
- PROMS (Patient Reported Outcome Measures)



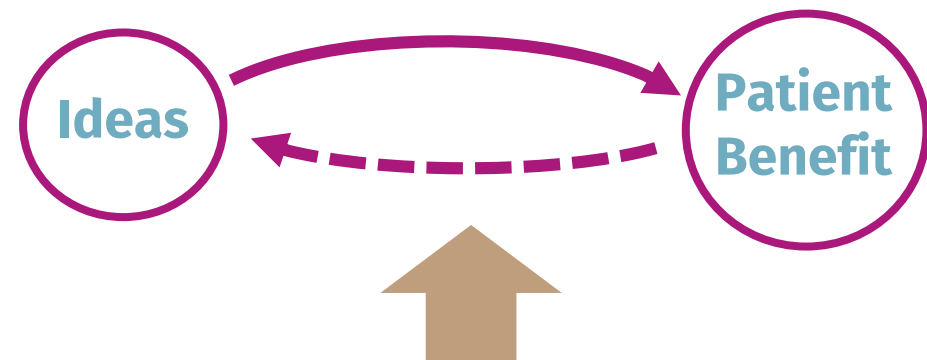
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Process – KPI's

- Proof of principle studies
- Academic first in man and clinical studies (IIT)
- Manufacturing allowance
- Ratio of filed patents to used patents
- Licensing, spin-offs, sales
- Bibliometrics
- External funding



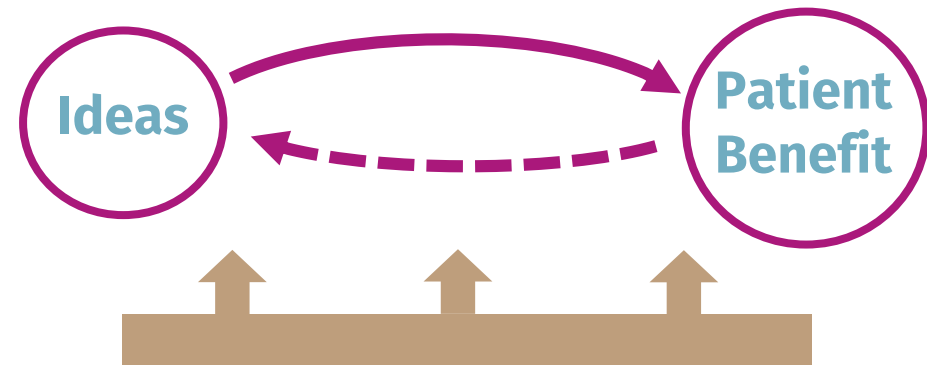
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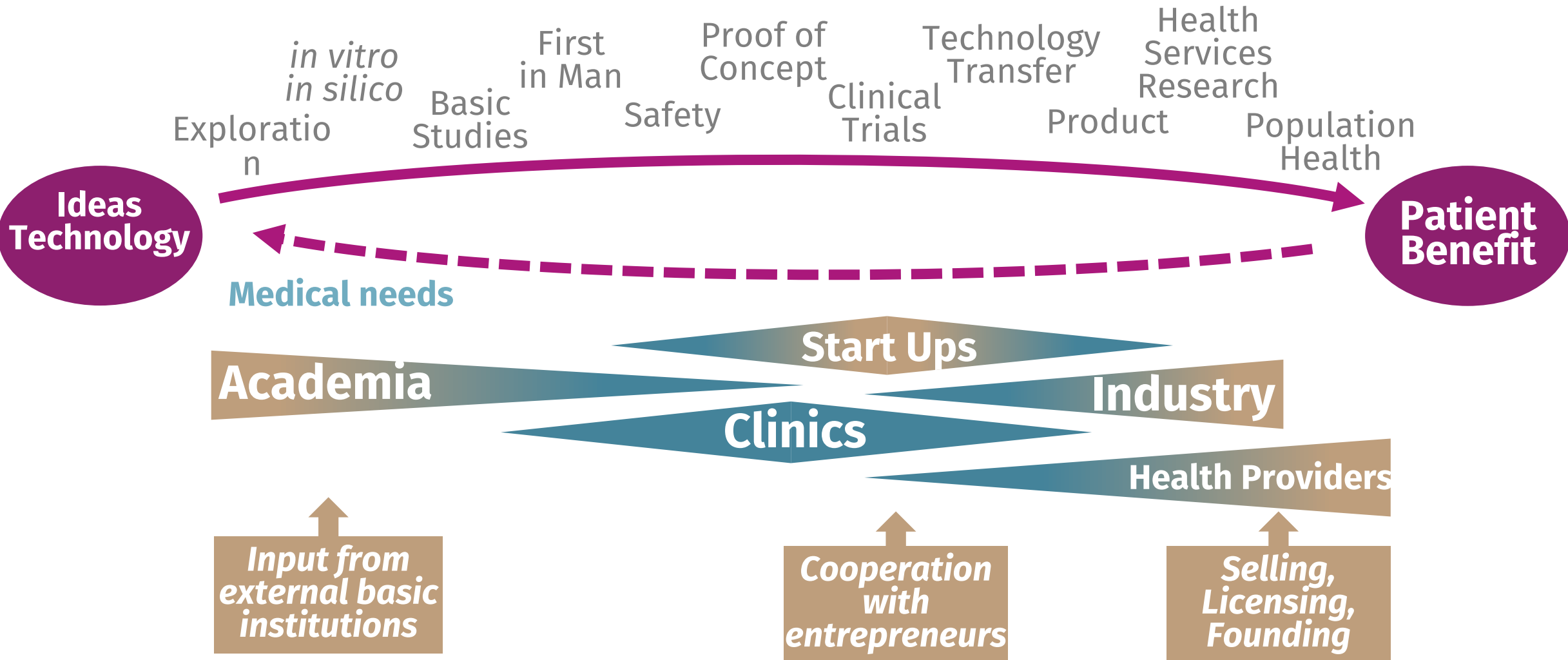
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Quality – KPI's

- Open Access publications
- Open Data / Open Science
- Publication of negative results
- ‚Confirmatory studies‘
- Diversity
- Inclusion
- Outreach

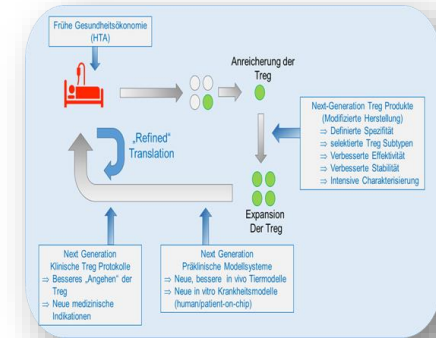


BIH: The Partnering Concept



Examples for Success: BIH-Regeneration

Regulatory T-Cells (Treg) for the Control of Unwanted Immune Reactions



Medical Need

Graft rejection in transplantation. Standard therapy (immune suppression) has many side effects

New Concept

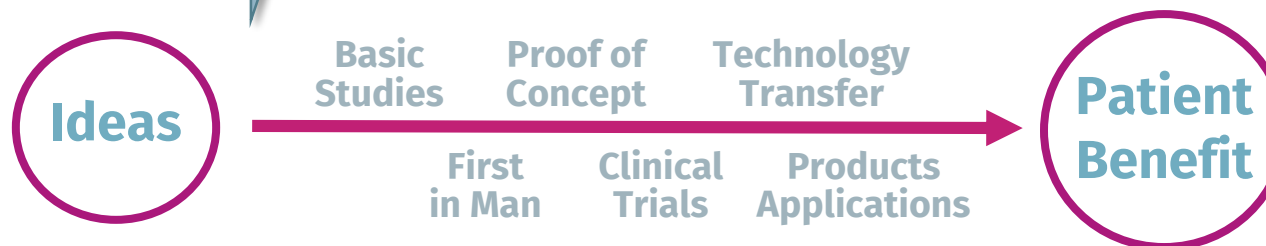
Selective blockade of pathological cells

Translational Steps

Preclinical Models
Biomarkers
GMP-Manufacturing
Legal-Affairs

Refined Translation

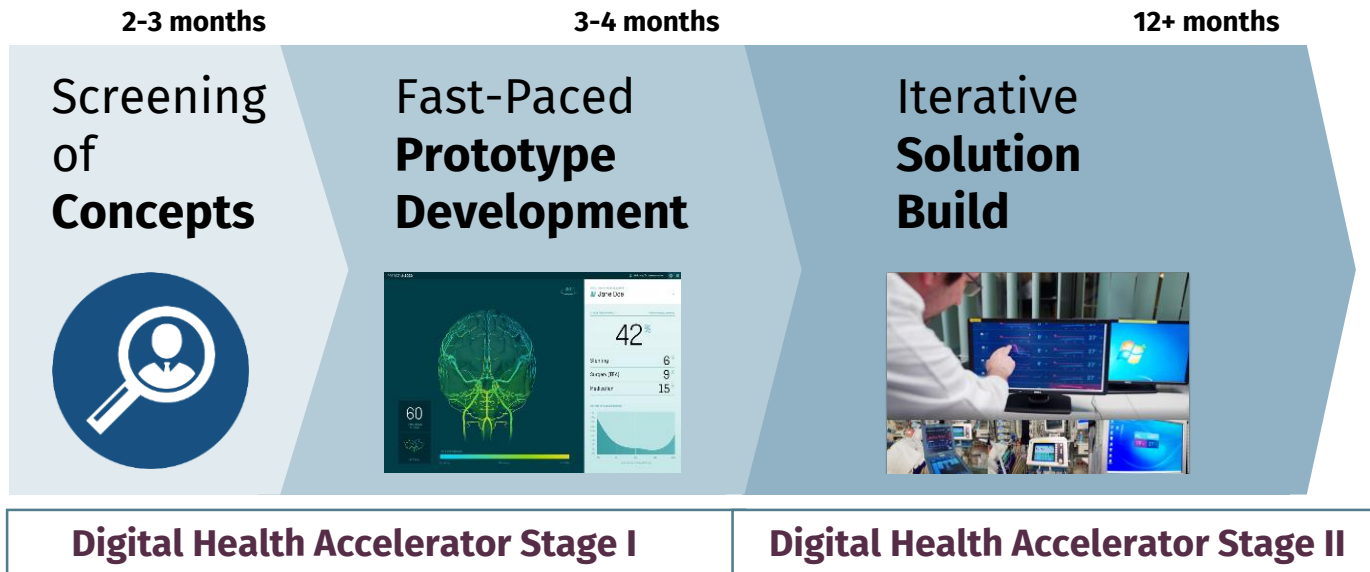
Next-Gen.
Treg Products
EU Grant RESHAPE
(2019;13.6 Mio €)



Examples for Success: BIH-Innovation

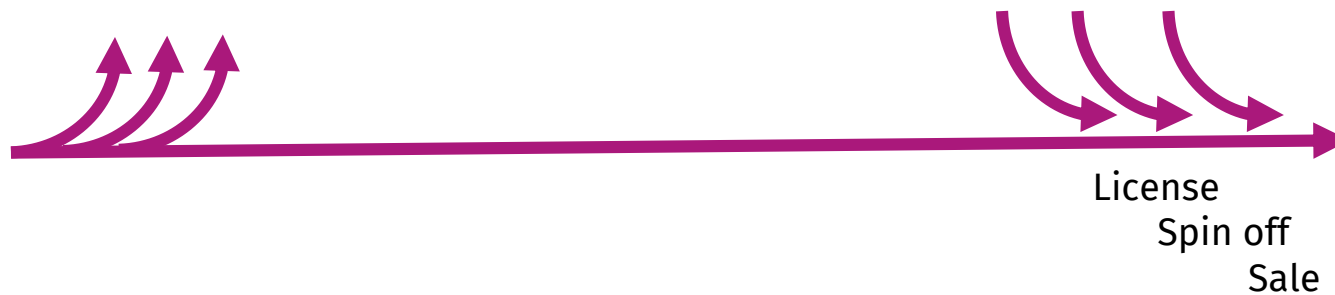
Digital Labs *PRODUCT + BUILD*

End-to-End Approach



In 2.5 Years:
>50
Concepts
leading to
4 Spin-Offs

Ideas



Patient Benefit





Neuartige Therapien
für personalisierte
Behandlungen



Thank You

FREI

STRA

STRA

FIRST TEAMS FROM BIH DIGITAL LABS COMPLETED THEIR PRODUCTS...



X-Cardiac: Predicting and preventing complications in intensive care units (ICU).

Problem: Taxing environment of an ICU leads to complications like post operative bleeding as well as renal failure and longer and riskier stays.

Solution/Product: X-cardiac is a unique monitoring solution for earlier detection of complication in an ICU by machine learning (algorithms are based on a cohort of approx. 50.000 patients).

Current Status: Minimum Viable Product (MVP) alpha version up and running. Adds a layer of clinically information on routinely collected data. MVP for research use is running at 65 beds at the German Heart Center Berlin (stable operations since April 2018). Clinical validation and regulatory certification in process. Management team completed. First negotiations with investors ongoing.



DentalXr.AI: Deep Learning for Dental Image Diagnostics.

Problem: The interpretation of dental x-rays is time consuming and limited accuracy leads to inconsistent decisions.

Solution/Product: Dental Xr.AI is an AI based diagnostic software tool, which provides higher accuracy and consistency (up to 40%). In addition it is time saving, which significantly reduces costs.

Current Status: Building the MVP and in parallel a validation study and modeling pipeline are ongoing. Regulatory approval in progress. Management team completed. Negotiations with investors.

...AND ARE READY FOR COMMERCIALIZATION AS SPIN-OFFS



AiGnostics: Precision in Computational Pathology.

Problem: Manual quantification is time-consuming, leads to inaccurate estimations and observer variability. In addition an ageing population leads to a huge increase in the number of diagnoses.

Solution/Product: AiGnostics is an explainable AI software, which identifies cancer cells and non-cancer tissue in histological samples and quantifies features more accurately and faster.

Current Status: Building the MVP and growing the data base with over 500,000 annotations. Pilot live at Charité. QM system implementation and test with first potential customer ongoing. Clinical validation and regulatory certification in process. Management team completed and fundraising initiated.



Platform for Accessible and Affordable Healthcare in developing countries.

Problem: 1 bn patients in fear of medical impoverishment with insecure income for healthcare providers. 180 bn \$ leakage of funds due to corruption (-50%).

Solution/Product: Empowering access to healthcare by a mobile health wallet, claim validation and quality assurance. The solution is connecting patient (secure payment) , provider (accurate payment) and sponsor (traceable impact).

Current Status: Launched in October 2018 in Madagascar. Currently 500+ patients and 150+ babies born in 10 medical centers. Tech development and fundraising ongoing. Regional expansion into Senegal and new verticals. Further team expansion.