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ESTABLISHING A NEW STATE-OF-THE-ART LIFE SCIENCE RESEARCH INSTITUTE: A BLUEPRINT FOR CLINICAL TRIAL CONTRIBUTION

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Abstract

The newly established Nova Institute for Medical Systems Biology (NIMSB) in Portugal is striving to set new standards in medical systems biology. This thesis explores the various challenges and opportunities facing the NIMSB, focussing on four key areas: local collaboration, biobanks, clinical trials, and industry relations. Based on interviews with 45 stakeholders and supplementary research, this study analyses and summarises the key strategies for the further development of the NIMSB in these 4 areas. A particular focus of this work is the development of a basic concept for how the institute can position itself with regard to clinical trials. The concept advocates to focus on advanced technologies to improve and secure clinical trial processes. Regarding the other three topics, the Institute is encouraged to proactively seek local and international partnerships, implement a centralized model for biobanking and foster innovation through long-term collaboration with industry leaders. These recommendations aim to create a strong and dynamic foundation for the NIMSB to make an important contribution to the global research landscape.

Keywords: Research Organizations, Systems Biology, Innovation, Biobanks, Clinical Trials, Key Collaborations, Industry Partnerships

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Establishing a New State-of-the-art Research Institute: The NIMSB (Group Part)

With 6 million new cases and 1.8 million deaths related to cardiovascular disease, and 2.7 and 1.3 million cancer diagnoses and deaths, respectively, chronic diseases are a major health, societal, and economic burden in the European Union (EU) (European Commission 2022; European Heart Network 2017). As the population ages, the challenge of managing chronic diseases becomes increasingly difficult, endangering the long-term viability of healthcare systems. The Nova Institute for Medical Systems Biology (NIMSB) is a newly founded, independent Center of Excellence (CoE) for Medical Systems Biology located in Oeiras, near Portugal´s capital city, Lisbon. It will research, identify, and prevent diseases by developing and implementing cutting-edge molecular profiling technologies. New diagnostic and therapeutic approaches focusing on diseases with high morbidity and mortality rates, such as (henceforth s.a.) cardiovascular, neurodegenerative, and cancer, will be key outcomes of research and innovation activities at the NIMSB. Its main objectives include (1) developing an excellent research program in Medical Systems Biology focused on single-cell multi-omics, human disease models (including organoids), and AI for health, (2) contributing to improving human health outcomes through precision and interceptive medicine, and (3) training a new generation of researchers and medical doctors in advanced digital-transformation technologies. The institute recently raised a funding of EUR 30 million, with equal contributions from Horizon 2020 as well as from national and regional funds from the Ministry of Science, Oeiras and Cascais city councils, and the greater Lisbon regional authority. These funds primarily aim to ensure the successful establishment of the NIMSB to meet its long-term objectives. A grant of this magnitude for a Portuguese research institution reflects the distinctiveness and the groundbreaking potential NIMSB’s research may have. Moreover, it allows the rare and unique opportunity for this work to undertake an analysis from a foundational, ground-zero perspective.

As part of the Horizon 2020 program, the NIMSB has teamed up with the Max Delbrück Center for Molecular Medicine (MDC) in Berlin, a major biomedical research institution within the Helmholtz Association, which is the largest national research community in Germany. The MDC is also home to the renowned Berlin Institute for Medical Systems Biology (BIMSB), a leader in applying cutting-edge molecular, cellular, and computational technology to health concerns, which will serve as a model for the NIMSB in terms of research objectives. Since the initiation of the project, the director of the new institute, Prof. António Jacinto, and his team closely collaborated with representatives of the MDC, s.a. the BIMSB director, Nikolaus Rajewsky, Dr. Stan Gorski, and others. Thereby, the NIMSB has and will further benefit from the MDC's expertise and experience in establishing the BIMSB, cutting-edge technology infrastructure, relationships with hospitals, and innovation, education, and training initiatives. The complementary skills and objectives of this partnership assist the NIMSB to remain viable and increase its global influence.

Following its inaugural meeting in October 2023, the NIMSB's development continues to progress. While precise objectives were defined, as previously stated, there are still specific components of the institute that require further refinement and elaboration to fully comprehend their potential contribution to the long-term sustainability of the institute. Four key components were defined in active collaboration with the Director of the NIMSB and our supervisor, Prof. Nuno Arantes-Oliveira, that require further investigation: (1) local collaborations, (2) biobanking, (3) clinical trials, and (4) industry collaborations. While there may be other crucial components, the rationale behind this selection derives from the examination of other prosperous global life science research institutes and the recognition that these components may collectively catalyze the NIMSB´s long-term sustainability and establish the NIMSB as an institute of excellence.

For each of these areas, the aim was to examine their unique opportunities and challenges in supporting NIMSB´s mission and objectives while simultaneously adding value to the broader research community. Additionally, the articulation of strategic and practical recommendations will lay a foundational framework, serving as a precursor to further investigation and the formulation of a comprehensive business plan. This thesis will introduce and discuss each topic sequentially to comprehensively understand their role in supporting the NIMSB´s long-term vision and contribution. The methodology is attached in Appendix 3 and an overview of all conducted interviews can be found in Appendix 4.

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Section A: Defining Key Collaborations (Group Part)

At the core of the NIMSB's mission is the creation of strong partnerships, vital for its integration into the scientific ecosystem. Recognizing the significance of this task, this thesis commits to delivering a strategic blueprint for these essential collaborations, aiming to facilitate the NIMSB's successful engagement within the research community. This includes a thorough investigation of the essential needs of the NIMSB and how distinct models of collaboration can fulfill these requirements to enhance its research capacity. The analysis will give a clear picture of the research institutes's objectives, the operational landscape, and the resources available. It outlines customized collaboration models intended to leverage potential partnerships and expected synergies while tackling foreseeable challenges. The findings of this project aim to provide a strong base for the NIMSB, offering concrete theoretical guidance and practical strategies during its early stages. It seeks to identify the crucial initial steps for establishing a strong network of stakeholders. Ultimately, it will lay the foundation for the NIMSB’s objectives to become an excellent research program in Medical Systems Biology, contribute to improving human health outcome, and offer training in advanced digital-transformation technologies (see detailed objectives in the introductory chapter).

1. NIMSB's Ecosystem: Needs and Opportunities for Collaboration (Group Part)

The international best practices highlight the significance of establishing a diverse local, national, and global partnership network. To transfer these insights and identify strategically beneficial collaborations for the NIMSB, it is imperative to examine the research institute's needs and available resources. These are derived from the NIMSB's pre-defined objectives as mentioned in the introduction (Jacinto, interview, September 29, 2023). The following paragraph outlines the primary needs of the NIMSB, which arise from the interview insights aligned with the described objectives.

1.1. Resource Needs (Group Part)

Required resources to establish a research ecosystem range from specific expertise, human resources, and sufficient funding to cutting-edge technologies. Attracting employees and building specialized expertise is particularly important to address complex research issues (Crespo, interview, October 10, 2023; Dìas, interview, October 12, 2023; Gomes, interview, October 27, 2023; Gorski, interview, October 11, 2023; Jacinto, interview, September 29, 2023). This is especially relevant for the NIMSB, given its focus on precision medicine and AI, which involve demanding tasks, s.a. analyzing big data and developing complex algorithms (Kennedy, interview, October 13, 2023; Leite, interview, October 18, 2023). Furthermore, it became evident that attracting key opinion leaders (KOLs) is essential due to their significant contributions to research. Recruitment is specifically challenging for areas of computer science and artificial intelligence (Dìas, interview, October 12, 2023). Potential underlying reasons stem from poor payment and strong competition among large companies when hiring employees. Thus, funding is required to provide attractive compensation to the staff (Dìas, interview, October 12, 2023; Gorski, interview, October 11, 2023). To retain qualified employees with competitive pay, a sense of belonging and overall employee satisfaction should be ensured (Crespo, interview, October 10, 2023; Dìas, interview, October

12, 2023). Pooling capacities between institutions can be useful for gathering skilled human capital (Agostinho, interview, October 24, 2023; Dìas, interview, October 12, 2023). Moreover, to lead groundbreaking research projects on early disease detection, the NIMSB must combine cutting-edge technologies, including (henceforth incl.) single-cell multi-omics, artificial intelligence, and disease models derived from patient data (Jacinto, interview, September 29, 2023). Enabling all required resources will thus demand substantial financial investment, which represents another crucial element of resources.

1.2. Educational Needs (Group Part)

To gain relevance within the research ecosystem and to meet the above-stated goal of training a new generation of researchers, the NIMSB needs to contribute in areas s.a. training and education. Therefore, the establishment of a Career, Education, and Training Office (CTO) and educational initiatives for researchers and clinicians are needed. Additionally, integrative education through close collaboration with the university may foster education synergies. A workforce demand was primarily identified in data science, bioinformatics, multi-omics analytics, and AI designed explicitly for use in biomedical and clinical settings (Jacinto, interview, September 29, 2023). Moreover, researchers at the NIMSB should be trained to effectively present the institute's strengths and research findings to the public, as many are not naturally skilled in this due to a focus on scientific pursuits (Leal, interview, October 19, 2023). As per section D, such training and education may also encompass teaching blocks within business and entrepreneurship to foster translational research.

1.3. Marketing Needs (Group Part)

According to the interviewees, the NIMSB should focus on raising awareness to attract different companies and partners. A crucial step in establishing a reputation is implementing a strong marketing strategy. The NIMSB’s capabilities need effective local and international marketing to attract potential partners (Gomes, interview, October 27, 2023;

Leal, interview, October 19, 2023). Communicating the NIMSB's value proposition among institutes is vital to identifying complementary stakeholders and working together efficiently. However, frequent communication problems among research institutions in Portugal were pointed out during the interviews (Gomes, interview, October 27, 2023). The lack of communication among organizations represents a challenge but can also be considered as an opportunity for improvement.

1.4. Opportunities for Biobanking (Group Part)

The decision on what biobanking format the NIMSB will engage and to what extent depend on external resources and still needs to be evaluated (Section B). However, collecting samples will be crucial for conducting research and sample analysis on a molecular level (Leal, Interview, October 19, 2023). Regardless of the advised model of biobanking, beneficial collaborations should be initiated with stakeholders, enabling or ensuring sufficient and diverse sample availability (Gorski, Interview, October 11, 2023). Additionally, expertise regarding the implementation of robust quality protocols, legal frameworks, and extensive organizational efforts, accompanied by sufficient financial resources, will be needed (Dìas, interview, October 12, 2023; Kennedy, interview, October 12, 2023; Leal, interview, October 19, 2023; Ng, interview, October 25, 2023). Further needs, opportunities, and challenges in terms of biobanking and sample collection for the NIMSB will be discussed in section B, "Biobanks".

1.5. Opportunities for Clinical Trials (Group Part)

Considering participation in clinical trials is crucial to the NIMSB as these trials are key to translating research findings into real patient benefits. Engaging in this area is critical to connecting with key stakeholders, including hospitals and pharmaceutical companies (Kennedy, interview, October 13, 2023; Leite, interview, October 18, 2023). Such involvement not only broadens the reach and deepens the research of the NIMSB but also

brings mutual benefits. This focus would demonstrate the NIMSB's commitment to bridging the gap between research and practical application and reinforces the NIMSB's role as a key player in the healthcare research community. In-depth insights into the fundamentals, strategies, and benefits of clinical trials are explained in section C

1.6. Industry Opportunities (Group Part)

Successful research outcomes require engagement with the industry (Crespo, interview, October 10, 2023; Gorski, interview, October 11, 2023). Collaborating with companies is intended to strengthen the reputation of an institute and boost funding. Furthermore, translating research results into marketable solutions eventually leads to the founding of start-ups, spinouts, and the formation of licensing agreements (Benz, interview, October 13, 2023; Gomes, interview, October 27, 2023; Leal, interview, October 19, 2023). In addition, job creation and advances in healthcare can increase the likelihood of governmental support (Leal, interview, October 19, 2023). Therefore, research institutes should actively approach companies, recognize their needs, and promote mutually beneficial synergies (Gorski, interview, October 11, 2023; Kolben, interview, October 17, 2023; O'Beirne, interview, November 16, 2023). Further information on this topic can be found in section D, "Industry Collaborations".

1.7. Regulatory Needs (Group Part)

Technology transfer (TT) involves a number of legal aspects, s.a. patent registration and intellectual property (IP) negotiations (Benz, interview, October 13, 2023). Additional information on the topic of industry engagement, incl. intellectual property and patents, is illustrated in Section D. Moreover, as already indicated, specific legal conditions apply to biobanking, and clinical trials require specialized legal support. Besides, many scientists lack the expertise to market their research findings, hindering the successful development of products (Gomes, interview, October 27, 2023). To reduce disagreements within research, it is

important to seek advice on legal issues, especially regarding IP sharing (Dìas, interview, October 12, 2023; Gorski, interview, October 11, 2023; Kennedy, interview, October 13, 2023). To function effectively within a research environment, the institutes should foster trust by offering an innovative and properly structured working environment by providing legal frameworks (Dìas, interview, October 12, 2023).

Undoubtedly, being at ground zero, the NIMSB will encounter challenges in building impactful collaborations. The groups of needs and opportunities critical for success that have been identified include resources (human resources, expertise, technology, funding, etc.), education, marketing and communication, industry engagement, legalities, and economic and social value creation. Focusing on the three components, namely effective communication, qualified human resources, and sustainable financial resources, will allow the NIMSB to prioritize its efforts strategically in the early stage to lay the foundation for achieving its objectives. In addition, participation in clinical trials, biobanking, and active industry engagement are crucial for promoting research excellence and impacting the health community, necessitating substantial efforts.

2. Available Capabilities (Group Part)

To effectively analyze what collaborations are key for success, besides illustrating the NIMSB's needs, it is crucial to highlight the available resources that serve as the institute's building block. These were mainly identified through interviews with the NIMSB's director and additional official internal documents.

2.1. Internal Capabilities (Group Part)

The NIMSB will provide diverse capabilities to the ecosystem, s.a. expertise, scientific approaches, data sets, services, and technologies. The establishment of the research institute will increase the critical mass of researchers and technicians by 300 people. The institute will set up 20 research groups with 12 principal investigators. Half of the NIMSB's capacity is

expected to be used for laboratory experiments and the remaining half for data analysis. Furthermore, the institute can offer a support infrastructure for single-cell genomics, single-cell proteomics and human organoids, data science and artificial intelligence, clinical research, and sample processing (Jacinto, NIMSB kick-off, October 23, 2023).

2.2. Cross-Functional Capabilities (Group Part)

Besides its internal capabilities, the NIMSB may refer to cross-functional capabilities provided by the MDC and Nova University. Given the close partnership, mutually beneficial synergies may evolve from, e.g., resource sharing. Further, given its renowned status, the MDC can support the research institute in building a favorable reputation. The acknowledgment, in turn, can help the NIMSB increase reliability, which will be useful to obtain additional funding, among other aspects. Furthermore, the NIMSB can benefit from the MDC's unparalleled experience from 31 years in its field (Max Delbrück Center 2023). The institute can seek advice regarding vital decision processes, developmental procedures, and other issues. In addition, the NIMSB is more likely to have access to their expert knowledge, technologies, and samples. In particular, MDC’s wide-ranging research connections can be crucial to the research center, as they involve further potential partners, incl. their expertise and resources. For example, the MDC is part of the ISAAC Foundation, a research network of 10 other institutes (Gorski, interview, October 11, 2023).

Furthermore, the Nova University in Lisbon is an internationally recognized public institution that conducts research and offers multiple study programs (Nova University Lisbon 2023). With its faculties, the university can support the NIMSB in gaining acknowledgment, as well as provide an extensive network, technology, and expertise in various disciplines. Above all, Nova University established a comprehensive innovation ecosystem consisting of many laboratories and scientific initiatives. The proximity of the university facilitates access to their resources (Jacinto, NIMSB kick-off, October 23, 2023). The university offers a

variety of degree programs, s.a. management, biomedical and biochemical engineering, social sciences, medicine, law, tropical medicine, public health, and other subjects. For example, they host a center for entrepreneurship, the Haddad Institute, which focuses on assisting students in turning ideas into start-ups (Nova School of Business and Economics 2023; Nova University Lisbon 2023). In addition, the Nova Medical School (NMS) conducts clinical trials through its Clinical Trials Unit (CTU) and is currently in the process of re-establishing its biobank based on the already available biobanking structures of the Centro de Estudos de Doenças Crónicas (CEDOC) (Calado, interview, October 26, 2023). Moreover, the NMS includes several research initiatives, incl. the Comprehensive Health Research Centre (CHRC), Center for Health Technology and Services Research (CINTESIS), iNOVA4Health, and ToxOmics. These programs include a wide range of interdisciplinary projects in healthcare, biotechnology, and other fields (Nova Medical School 2023). Due to the close partnership between the NIMSB and Nova University, the engagement with students and, hence, identifying potential new talent will be facilitated. Additionally, Nova University provides teaching and training programs as well as funding opportunities (Jacinto, NIMSB kick-off, October 23, 2023).

2.3. External Capabilities (Group Part)

Despite science operating within a global network, certain resources must be in physical proximity. Institutions within Oeiras, Lisbon, and the surrounding area are being examined to identify locally available capabilities, which means that they can be outsourced. The organizations introduced are intended to provide insight into several potentially valuable external resources in the immediate vicinity.

The research center will be located in a large building near the research institutes Chemical and Biological Technology António Xavier (ITQB), Institute of Experimental and Technological Biology (iBET), National Institute of Agricultural and Veterinary Research

(NIAV), and the Gulbenkian Institute of Science (IGC). These organizations are active in various disciplines, s.a. biomolecular medicine, biomedical science, veterinary medicine, systems biology, precision medicine, advanced therapeutics, biotechnology for sustainability, and agriculture. Moreover, the Oeiras campus employs more than 2000 people, incl. doctoral and master's students (Jacinto, NIMSB kick-off, October 23, 2023). Other relevant institutions in the Lisbon area are the Institute of Molecular Medicine of Lisbon (IMM) and the Portuguese Oncology Institute (Instituto Português de Oncologia; IPO). The IMM specializes in biomedical, clinical, translational, and basic research. Additionally, it owns a biobank, incl. an extensive collection of biological samples and clinical data (Dìas, interview, October 12, 2023). The IPO is the largest Portuguese cancer hospital and also offers sample collections from its own biobank (IPO Lisboa 2023).

Additionally, the Catholic University of Lisbon offers various degree programs in medicine, anthropology, biology, chemistry, economics, and other subjects. The university maintains more than 100 scientific facilities and 17 scientific centers. Similarly to Nova University, this can reflect a promising opportunity for relevant talent acquisition. Among others, they offer research in the field of healthcare and biomedicine, collaborating with the Hospital da Luz and conducting research on the Oeiras campus at the IGC (Universidade Católica Portuguesa 2023).

There are hospitals located in the vicinity of the future NIMSB that conduct clinical trials and are specialized in various fields, e.g., the Hospital da Luz and the CUF. The Hospital da Luz belongs to the largest and most modern private hospitals in Portugal, where all major focus areas are represented. Furthermore, they focus on primary care and complicated surgeries (Hospital da Luz 2023). The CUF comprises 24 clinics throughout Portugal dedicated to investigation, development, and training. The clinic also represents many medical disciplines, s.a. cardiology, gynaecology, and oncology (CUF 2023).

The local ecosystem of the NIMSB also includes access to industrial collaboration, hence an opportunity for, e.g., joint research as well as financial returns through licensing agreements. The Tagus Park Oeiras, a hub for technology, communication, healthcare companies, and start-ups, is located close to the future NIMSB site. The innovation park includes 160 companies and 20 start-ups fostering different areas of expertise. The companies focus on designing technologies while working cross-disciplinary (Taguspark 2023). In Lisbon, relevant companies include the healthcare service company Ophiomics, which focuses on applying advanced genomics and bioinformatics technologies. Ophiomics develops personalized solutions for precision medicine and diagnostics in oncology (Ophiomics 2023). There are also many other startups in the region, s.a. Plux, which specializes in creating biomedical solutions for education, research, and healthcare, contributing to an innovative ecosystem (Plux 2023). Additionally, three of the largest pharmaceutical companies, Novartis, Bayer, and Roche, are represented near Lisbon (Bayer 2023; Novartis 2023; Roche 2023).

To summarize, the NIMSB is equipped with valuable resources, s.a. technologies, expertise, and facilities and has established significant initial connections through its collaboration with Nova University and the MDC. Furthermore, it will benefit from its proximity to a diverse and solid innovation ecosystem. While assessing potential gaps within this ecosystem, it is essential to recognize that the foundation of the NIMSB was driven by specific needs, especially by the absence of specialized technologies in the local region (Jacinto, interview, September 29, 2023). Additionally, the interviews have uncovered a need for focused legal support within the local ecosystem (Crespo, interview, October 10, 2023; Santos, interview, November 14, 2023).

3. Practical Recommendations (Group Part)

Drawing upon the conclusions gained from expert interviews and literature review, the newly established NIMSB should prioritize certain recommendations. The proposal encompasses actionable steps and theoretical considerations, laying the foundation for achieving the objective mentioned above.

The development of groundbreaking life science is based on an extensive global network, which implies that research institutes cannot function in isolation. Diverse collaborations with acknowledged local, national, and international organizations are crucial to foster long-term success. Identified relevant requirements, s.a. improving marketing and communication, developing a skilled workforce, securing financial support, and establishing regulatory frameworks, should be addressed as top priorities by the NIMSB. The following partnership models, leading to mutually beneficial synergies, should be applied to tackle the critical needs:

(1) The NIMSB should prioritize the ***"Collaborative Research Project Model"***, focusing on ***sharing resources*** to enhance a strong positioning within the ecosystem and facilitate collaboration. The strategic approach aims to provide and leverage capabilities to receive support from potential partners. It is recommended to provide internally available and easily accessible resources, s.a. specialized technologies and expertise that have been identified as lacking within the ecosystem. Sharing resources simultaneously supports the NIMSB in developing critical resources, especially in the initial phase when significant investment is required.

(2) In the early stages, it is crucial to engage proactively in ***"Strategic Marketing Partnerships"*** through, e.g., events to achieve an impactful introduction of the NIMSB. Concurrently, these events aim to collaboratively promote the combined strengths of all partners, effectively presenting Oeiras Valley as a unified entity. The NIMSB has to

become a place for fostering exchange and TT in an innovative and inspiring research environment. This setting also enables the NIMSB to advocate for its specific needs, s.a. funding, legal advice, staffing, and training programs. The local connections, initially strengthened by sharing resources and the reputation of Nova University and MDC, facilitate the attraction of national and international partners. The participants of the venue will provide new collaboration opportunities, incl. various benefits, eventually covering the NIMSB´s focal needs.

(3) ***Collaborations with hospitals or clinics, biobanks, and pharmaceutical companies will be fundamental*** for effectively addressing the diverse critical needs of the NIMSB. Different collaboration models in these fields should be implemented, supporting the research institute in building essential resources and adding value to the ecosystem. For instance, engaging with hospitals, clinics, and biobanks provides access to core research assets, s.a. human-biological samples, clinical data, and expertise. Furthermore, industry partnerships are crucial for technology transfer, generating sustained income, and eventually enhancing societal influence. While the topics of biobanking, clinical trials, and industry collaborations have been briefly discussed, their importance and impact on the overall concept of the NIMSB and its core objectives have yet to be analyzed.

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Section B: Opportunities and Barriers of Biobanking (Group Part)

The opening chapter of this thesis provides an outline of the main objectives and vision of the NIMSB, emphasizing certain areas that have not yet been fully defined. Among the focus areas is the field of biobanking or the process of acquiring samples for the NIMSB. The previous chapter on local collaborations already stressed the importance of establishing a local collaborative network, incl. stakeholders within the biobanking network. The present chapter raises significant questions regarding the opportunities and barriers that the NIMSB

encounters in utilizing biobanking to advance research and its recognition in the wider scientific community. Thus, the following investigation aims to provide insights into the practice and feasibility of integrating biobanking within the NIMSB's activities. This includes a fundamental examination of biobanking, encompassing its integral elements and inherent value proposition. Subsequently, the benefits and challenges associated with different approaches to collecting and sharing samples, specifically in relation to the NIMSB, are comprehensively analyzed. Finally, strategical and practical recommendations are provided for the NIMSB in implementing biobanking or sample collection procedures. These recommendations aim at creating mutual benefits for the NIMSB and the broader research community.

1. Value Creation and Impact Generation Through Biobanks (Group Part)

Biobanks have a crucial role in advancing medical science, (systems) biology, and healthcare delivery by serving as repositories for biological specimens (Kinkorová and Topolčan, 2020, 333-341). Biological repositories, as emphasized by Pelisek et al. (2019), are carefully constructed to enhance our understanding of various diseases and are vital for the progress of novel and pioneering treatment strategies. The extensive collection of patient samples can help in promoting personalized or precision medicine, incl. prevention, diagnosis, treatment, and personalized monitoring (Kinkorová & Topolčan, 2020). Biobanks play a crucial role in coordinating and mediating between medical institutions (i.e., clinics and hospitals), research institutions, and pharmaceutical companies (Abdulghani, interview, November 22, 2023; Dìas, interview, October 12, 2023; Kennedy, interview, October 13, 2023; Penney, interview, November 27, 2023). When executed properly, Biobanks can effectively fulfill their primary objective of generating impact for each of these stakeholder groups. This will be further elaborated in the subsequent discussion (Castillo, interview, November 22, 2023; Divers, interview, November 15, 2023).

1.1. The Medical Perspective (Group Part)

From a medical standpoint, biobanks support the advancement and validation of novel diagnostic techniques, empower individualized care, and strengthen the surveillance and management of chronic and infectious illnesses through organized and processed sample provision. Thereby, patients benefit from precise diagnoses, individualized treatment strategies, and perhaps earlier intervention, all of which can significantly enhance their prognoses and long-term health. Furthermore, the availability of a diverse collection of biological specimens facilitates our understanding of disease progression and response to therapy. This significantly supports healthcare professionals in generating accurate medical judgments (Hewitt, Watson, and Dhir, 2014, 4-9). The knowledge transfer and technological innovations that occur as a result contribute to the overall improvement of patient care and medical procedures. Biobanks may also add value in clinical trials conducted by investigators, pharmaceutical companies, or clinical research organizations. During clinical trials patient biological samples and their associated data are collected and may be integrated into biobanks for future and retrospective research (see definition of retrospective research in Appendix 2) (European Commission 2012; Mouta, interview, November 3, 2023). This interaction between biobanks and institutions conducting clinical trials is further elaborated in section C.

1.2. The Scientific Perspective (Group Part)

For biomedical and scientific research, researchers and research institutes utilize specimens to understand complex diseases at the molecular level (Dìas, interview, October 12, 2023; Gorski, interview, October 11, 2023; Kaunisto, interview, November 10, 2023; Michalska-Falkowska, interview, October 17, 2023). Biological repositories guarantee the quality and integrity of research specimens by providing a structured collection and preservation of specimens. This is essential in assuring more accurate dependability and replicability of research findings (Stege, interview, December 12, 2023). Ashley Sanders,

Group Leader at the BIMSB, specifically pointed out the significance of biobanks in facilitating the transfer of research findings on single cells from one patient to multiple others by analyzing organized and processed samples (Sanders, interview, December 13, 2023). In addition, biobanks facilitate cooperation among academics and research institutions and across several other disciplines, forstering the scientific discourse and accelerating the rate of advancement in fields, s.a. genomics, proteomics, and epidemiology (Watson, Barnes, and Datta 2019). They serve as intermediaries between clinical research units and research groups conducting specialized research initiatives by storing specimens in an organized way for prospective research as was emphasized by Sanders during her lecture at the NIMSB kickoff.

1.3. The Commercial Perspective (Group Part)

Biobanks serve as a gateway between academic and scientific research, and industry, facilitating the rapid transformation of research discoveries into marketable assets and services. For instance, pharmaceutical organizations employ biobank resources to expedite drug research and development, hence decreasing the time and expenses associated with such procedures. In addition, biobanks offer useful data that can be utilized to discover new therapeutic targets or categorize people for clinical trials, thereby improving the efficacy of drug development processes (Zika et al. 2011, 96-103). This was also pointed out by the Vice President of Bayer US, as pharmaceutical companies like Bayer strongly benefit from biobank collaboration at the beginning of the drug development process to identify targets and their prevalence and later on for support in sample acquisition (Penney, interview, November 27, 2023). Similarly, when engaging in clinical trials, pharmaceutical companies may distribute specimens to biobanks for future research purposes after their own analysis objective has been met (Kennedy, interview, October 13, 2023). There are four key factors that pharmaceutical companies may look for in biobank partners, namely (1) sample availability (i.e., the required type of sample), (2) hospital relationship, (3) strong documentation around consent enabling

sample and data sharing with industry, and (4) a strong database and infrastructure which ensure high sample and data quality. Besides, start-ups can benefit from biobanks to facilitate innovation and advance the development of novel diagnostics, treatments, and medical technology. Similarly, as with pharma companies, biobanks enable smaller businesses easy access to top-notch biological samples and related data, fostering an environment where they can spur innovation, create economic worth, and ultimately enhance global health outcomes.

2. Evaluation of Different Models of Sample Sharing for NIMSB

2.1. The Centralized Biobanking Model

2.1.1. Challenges of a Centralized Biobanking Model (Group Part)

The establishment of a biobank in the NIMSB also presents notable obstacles that must be taken into account. First, it is associated with ***substantial expenses*.** According to the Head of Biobanking at the Victorian Cancer Biobank in Australia, the majority of biobanks will only be able to cover a mere 20 percent of their expenses. The costs arise from various factors, incl. (1) physical facilities, e.g., lease, electricity, and water; (2) equipment for specimen processing and storage, incl. freezers, liquid handling machinery, and cabinets; (3) staffing and administration, (4) transportation and logistics, incl. samples collection and transportation, (5) IT and data management, incl. software and hardware for data storage and analysis, and from (6) marketing and outreach activities for donor community engagement and education (Campbell et al. 2018; Calado, interview, October 26, 2023; Kaunisto, interview, November 10, 2023; Ng, interview, October 25, 2023; Stege, interview, December 12, 2023). Since biobanks are bound to keep a non-profitable status mandated by law, it is important to implement a solid cost-recovery model (Abdulghani, interview, November 22, 2023; Dìas, interview, October 12, 2023; Stege, interview, December 12, 2023). This must be considered for any cost and price specifications of to be shared sample and data collections. Additionally, the NIMSB should try to build up a strong industry collaboration network and

benefit from medical treatment patent-, licences-, and partnership agreement profits. These profits are frequently reinvested in biobanks, positively influencing their long-term sustainability and ongoing significance in biomedical research and clinical trials (Dìas, interview, October 12, 2023, Gomes, interview, October 27, 2023).

Secondly, building up a biobank is a ***highly complex and lengthy process***, therefore requiring a stringent strategic and operational guideline with the according expertise, as was also highlighted in section A. The entire process of defining and implementing consecutive structures and operations should not be underestimated. For example, a challenging aspect refers to identifying the specific requirements of sample requests from researchers in order to be able to provide the appropriate and necessary samples. This is subsequently followed by an extensive and time-consuming sample collection process (Ng, interview, October 25, 2023; Stege, interview, December 12, 2023). It will be essential for the NIMSB to clearly outline its primary areas of research and to define the corresponding sample types that can support progress in these research areas. For example, even while wanting to collect specimens of a more common cancer type like breast cancer, it is necessary to accurately determine the precise type and stage of the cancer. If researchers do not have access to this specific sample collection, they must be willing to utilize alternative resources (Ng, interview, October 25, 2023; Kaunisto, interview, November 10, 2023). The limited sample storage capacity of biobanks aggravates this challenge. Additionally, due to the NIMSB's aim to analyze omics data, which involves a highly technical and complicated process, it will be specifically important to implement a solid IT infrastructure (see definition of omics data in Appendix 2) (Abdulghani, interview, November 22, 2023, Stege, interview, December 12, 2023).

Furthermore, as explicitly discussed in section A, the NIMSB has not yet formed any sort of partnership with a nearby hospital. However, such a ***partnership is highly crucial*** and should be established from the outset in order to ensure the consistent acquisition of samples

(Abdulghani, interview, November 22, 2023). As emphasized by the Head of Biobanking Development at BBMRI-ERIC, it is much more convenient to partner with local hospitals (i.e., in Oeiras) in terms of transportation and logistics. Hospital da Luz has previously partnered with several biobanks in Lisbon and is now initiating a larger collaboration with the clinical academic center of the Catholic University of Portugal (Leite, interview, October 18, 2023). Section A also provides a deeper outlook into potential collaboration models with hospitals in the Lisbon area.

A final obstacle arises from the ***competitive biobanking landscape*** in the Lisbon region (Abdulghani, interview, November 22, 2023). This landscape already includes well-established biobanks like the IMM Biobank or the Champlaumidaud Foundational Biobank, as well as the formerly called CEDOC biobank of the Nova Medical School. The previous analysis of sample collections in Portugal has shown that the diversity of sample collection in the Lisbon area is currently rather well-balanced. However, the NIMSB should be cautious of potential overlaps as it establishes itself as a biobanking organization in it this environment. During the conversation with the Biobanco IMM and the Nova Medical School Biobank, both parties expressed genuine interest in collaborations with the NIMSB and emphasized the importance of maintaining distinct areas of focus for sample collecting in order to prevent any potential overlap (Leite, interview, October 18, 2023; Dìas, interview, October 12, 2023). With a centralized biobank, it will be crucial for the NIMSB to set itself apart from other biobanks on a national and international level through specialized samples and high quality data collection (Abdulghani, interview, November 22, 2023).

3. Strategic Insights and Recommendations for Biobanking for the NIMSB (Group Part)

The previous analysis and exploration of interview insights, along with the literature review, do not suggest a one-sided solution for the integration of biobanking at the NIMSB.

Since the samples are definitely required for single-cell multi-omics analysis, it is out of the question for the NIMSB to collect samples. However, the way in which this happens follows a complex and strategically crucial decision-making process and should be considered most carefully. Taking into account both the benefits and challenges of the previously analyzed integration models and considering the complexity of establishing a biobank, **it is recommended that the NIMSB adopts a combination of the centralized and external sample acquisition model**. This would mean that the NIMSB develops additional biobanking facilities at the Oeiras campus on a smaller scale (incl. storage and processing facilities) as an extension of an already established biobank of another institution. An illustration of this approach can be found in Figure 6 in Appendix 14. In this case, the NIMSB's biobank would operate as a joint entity alongside the biobank of the other institute, hospital, or university, e.g., the Biobanco IMM, the Biobank of the Nova Medical School, or the Portuguese Oncology Institute (IPO). To comprehend the final recommendation, it is useful to recollect the key components of biobanking. These four points were also inferred from the interview findings and the definition and purpose of biobanking: (1) structured and ethical sample collection and processing (i.e., quality control, ELSI compliance, and robust IT infrastructure), (2) strong collaborations for sample acquisition, (3) sustainability and funding, and (4) impact generation. These should be considered in any decision-making process. Adopting the described model can have a positive reciprocal effect on all four components, which will be further elaborated in the following.

3.1. Structured and Ethical Sample Management Through Shared Resources (Group Part)

A combined model will ensure a more structured and ethically-correct sample collection and management from the beginning of the project due to the opportunity to leverage already established structures and organizations provided by another biobank or

institution, as well as the accumulated industry knowledge and expertise around biobanking. This includes quality control, compliance with ELSI, and the IT and data management infrastructure. Establishing organized processes and structures to ensure high-quality samples is highly complex and requires significant effort. Like many other institutions, the Nova Medical School dedicated a minimum of three years to establishing the present state of its biobank by conducting visits and engaging in discussions with experts from other biobanks in Portugal and Europe (Calado, interview, October 26, 2023). The NIMSB can greatly benefit from this unique expertise and the opportunity of knowledge transfer. Furthermore, leveraging this knowledge in understanding the multifaceted aspects of ELSI and putting them into practice in the correct way will offer another great opportunity to the NIMSB when engaging in the collection of samples. It will not only support the NIMSB in gaining the public's and patient's trust but also in ensuring a renowned positioning within the research and life science industry community, which is also crucial for funding. Although there are many available resources and best practices from networks, s.a. the BBMRI-ERIC, the ability to leverage insights from a partnering already experienced institution or even benefit from their certifications can make a substantial difference (BBMRI-ERIC 2023). It also facilitates better understanding of local needs and requirements. Adopting a combined model is additionally advantageous in the development and enhancement of a robust IT and data management infrastructure. The NIMSB biobank may be able to benefit from shared and existing resources in terms of IT management systems and already built-up infrastructure from the collaborating biobank.

3.2. Stronger Collaboration and Better Sample Acquisition (Group Part)

In a combined model, the NIMSB will benefit from **already established partnerships**, not only with pharmaceutical companies but also with renowned hospitals in the wider Lisbon area, s.a. Hospital da Luz, CUF, or the Portuguese Oncology Institute (IPO)

(i.e. the largest cancer hospital in Portugal). Additionally, such a combined paradigm would significantly increase the amount and **diversity of sample sets** and simplify the sharing processes of those samples and their associated data between two joint entities. For example, the NIMSB and Nova Medical School's biobank could optimize their resources by strategically coordinating their sample collections. Redundancies can be avoided when each biobank focuses on distinct types of samples, enabling a synergy effect where both benefit from the unique and complementary nature of each other's repositories. This collaboration would enhance the efficiency of both biobanks and additionally expand the scope and depth of their research possibilities.

3.3. Improving Sustainability and Funding (Group Part)

Although the combined model would still require substantial financial investment, expenses could be reduced through **shared resources** for marketing, IT management, staffing (e.g., quality and legal assurance), and other biobanking elements. As mentioned, a detailed and reliable cost-recovery model should be created for this purpose (Abdulghani, interview, November 22, 2023). Given the substantial rise in energy and electricity costs, these concerns will become increasingly relevant (Abdulghani, interview, November 22, 2023). This can be achieved, for instance, by fostering **strong engagement with the pharmaceutical sector and grant givers** to generate revenue for re-investment in Research & Development by filing licenses and patent applications and gaining revenue through partnership agreements (Michalska-Falkowska, interview, October 17, 2023). Furthermore, teaming up can improve opportunities for funding as mentioned in chapter 6.3 .

3.4. Ensuring Impact Generation (Group Part)

As was emphasized by the Retired Director of the KI Biobank and derived form the purpose of biobanking, generating and measuring quantifiable impact as a biobank is crucial and should not be overlooked. Useful KPIs may be, for example, the number of supported

projects through sample distribution. In the recommended model, this impact might be even stronger than in a centralized biobank model only due to several reasons. The **reduced time and effort** regarding all administrative and organizational tasks that a combined model entails should rather be allocated to **advancing processing and analysis** of the specimen collections. This has substantial impact on the research projects quality analyses and outcomes. Advanced analyses technologies, s.a. single-cell multi-omics or AI, and their potential for improved patient health outcomes will be further elaborated in section C.

4. Conclusion (Group Part)

In conclusion, while biobanking is a highly complex and costly matter, its potential to provide value both to the NIMSB's research progress as well as to the wider research community both locally and internationally is substantial. The analysis has outlined that the benefits clearly outweigh the challenges in a combined model for biobanking. Considering the unique positioning and available network of the NIMSB, it is strongly advised for the NIMSB to collaborate closely with this network and leverage existing infrastructures, expertise, sample collections, and partnerships when engaging in biobanking and building up internal storage and processing facilities. When executed adequately, this step can represent an important milestone in the NIMSB's objectives to develop and position itself as a world-class research program in Medical Systems and advance human health outcomes.

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Section D: Forging Ties with Industry (Group Part)

As highlighted in preceding sections, forging ties with industrial partners is essential for cultivating a stellar reputation of becoming a state-of-the-art research institute for systems biology. Collaboration with industry is not just instrumental in securing the financial viability of the institute; it will lay the foundation for developing an excellent research program by funding capital-intensive elements, s.a. biobanking. These elements in turn will enhance

NIMSB's distinctiveness and reciprocally augment the scientific progress of its industrial collaborators, especially in areas impacting patient outcomes.

This section aims to methodically articulate the significance of synergistic engagements between academic institutes and the industrial sector. After explaining what objectives and constraints NIMSB may have, different paths of collaboration with industry are highlighted and assessed. Subsequently, the requisite organizational frameworks that facilitate effective knowledge transfer are exemplified, and different formats of technology communication are outlined. Lastly, this section will provide an overview of potential challenges and a future outlook coupled with practical recommendations.

1. The Importance of Collaboration Between Research and Industry (Group Part)

Over the past 50 years, there has been a significant increase in collaborative life science research agreements between corporations, academic institutions, and non-academic research institutions. This trend stems from a noticeable shift in corporate strategy; life science companies, after consistently scaling back their investments in early-stage research, are now actively seeking partnerships with universities and research institutes. By engaging with these (academic) institutions, they aim to tap into the top-tier expertise and specialized knowledge in various scientific fields, effectively outsourcing their need for foundational research and thus saving costs (Lutchen 2018). For research institutes, partnering with industry is essential to maintain sustainable operations. The significance of such collaboration is shown by the well-regarded Vlaams Instituut voor Biotechnologie (VIB) or Massachusetts Institute of Technology (MIT), where revenue generated from industry collaborations exceeds 15 percent and 20 percent respectively of their annual budget. Notably, all profits from these activities are directly reinvested into further research efforts, which in turn benefits the scientific outcomes and, conversely, the overall reputation of an institute (Durinx, interview, November 8, 2023) (Roberts, interview, December 4, 2023).

The outputs of these partnerships, however, are even more impactful, as translational biomedical research significantly contributes to economic growth, especially when considering the creation of jobs and new companies (Jacinto, interview, September 30, 2023). Moreover, collaboration increases the efficiency of translational processes and garners benefits in biomedical research (Portilla & Alving 2019). Thus, research and industry collaborations can accelerate the introduction of groundbreaking pharmaceuticals and medical technologies, yielding significant benefits for public health (Martin 2002).

2. NIMB'S Vision, Capabilities, and Objectives (Group Part)

For the impact of collaboration outcomes between industry and research institutes to be significant, partnerships need to meet the institutes' notion of its vision, capabilities, and overall objectives. Thus, the following sections propose collaboration models aimed at fulfilling the NIMSB's objectives of becoming a CoE in the field of Medical Systems Biology. Other underlying goals specifically relevant to this section include creating sustainable long-term employment for at least 200 individuals funded by the NIMSB's core budget or additional grants and laying the foundation to spin off several start-ups (Jactinto, interview, September 30, 2023). Hence, identifying ways to sustain as an institute, independent from subsidies in the long run, is crucial and needs to be considered a priority within the NIMSB team. Even though the NIMSB may have the capability of materializing single-cell multi-omics to clinical practice in Portugal faster, some constraints will need to be considered in the context of serving the industry (Teaming document). Next to the relatively small size of this institute within Europe and beyond, the technology can at first be classified as a low Technology Readiness Level (TRL) ranging from TRL-1 to TRL-3 (Jacinto, interview, September 29, 2023) (Table 3, Appendix 21) thus making it at first challenging to be regarded by industrial partners (Section C) and to count on industry as a steady source of income. For the industry, it will be crucial to move up the TRL to stages like TRL 7; otherwise, the

industry will consider it fundamental research with a very long timeline towards commercialization (Leal, interview, October 19, 2023). Such constraints will need to be considered for the strategic planning of industrial partnerships.

3. Models of Industry Collaboration

3.1. Partnership Scope Selection Process (Group Part)

The desired scope and depth of a partnership may depend on the specific technology and company. For instance, a research institute may opt for a singular, preferred industrial ally, securing steady funding but potentially sacrificing operational flexibility due to exclusive commitments. The AstraZeneca-Oxford collaboration is a prime illustration of such a model, underscoring, however, the necessity for a research institution to be highly esteemed to attract such exclusive partnerships. Most of the research institutes decide on a “crowdfunding” model, implying that there are several different potential partners and projects stemming from a case-by-case evaluation. This latter approach may result in a more mutually beneficial dynamic for the NIMSB, allowing greater flexibility and independence for both parties (Mouta, interview, November 3, 2023). Apart from the number of partnerships set up, there is, according to Christine Durinx, the Co-Managing Director of VIB, a general notion that the ideal partnership should be long-term, partners are considered equal, and resources and skills are complementary (Durinx, interview, November 8, 2023).

In terms of relevant industries for an institute in the medical systems biology space, pharmaceutical and biotechnology players will undoubtedly be primary targets for industrial partnerships, considering their direct relevance. However, given systems biology’s involvement in substantial data generation, it may be beneficial for the NIMSB also to consider collaborations with companies specializing in computational fields like big data and data analytics. Data analytics companies are likely to seek expertise in interpreting the complex datasets that systems biology produces (O’Beirne, interview, November 16, 2023).

3.2. Spinouts

3.2.1. The Impact of Spinouts beyond the NIMSB (Group Part)

The contribution of spinout infrastructure to industry is undeniably significant. However, its impact extends even further, positively influencing the entire local ecosystem surrounding it, which, as per section A, is crucial for the NIMSB. While there may be no institutional preference between licensing technology or forming spinouts, spinouts play a crucial role in enhancing an institute's prestige. Despite the higher risks and longtime horizons until payout associated with spinouts, particularly in medical fields, they significantly boost a region's attractiveness and economic standing by creating high-quality employment opportunities and drawing in skilled professionals, as well as domestic and international funding. They initiate a self-reinforcing cycle of growth. This cycle begins with fostering entrepreneurial mindsets, leading to the creation of an entrepreneurial hub. This hub, in turn, attracts additional startups, further amplifying job creation and increasing funding opportunities. This dynamic cycle not only benefits the immediate environment but also contributes to broader regional development (Dominguez, interview, November 8, 2023). Given the NIMSB's ambition and philosophy of significantly contributing to economic growth, job creation, and the formation of new companies, the development of pathways leading to spinout formations is unquestionably a vital strategy.

3.3. Communication and Outreach

3.3.1. Dual Communication Models (Group Part)

A well-structured TTO plays a crucial role in managing the dual dynamic of either proactively promoting an institute's capabilities to the industry (open communication) or allowing the industry to influence research for its benefit (closed communication). To navigate this dual role effectively, the institute must be flexible and proactive in communicating its knowledge and expertise (Vidal, interview, December 7, 2023). It should

clearly articulate its high-level mission goals as well as the specific objectives of each research line. Simultaneously, the TTO should manage a portfolio of technologies and assets that are available for external collaboration (Santos, interview, November 14, 2023).

Industrial partners often pursue two main paths in collaborations: *"You want strategic collaborations with incredibly prominent figures in the field, or you need a specific collaboration because somebody has a specific model or a specific method that you want to tap into"* (Penney, interview, November 27, 2023), highlighting the necessity to develop specialized technologies that address the unmet needs of the industry. This could include services s.a. conducting genome analyses, managing and cataloging biosamples (section B), and clinical trial support tools (section C). This strategy is especially pertinent to the NIMSB, considering the potentially lengthy process involved in recruiting such prominent figures.

Additionally, the innovation office is responsible for protecting intellectual property and serving as a bridge between the institute and various external stakeholders. By adeptly handling both inward and outward engagement, the NIMSB's TTO can play a pivotal role in advancing the institute's research and innovation goals (Santos, interview, November 14, 2023).

4. Challenges (Group Part)

Setting up a successful TT framework at the NIMSB will undoubtedly come with challenges. Firstly, given that Systems Biology is a relatively new science and lacks a substantial track record in drug development (O'Beirne, interview, November 16, 2023), the NIMSB's technologies might initially be at a low TRL. Therefore, setting realistic expectations for the timeframe of translating systems biology research into marketable products or licensed deals is crucial. Moreover, there is a need for the NIMSB to offer novel and distinct scientific contributions that set it apart from industry capabilities despite the industry's larger financial resources (Vidal, interview, December 7, 2023). Secondly, being

based in Portugal presents challenges due to limited university-industry linkages in the national economy (Teixeira and Monteiro 2018), yet this also opens opportunities for the NIMSB to bridge this gap. Thirdly, the success in translation, particularly for spinouts, greatly depends on the entrepreneurial mindset within the NIMSB's staff, a trait found challenging to cultivate in the scientific community (Roberts, interview, December 4, 2023).

5. Practical Recommendations (Group Part)

Drawing upon the insights of various decision makers from the perspective of renowned life science research institutes and universities as well as relevant, influential pharmaceutical representatives, allows for a comprehensive framework of recommendations on how the NIMSB can forge ties to the industry for ensuring long-term success. Long-term success in this context is defined as reaching the NIMSB’s research, societal, and financial goals.

The insights and recommendations from this study can be organized into two primary strategic visions for guiding the NIMSB's operations and a key recommendation for a foundational structure to support these strategies (Figure 9, Appendix 27).

First, the NIMSB should position itself as ***fulfilling a role as a connector*** in the single-cell multi-omics field, fostering a collaborative environment, mutual learning, and innovation. It should pursue dynamic, long-term, and equitable industry partnerships and aspire to become a hub in the field. There is an increasing trend of companies seeing value to be connected within an innovation ecosystem (Roberts, interview, December 4, 2023). Further, there is sufficient evidence that both industry players and institutes prefer long-term, ongoing collaboration. The NIMSB should provide a platform facilitating connections between industry partners, researchers, governmental institutions, investors, and startups, e.g., in terms of organizing events, meet-ups, etc. Fostering an industry partnership model or

ongoing strategic collaboration and integrating them into the NIMSB ecosystem may reflect an ideal way to ensure a constant, long-term connection and exchange.

The second is to position the NIMSB as a leader in ***driving entrepreneurship***. It should actively support a sustainable and diverse spinout pipeline, maximizing opportunities for growth and impact. Moreover, focusing on providing adequate tools and support for spinouts is key - e.g., through connecting entrepreneurs with potential investors has proven to work well in other institutes. Given the resource-intensive nature of these support systems, the NIMSB needs to explore how it can indirectly benefit, s.a. becoming a shareholder through external trustee arrangements. Effectively managed, a thriving spinout ecosystem can significantly align with the NIMSB's objectives in economic and scientific contributions, thereby yielding substantial societal benefits in the Lisbon region and beyond.

Lastly, the successful implementation of the previous two recommendations mandates a ***strong operational and agile foundation***, ensuring the NIMSB is administratively effective and strategically positioned for long-term success. One element of this is a well-functioning TTO both in terms of size and the appropriate governance structure and backgrounds in place. To build ties with the industry successfully, it is crucial to attract scientists, professors, transfer managers, and decision-makers within the NIMSB who, in the best case, have experience working in or with the industry to understand their needs. Next, the NIMSB should attract profiles that are driven by NIMB's visions mentioned above, which is why the proper external articulation of these values is imperative. Furthermore, the NIMSB will need to set tangible, goal-oriented KPIs that are not just tracking research-focused goals but measure status in terms of industry ties, e.g., number of industry partnerships or TRL progression. The NIMSB’s strategic focus should be consistently directed towards building up and diversifying its portfolio with an eye on long-term sustainability beyond the initial funding. For example, the NIMSB should proactively focus on setting up the requisite

infrastructure for facilitating spinout creation since the return on investment may be stretched for several years; hence, initiating this process in the early stages of the institute's development is advisable to ensure a robust portfolio in the future. While maintaining its autonomy, the NIMSB should consider partnerships with independent TT companies to reduce the high costs of establishing a wide range of industry collaboration opportunities, enabling it to achieve its vision of a diverse and dynamic portfolio.

Final Conclusion (Group Part)

To summarize, the preceding analysis substantially contributes to the overall development of a foundational framework instrumental in the NIMSB's overarching developmental strategy. It lays the groundwork for further investigations and complements the comprehensive business plan. The four components can be seen as fundamental building blocks of the "House of the NIMSB" (Figure 10 in Appendix 28). Together with other essential building blocks, they constitute the foundational structure of the house, collaboratively aiding the NIMSB in realizing its vision of establishing a prominent position within the research ecosystem. The key findings of each focus topic can be summarized as follows:

(1) At its core, research is fundamentally driven by cooperative initiatives. Hence, engaging in local and global partnerships is crucial for the NIMSB to establish its position through the contribution of its unique capabilities and effective utilization of available resources.

(2) Centralized collaborative biobanking has the potential to expedite and bolster the NIMSB's research goals while also making a significant contribution to the research community.

(3) The NIMSB can distinguish itself among peer institutions by leveraging its cutting-edge technologies in clinical trials. Embracing a forward-thinking approach positions the NIMSB uniquely within the evolving landscape of clinical trials. It

equips the institute to address future challenges and opportunities in the healthcare community.

(4) The NIMSB will achieve its outlined objectives by becoming an innovation and entrepreneurship hub and forging long-term and equitable industry partnerships while building on a strong operational foundation beyond initial funding.

Adopting these recommendations will position the NIMSB at the forefront of healthcare research and innovation, enabling the institute to effectively meet its research objectives while making a profound and lasting impact to the healthcare community.

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Section C: A Blueprint for Clinical Trial Contribution (Group Part)

Recognizing the significance of collaborations and biobanking for accelerating research and extending the NIMSB´s reach within the previous sections, the present research shifts focus to exploring the institute´s potential contributions to the clinical trials sector. The critical role of clinical trials in healthcare, coupled with the current demand for rapid technological innovation (Hardman et al. 2023, 1-11), highlights the importance of the NIMSB in exploring these opportunities. This analysis aims to uncover how the NIMSB can utilize its capabilities to enhance its scientific and societal impact significantly, underlining its relevance in health sciences and its prominence in the academic community. The following section will provide a comprehensive overview of clinical trials, starting with their definition and importance in clinical research. This will be followed by an exploration of the clinical trials market, identifying key trends and challenges pertinent to the NIMSB. The analysis will then delve into potential contribution opportunities for the NIMSB, ensuring alignment with market needs identified earlier. Finally, the strategic benefits of these potential contributions will be examined, leading to tailored recommendations for effective implementation. This

approach aims to map out a clear pathway for the NIMSB´s meaningful engagement in clinical trials, enhancing its role in advancing healthcare research.

1. Understanding Clinical Trials

The World Health Organization (WHO) defines a clinical trial as any research study that prospectively assigns human participants or groups to one or more health-related interventions to evaluate their effects on health outcomes. These trials encompass a wide range of interventions, incl. drugs, surgical procedures, medical devices, behavioral treatments, and preventive care. Before their initiation, clinical trials require careful design-, review-, and approval processes (World Health Organization 2020). Another crucial aspect is the diversity of participants in clinical trials, which is why it should be ensured to involve individuals from various age groups, health conditions, races, genders, ethnicities, and cultural backgrounds. This is essential to increase the probability of finding universally safe and effective treatments and procedures (National Institute on Minority Health and Health Disparities 2023).

1.1. The Clinical Trials Process in Context of Drug Development

To fully understand the clinical trials process, it is essential to understand the broader spectrum of clinical research. The drug development process serves as a basic framework that can be used to explain the entire clinical research process, thereby clarifying the role of clinical trials in the context of developing new treatments. An illustration of the drug development process can be found in Figure 7 in Appendix 15.

In the initial stage of drug development, the ***discovery phase*** refers to exploring new insights about diseases, testing numerous compounds for therapeutic potential, and identifying promising candidates from existing treatments or through innovative technologies. Subsequently, during the ***development***, these selected compounds undergo detailed studies to determine their absorption, metabolism, potential benefits, optimal dosages, side effects, and

effectiveness, setting the stage for their progression into preclinical research. The development phase is followed by another preliminary stage of clinical trials, ***preclinical research***, which is mainly conducted by academic and research institutions or pharmaceutical and biotechnology companies. This includes assessing the potential toxicity of a drug using in vitro (lab) and in vivo (animal) studies (Food and Drug Administration 2018). Although not extensive in scale, these studies are pivotal in narrowing down promising drug candidates and ensuring that only the most viable options enter human trials (ALS Therapy Development Institute 2023).

Once sufficient data has been collected, the ***initiation of the clinical trial*** starts. Clinical trials are generally divided into two categories. They can be industry-sponsored, usually by pharmaceutical companies or investigator-initiated, where individual researchers or clinicians lead the study. In the case of investigator-initiated trials, sponsorship can come from various sources, incl. individual donors, government agencies, private organizations, or other entities (Leite, interview, October 18, 2023). Initiators are responsible for creating a clinical trial protocol. This protocol outlines the background and purpose of conducting clinical trials, details the specific research questions to be investigated, and entails information about the trial design. Additionally, it includes a comprehensive examination of ethical considerations to ensure that the clinical trial meets the highest standards of ethical practice and participant safety (Cipriani and Barbui 2010, 116-17). The protocols are required to undergo review by a third-party board, known as an Institutional Review Board (IRB) in the US or an Independent Ethics Committee (IEC) in other countries (AbbVie Inc., n.d.). Once the protocol receives approval, the next step is to select a site where the clinical trial will be conducted. This selection is a collaborative process involving several key stakeholders of the clinical trial process. Selecting the appropriate sites is a key factor in ensuring the success of the trial in terms of patient recruitment, data quality, and compliance with regulatory requirements.

Clinical trial sites are primarily hospitals and medical centers but can also be universities or academic medical facilities, as well as other healthcare centers (Hurtado-Chong et al. 2017, 1-7). After the site has been selected, the clinical trial can begin. The responsibility for conducting the trial under the defined protocol then lies with a clinical trial coordinator, who can be employed by the clinical trial site or the initiator and is usually based at the selected trial site (Barros, interview, October 31, 2023). Clinical trials are carried out in phases, each serving a different purpose. The phases are described in more detail in Table 2 (Appendix 16):

(1) ***Phase I trials*** (several months) primarily assess the safety and dosage of the drug, involving 20 to 80 participants who may be healthy volunteers or patients with the disease, to understand the treatment's interactions within the human body. Around 70 percent of drugs move to Phase II (Food and Drug Administration 2018).

(2) ***Phase II trials*** (several months to two years) extend the focus to efficacy and side effects, targeting several hundred patients diagnosed with the disease to gather safety information, refine the research approach, and define the design of subsequent Phase III protocols. Around 33 percent of drugs move to Phase III (Food and Drug Administration 2018).

(3) ***Phase III trials*** (one to four years), with 300 to 3000 participants, further evaluate the treatment's efficacy and monitor adverse reactions to ascertain its therapeutic value for a wider patient population. They provide most of the safety data. Following the successful completion of Phase III, the next step is the commercialization of the medical treatment. Around 25-30 percent of drugs move to Phase IV (Food and Drug Administration 2018).

(4) ***Phase IV trials***, which are conducted post-market authorization, are concerned with long-term safety and efficacy, drawing on data from several thousand diverse patients (Food and Drug Administration 2018).

Throughout each of the four phases, samples are collected and analyzed to meet the unique objectives of each phase. At any stage of this process, a Contract Research Organization (CRO) can be hired to support various phases of the clinical trial process (Pharmaceutical Product Development 2022).

1.2. The Importance of Clinical Trials

Clinical trials are instrumental in improving our understanding of diseases and refining treatments (Jager 2023, 93-98). Jager (2023) further emphasizes the role of clinical trials in validating the safety and efficacy of new interventions, which form the basis for regulatory approval and widespread use. According to the FDA, clinical trials are vital in refining existing treatments, optimizing their use, and ensuring their safety across diverse populations. Through such comprehensive and carefully regulated studies, clinical trials offer a rigorous pathway to advancing healthcare and ensuring that new and current treatments meet the highest standards of care for all population segments (Food and Drug Administration 2023c).

Additionally, the significant financial investment in clinical trials, with median costs per approved drug at USD 48 million (USD 20 to USD 102 million) and individual trial costs averaging USD 19 million (USD 12 million to USD 33 million), underscores their crucial role in medical research development (Moore et al. 2020, 1-5). Despite this financial burden, the number of clinical trials worldwide has increased from 2,408 in 1999 to almost 54,952 in 2022 per year. This remarkable increase of more than 2000 percent indicates a growing global emphasis on medical research and innovation (World Health Organization 2023). This increase highlights the critical role of clinical trials in advancing medical knowledge and improving patient care, as well as the potential for research institutions like the NIMSB to enter this expanding field.

2. The Clinical Trials Market

To effectively position the NIMSB in the evolving clinical trials landscape, it is essential to gain a comprehensive understanding of both the global and the Portuguese markets. The clinical trials market is increasingly characterized by its internationalization and globalization, a trend that underscores the importance of understanding the broader, worldwide context (Mouta, interview, November 3, 2023). By thoroughly analyzing the different aspects of these markets, the NIMSB can develop a sound strategy that strengthens Portugal's competitive position in the global market and ensures locally relevant and effective contributions to clinical trials.

2.1. Understanding Today's Global Clinical Trials Market

The global clinical trials market was estimated to be between USD 49.8 billion and USD 54.24 billion in 2022. The market is expected to see a compound annual growth rate (CAGR) of 5.8 percent to 6.9 percent between 2023 and 2030, resulting in a market size of USD 78.3 billion to USD 92.45 billion by 2030. This growth expectation is due to the integration of cutting-edge technologies, an increase in the prevalence of chronic diseases, the expanding field of precision medicine, the increasing globalization of clinical trials, and the rising demand from developing nations. Additionally, pharmaceutical and biotechnological companies' significant investments in research and development (R&D) contribute to this upward trend (Grand View Research 2022a; Fortune Business Insights 2023). The global R&D spending from the pharmaceutical industry in 2022 was estimated to be approximately USD 244 billion, a substantial increase compared to USD 137 billion in 2012 (Mikulic 2023). In 2022, North America accounted for a major market share of around 50.5 percent, largely due to its high investment in R&D and early adoption of cutting-edge technologies in clinical trials. Key industry players, s.a. IQVIA, Pfizer, Pharmaceutical Product Development, LLC, and Laboratory Corporation of America Holdings are not only capturing a considerable global

market share in 2022 but are also at the forefront of rapidly integrating advanced technologies to enhance healthcare outcomes and driving market growth (Grand View Research 2022a; Fortune Business Insights 2022).

This evolving landscape presents unique opportunities to the NIMSB for strategic engagement. The NIMSB's objective to focus on chronic diseases, precision medicine, and cutting-edge technologies is very much in line with the market trends that are responsible for market growth. This strategic alignment underlines the potential opportunities for the NIMSB to make an impactful contribution to the clinical trials market.

2.2. Current State of The Portuguese Clinical Trials Market

Understanding the Portuguese clinical trials market where the NIMSB will operate provides an inherent advantage, enabling the institute to tailor its approaches to align with regional needs and regulations. The local context allows the NIMSB to focus its research efforts on health priorities and challenges specific to Portugal, thereby fostering meaningful collaborations. This enhances the NIMSB´s relevance and positioning in the clinical trial landscape and paves the way for impactful, locally relevant research.

2.2.1. Dynamics in and Current Status of Portugal's Clinical Trials Landscape

The clinical trials sector in Portugal shows a fluctuating but overall positive trend. From 2021 to 2022, the number of submitted clinical trials increased from 175 to 230, of which the pharmaceutical industry sponsored 212. The number of approved trials rose from 144 to 152. Phase III trials dominated with 128 applications in 2022, followed by Phase II trials at 55 applications, while Phase IV trials had the fewest, with only nine applications. The most studied therapeutic areas include antineoplastic and immunomodulatory drugs, studies on the central nervous system, the gastrointestinal tract and metabolism, as well as the cardiovascular system (Infarmed I.P. 2022).

Despite the positive trend of submitted clinical trials, Portugal lags behind other European countries of similar size in terms of the number of participants recruited per million inhabitants (Grand View Research 2022a). Also, the time to receive approval for clinical trials has increased from an average of 32 calendar days in 2020 to 87 days in 2022 (Infarmed I.P. 2022). This duration exceeds the average in other European countries, affecting market dynamics and preventing rapid progress (Leal, interview, October 19, 2023). The extended approval times can be largely attributed to the increasing complexity of these trials, which requires a more comprehensive review process. In particular, trials involving innovative therapies, complex designs, and integrating advanced technologies require a higher level of review and a more detailed assessment (Infarmed I.P. 2022; Leite, interview, October 18, 2023).

2.2.2. Portugal's Regulatory Landscape

The regulatory environment in Portugal plays a crucial role in shaping the pace and nature of clinical trials. As a member of the European Union (EU), Portugal must comply with EU-wide regulations. The EU introduced the Clinical Trials Information System (CTIS) on January 31, 2022, representing a substantial development in the regulatory framework for clinical trials in Europe. CTIS is now the obligatory platform for submitting all new clinical trial applications throughout the EU and the European Economic Area (EEA). This platform integrates the application, evaluation, and documentation stages of clinical trials across up to 30 EU/EEA countries. The CTIS replaces the need for separate submissions to national competent authorities and ethics committees. It provides a single, publicly accessible database that improves efficiency and transparency for healthcare professionals, patients, and other stakeholders. This reduces administrative burdens for researchers and pharmaceutical companies and ensures a consistent approach to governing clinical trials across Europe (European Medicines Agency 2023). Overall, this may positively influence the time of

receiving approval for clinical trials. In addition, Portuguese researchers and pharmaceutical companies are required to align with the national legislation Law No. 21/2014 of April 2016 (Clinical Research Law), as amended by Law No. 73/2015 of July 27 and Law No. 49/2018 of August 14, where clinical trials require approval from the Ethics Committee in Portugal (CEIC) and authorization from the Director Council of Infarmed, I.P. (Carvalho et al. 2021; European Network of Research Ethics Committees, n.d.; National Registry for Clinical Studies, n.d.).

2.3. Challenges within the Clinical Trials Landscape

Considering the complexity of clinical trials, it is crucial to understand the challenges in this sector to ensure a strategically beneficial positioning for the NIMSB. Globally, the clinical trials market faces challenges that include patient recruitment difficulties, leading to low-value trials and wasted resources. Further challenges are increasingly complex clinical trial designs, regulatory hurdles, talent shortages, and the need to keep pace with ongoing technological advancements and innovations. Other significant obstacles include patient retention, ensuring diversity in trials, managing rising costs, and handling the rise in data volume and complexity (Bentley et al. 2019, 183-93; Pharmaceutical Product Development 2022; Soto 2023).

In Portugal, the clinical trials market faces unique barriers that affect its international competitiveness. Besides the aforementioned issue of long approval times for clinical trials, Portugal's national healthcare system lacks efficient organization, leading to inefficient collaboration among hospitals. This inefficiency is evident in clinical trials conducted at multiple sites across the country, where the absence of optimal referral pathways, which are commonly seen in other countries, hinders optimal coordination and patient recruitment. These infrastructural inadequacies and organizational and regulatory hurdles present significant obstacles for industry- particularly investigator-initiated clinical trials when

combined with limited funding and expertise. Consequently, Portugal´s attractiveness in the global clinical trials arena is diminishing (Carvalho et al. 2021, 80-83; Madeira et al. 2016, 141-48; Roche, interview, November 3, 2023).

2.4. Emerging Trends Shaping the Clinical Trials Landscape

Currently, research institutions, s.a. the NIMSB, have a relatively limited involvement in clinical trials. This highlights the need to explore their potential for greater future engagement, which is why a thorough analysis of emerging trends within the clinical trials sector will follow. The sector is experiencing a transformative shift towards innovative solutions. This development aligns closely with the strategic direction of the NIMSB. Emerging trends, s.a. precision medicine, Artificial Intelligence (AI), the use of Real-World Data (RWD), Real-World Evidence (RWE), and Decentralized Clinical Trials (DCT) are becoming significant driving factors. These advances not only improve the efficiency and effectiveness of clinical trials but also open opportunities for the NIMSB to make significant contributions in this field. In the following, key trends - precision medicine and AI - will be explained in more detail. Additional information on RWD and RWE can be found in Appendix 17 and more details on DCT is provided in Appendix 18.

2.4.1. Precision Medicine

The global market for precision medicine, valued at USD 72.73 billion in 2022, is projected to reach USD 175.6 billion by 2030. This growth represents a CAGR of 11.52 percent (Strategic Market Research 2022) and fits seamlessly into the NIMSB's research focus. Precision medicine is revolutionizing the healthcare market by shifting from the traditional "one-size-fits-all" method to a tailored strategy that personalizes therapies based on individual molecular profiles, ensuring that each person receives a specifically designed treatment for optimal efficacy (Naithani et al. 2021, 249-57). Mouta, the Principal Global Medical Leader of Breast and Gynaecological Cancers at Roche, along with other experts in

the field, underscores the significance of this emerging trend in the context of clinical trials, particularly in oncology. This aligns with the NIMSB's research focus on cancer. In oncology, breast cancer was considered as a single disease in the past. However, recent progress in precision medicine has revealed that breast cancer consists of at least three distinct subtypes. These subtypes show distinct symptoms and respond differently to treatments (Roche, interview, November 3, 2023). This new understanding significantly influences clinical decision-making by allowing for more targeted and effective treatment strategies based on patient-specific characteristics. Through this, the participant selection process improves by dividing patients into more precise subgroups based on their genetic makeup, e.g., biomarkers (Gomes, interview, October 27, 2023; Wang & Wang 2023, 3837). This advancement can streamline the selection process, reduce patient recruitment challenges, and speed up the development of treatments, increasing the overall efficacy of clinical trials (Gomes, interview, October 27, 2023).

Central to this shift is the incorporation of single-cell multi-omics, a technology that will be integral to the NIMSB and pivotal for analyzing molecular mechanisms at the cellular level, providing detailed insights into patients´ disease profiles (Pammi, Aghaeepour and Neu 2023, 308-15). This advanced technique allows researchers to analyze the complex heterogeneity of cell populations in patient samples, providing high resolution of cellular responses to therapeutic interventions. By integrating multi-omics data at the single-cell level, it is possible to detect the specific cell types that respond to treatment and to identify molecular signatures that predict therapeutic success (Kennedy, interview, October 13, 2023; Zielinski et al. 2021, 590742). These breakthroughs facilitate the creation of new clinical trials aimed at reevaluating existing drugs by analyzing them at a single-cell level, enabling more comprehensive analysis of events during clinical trials, expanding the scope of potential

drug targets, and stratifying patients more accurately. This, in turn, significantly increases the success rate of clinical trials (LifeTime Initiative 2020).

Currently, the application of single-cell multi-omics technologies in clinical trials is largely experimental and not yet a standard practice for patient selection. It is mainly used for retrospective or simultaneous studies that analyze patient material collected during trials or utilize non-patient sources like animal and in vitro models (see definition of retrospective studies in Appendix 2) (Kolben, interview, October 17, 2023; Roche, interview, November 3, 2023). While single-cell multi-omics approaches hold immense promise for clinical trials in the future, they also bring significant challenges. It deals with complex and large-scale data, which can be hard to manage and understand. Ensuring data accuracy is essential in avoiding misleading conclusions, as mistakes or inconsistencies in data can significantly impact the outcomes. Additionally, there is a need for powerful computational tools capable of handling and analyzing this vast amount of data efficiently. These tools must be robust and user-friendly to facilitate widespread adoption. Equally important is the need to train end-users, incl. researchers and clinicians, in the effective use of these technologies to ensure their optimal application. Alongside this training, there must be an investment in infrastructure to support these advanced techniques, which includes both hardware to perform the analyses and software to process the data (Zielinski et al. 2021, 590742).

As technology continues to advance, allowing us to identify even finer details of a disease, it is expected that clinical trials will increasingly incorporate this personalized approach. The future of clinical trials in the era of precision medicine will likely consist of more targeted, biomarker-driven trials that offer treatments tailored to individual patient profiles, leading to more effective and efficient therapeutic outcomes. However, while the full potential of these advanced technologies in precision medicine is recognized, the pathway to

its seamless integration into clinical trials is not yet clearly defined (Bayer, interview, October 17, 2023; Höpken, interview, November 28, 2023; Roche, interview, November 3, 2023).

2.4.2. Artificial Intelligence

The global market for Artificial Intelligence (AI) in clinical trials, estimated to be worth USD 1.4 billion in 2023, is expected to increase at a CAGR of 16 percent between 2023 and 2035 (Research and Markets 2023b). This development aligns well with the NIMSB's future emphasis on AI in health. AI can revolutionize clinical trials by refining study designs and enhancing the overall outcomes of clinical trials, notably through increased accuracy and efficiency in testing. It facilitates improved participant recruitment and retention, leveraging predictive analytics for more effective engagement and management. Additionally, AI is used for real-time safety monitoring, a key feature, ensuring ongoing vigilance throughout the clinical trial process. Furthermore, it supports more precise site selection and the performance of detailed data analysis, thereby streamlining the evaluation of treatments. This results in a faster development process for safer and more effective therapeutic solutions (Research and Markets 2023a; Medable, Inc 2023).

Building on these broad applications, AI's role becomes even more pivotal when applied to the field of single-cell multi-omics in the context of precision medicine by uncovering hidden relationships and interactions. Analyzing single-cell multi-omics data requires AI algorithms to integrate different types of data that are critical for understanding disease mechanisms and drug responses to ultimately gain meaningful insights. These algorithms have the ability to better understand the physiological state of a patient, to facilitate accurate diagnosis, and to predict and enable precise and personalized treatment strategies (Pace Ventures 2023). In early-phase clinical trials, s.a. Phase I and II, and especially in oncology, AI-enabled real-time data analysis supports agile decision-making and trial adaptation. This underscores the importance of AI in facilitating swift, accurate

assessments of drug safety, dosage, and efficacy, which is critical for rapidly determining a drug´s potential (Askin et al. 2023, 203-13). Beyond the scientific aspect, AI enhances operational efficiency in clinical trial management, logistics, and administrative processes, making the overall execution of trials more streamlined and effective (Iacona and Khan 2019). An example of its application in operational efficiency is its use in patient allocation in randomized trials (Roche, interview, November 3, 2023).

While AI presents significant opportunities, it also comes with challenges that need to be carefully navigated. Ethical considerations and regulatory challenges are the biggest hurdles to the integration of AI. Ensuring data privacy is critical as AI involves handling sensitive patient data. In addition, mitigating bias in training data and maintaining transparency is crucial to ensure fairness, trust-building, and accuracy. Managing these barriers is necessary for a responsible and effective integration of AI in clinical trials (Alsumidaie 2023; Askin et al. 2023, 203-13).

3. Assessing the NIMSB's Potential Contributions to Clinical Trials

The systemic challenges in the Portuguese clinical trials industry (Chapter 2.3.) require multi-layered interventions that go beyond the capabilities of a single research institution. Further, the previous discussion and the interview insights have revealed that clinical trials are an extremely complex field. There seems to be a scarcity of research institutes like the NIMSB that are actively involved in clinical trials. However, discussions with various stakeholders have also highlighted the NIMSB's advantageous position in contributing to the improvement of clinical trials. For example, the NIMSB's targeted focus on research and innovation in precision medicine, especially in single-cell multi-omics and AI, is closely linked to current trends in clinical trials, enabling the NIMSB to respond to diverse needs in this area.

In the initial meeting with Jacinto, it was explicitly stated that the NIMSB would not be setting up its own clinical trials unit (CTU). Consequently, the NIMSB must identify different modes of contribution. For that, the institute will depend on strategic partnerships with pharmaceutical companies, hospitals, and other stakeholders involved in clinical trials. This collaborative approach will pave the way for a robust and sustainable strategy that positions the NIMSB well in the ever-growing field of medical research.

3.1. NIMSB´s Cutting-Edge Technologies in Clinical Trials

The NIMSB is well-positioned to contribute to clinical trials through its advanced technological capabilities. By specializing in single-cell multi-omics (Chapter 2.4.1.) and AI (Chapter 2.4.2.), both of which are in high demand in clinical trials, the NIMSB has the potential to leverage its knowledge and significantly contribute to clinical trials. By facilitating the rapid adoption and integration of these cutting-edge technologies into clinical research, the NIMSB can play a prominent role in refining research methodologies, improving data accuracy, and ultimately leading to more effective and personalized treatments for patients (Bayer, interview, October 17, 2023; Bertero, interview, November 7, 2023; Leite, interview, October 18, 2023; Penney, interview, November 27, 2023; Roche, interview, November 3, 2023; Silva, interview, October 26, 2023; Vidal, interview, December 12, 2023).

3.1.1. Contribution to Translational Research

The NIMSB's strong technological capabilities are projected to impact translational research significantly, especially in clinical trials. An introduction to translational research is provided in Appendix 19. Discussions with several pharmaceutical companies have shown that a partnership will greatly benefit the NIMSB. These companies are the initiators of most clinical trials and have the necessary financial resources and interest in advanced technologies like those developed by the NIMSB (Bayer, interview, October 17, 2023; Roche, interview, November 3, 2023). With its expertise in single-cell multi-omics and AI, the NIMSB can

provide accompanying research by offering in-depth background analysis and a comprehensive understanding of clinical trial processes. This is vital for better understanding complex biological pathways and diverse patient reactions to treatments. The NIMSB's capabilities are particularly helpful in conducting parallel correlative studies alongside clinical trials. These studies are designed to provide deeper insights into biological mechanisms and patient variability without directly impacting study design or therapeutic decisions, as highlighted by experts s.a. Mouta and Kolben, the Global Head of Early Clinical Development Oncology at Bayer. Another key aspect of the NIMSB´s contribution is the comprehensive analysis of the immune response before and after treatment. This approach helps in identifying crucial biomarkers to advance personalized treatment strategies, guiding therapeutic decisions, and monitoring the efficacy of interventions (see definition of biomarker in Appendix 2). The analysis may also contribute to the development of new prognostic tools and therapeutic targets, enhancing patient-specific care. The integration of AI in this process is essential to interpret complex data generated from single-cell multi-omics technologies (Höpken, interview, November 28, 2023). This approach exemplifies how the NIMSB's advanced technologies can be applied in practice, effectively linking basic biological research and clinical applications and achieving remarkable progress in translational research (Roche, interview, November 17, 2023).

3.1.2. Contribution to Patient Stratification

Looking ahead, the NIMSB´s role in patient stratification using its advanced technologies could greatly enhance the decision-making process in the participant recruitment of clinical trials. Patient stratification involves categorizing patients into subgroups based on the presence or absence of particular disease characteristics (Abdelnour et al. 2022, 112). Although these advanced technologies have not yet been developed to the point where they can accurately stratify patients, as was noted by Mouta, their potential impact on the future is

significant. The goal is to categorize patients based on their biological, clinical, and demographic characteristics, subsequently testing new treatments for these specific groups (Coelho 2023; Gomes, interview, October 27, 2023; Lange, interview, December 5, 2023). By understanding the unique molecular patterns of patients, the NIMSB can facilitate more accurate participant selection, potentially reducing the number of patients needed in a trial and enhancing the overall quality and relevance of clinical research (Gomes, interview, October 27, 2023). A key aspect where the NIMSB could make a significant contribution regarding patient stratification is the development of companion diagnostics (see definition of companion diagnostic in Appendix 2). These specialized medical devices or tests are essential for tailoring specific treatments to individual patient profiles and depend on the identification of accurate and reliable biomarkers or genetic data. The NIMSB's cutting-edge technologies could help overcome one of the biggest challenges in patient stratification by improving biomarker discovery and validation through the development of companion diagnostics (Gomes, interview, October 27, 2023; Lange, interview, December 5, 2023). This capability not only helps to make patient stratification more feasible for different diseases but also promises to reduce the time and cost of drug development, thereby increasing the overall efficacy of clinical trials (Coelho 2023) .

By aligning its cutting-edge technologies with the evolving needs of the clinical trials industry, the NIMSB will be positioned to become a relevant partner in advancing clinical trial methodologies. Particularly in the area of precision medicine and personalized treatment strategies, the role of the NIMSB in patient stratification and decision support for clinical trials represents a significant step toward more efficient, effective, and patient-specific clinical research outcomes.

3.1.3. Preconditions for Applying Cutting-Edge-Technologies

For putting the NIMSB in a position to provide the contributions mentioned under Chapter 3.1.1. and 3.1.2. the NIMSB needs to focus on integrating its cutting-edge technologies into clinical trials. As Penney, Vice President and Global Head of Oncology Precision Medicine of Bayer US, pointed out, this aspect is decisive for thorough analytical validation of these technologies. The NIMSB needs to prove that technologies, s.a. single-cell multi-omics, are not only accurate and consistent but also tailored for specific applications. For single-cell multi-omics to be effectively applied to clinical samples, there needs to be a high degree of confidence in both the test and the algorithm used, which directly impacts the reliability of clinical trial outcomes. Partnerships with biobanks or a centralized NIMSB biobank for sufficient sample collection are crucial for assay validation to ensure the readiness of these methodologies for clinical application (Section B). The journey from technological innovation to clinical application involves navigating these complexities to ensure that the NIMSB´s technologies can effectively contribute to understanding drug mechanisms and resistance patterns, thereby enhancing the efficacy and precision of clinical trials (Penney, interview, November 27, 2023).

3.2. Exploring Additional Potential Contributions of the NIMSB to Clinical Trials (Group Part)

In addition to its crucial contributions to translational research and patient stratification, the NIMSB can extend its influence to several other vital areas and challenges of clinical trials. This broader engagement enables the NIMSB to effectively utilize its expertise and resources to improve various facets of the clinical trial process.

3.2.1. Training and Educational Initiatives (Group Part)

Discussions with Barros, the Director of CUF Academic Center, Leite, the Executive Director of Hospital da Luz and Calado, the Vice-Dean for Research at NOVA Medical

School, have highlighted the critical need for enhanced skills in AI and single-cell multi-omics within clinical trials. The NIMSB can meet this demand by offering specialized training programs tailored for medical staff, particularly in hospitals keen on adopting these innovations. Such initiatives would align with the NIMSB's objectives to train a new generation of researchers and medical doctors (Jacinto, interview, September 29, 2023). By addressing this knowledge gap, the NIMSB can empower healthcare professionals with the necessary skills to effectively utilize advanced biomedical technologies and data analysis techniques, ultimately enhancing the application of these technologies in clinical settings (Barros, interview, October 31, 2023; Leite, interview, October 18, 2023; Calado, interview, October 26, 2023). In addition, the NIMSB can contribute through guest lectures and joint workshops focusing on the latest clinical trial trends and innovations. These efforts foster continuous learning and knowledge exchange among healthcare professionals, benefiting everyone involved in clinical trials and patients.

3.2.2. Management of Clinical Trial and Data (Group Part)

The NIMSB's expertise in AI and complex data analysis can significantly improve the management and analysis of clinical trial data by increasing the depth and quality of research. By using AI to interpret datasets from single-cell multi-omics derived from patient samples, the NIMSB can significantly improve data quality and optimize the efficiency of the research process itself (Jacinto, interview, September 29, 2023; Leite, interview, October 18, 2023). In addition, the NIMSB's potential to provide advanced AI-powered management systems could revolutionize clinical trial workflows and increase efficiency from patient recruitment to data analysis. By using these systems, institutions, s.a. CUF, could experience a paradigm shift in the coordination of clinical trials, leading to a more seamless and integrated conduct of research activities (Gouveia, interview, November 14, 2023). The broader application of the

NIMSB's data management and process optimization expertise could improve clinical trial operations, potentially setting new benchmarks for efficiency and reliability in clinical trials.

3.2.3. Patient-Centric Approaches (Group Part)

The NIMSB's adoption of patient-centered approaches promises significant improvements in clinical trial participation and participant diversity. Community outreach programs that communicate the information and relevance of clinical trials could effectively increase trial participation and retention, demonstrate the NIMSB's commitment to advancing medical research, and underscore the importance of clinical trials to the healthcare system. In addition, the NIMSB can increase diversity in patient recruitment through its connections to diverse populations in Portuguese-speaking countries in Africa and South America. This strategy aligns with the globalization trend in clinical trials. It ensures broader applicability and reliability of medical treatments across different demographics, improving the overall impact for stakeholders and patients worldwide.

3.2.4. Science-Based Venture Building (Group Part)

The NIMSB is set to transform clinical trials by incubating startups focused on technologies like patient safety monitoring devices. Emphasizing the development of AI-driven diagnostic tools and data analysis platforms, this initiative addresses the needs of DCT, RWD, and RWE (Appendix 18, Appendix 17).

4. NIMSB´s Strategic Benefits for Clinical Trial Support (Group Part)

The strategic involvement of the NIMSB in clinical trials, as outlined in Chapter 3.0., presents a spectrum of advantages that align with the institute's core objectives. These benefits extend beyond commercial success, encompassing a profound impact on medical research and the enhancement of patient outcomes.

4.1. Collaboration and Resource Access (Group Part)

Given that the NIMSB does not conduct clinical trials itself, its contributions to this field are realized through strategic collaborations. These partnerships are instrumental in providing the NIMSB with significant resource access. Collaborating with pharmaceutical companies, s.a. Bayer, offers the NIMSB access to extensive compound libraries and sample collections, exceeding the typical scope of academic research and valuable pharmaceutical expertise (Gorski, interview, October 11, 2023). Integrating the NIMSB's advanced technologies with the extensive resources of pharmaceutical companies enriches the NIMSB's research on the one hand and provides pharmaceutical partners with access to high-resolution technologies beyond commercial products on the other hand - both to their mutual benefit.

Similarly, partnering with hospitals offers the NIMSB access to diverse clinical samples and data critical for developing and testing innovative technologies. In addition, through collaboration with clinicians, the NIMSB can align its research with unmet medical needs. It enables a more manageable transition from preclinical research to clinical trials, thereby creating opportunities for new patient treatments.

These partnerships often evolve into long-term collaborations that ensure ongoing access to resources on both sides and a steady bidirectional stream of clinical data, increasing the scope and impact of the NIMSB's and their partner´s research efforts.

4.2. Innovation and Revenue Generation (Group Part)

By offering its advanced technological capabilities in AI and single-cell multi-omics analysis as a service to pharmaceutical companies, the NIMSB positions itself as a valuable collaborator in the clinical trial process. This engagement strategy not only fosters TT paths and profit sharing but also catalyzes the development of the NIMSB´s cutting-edge technologies. Such collaborative efforts result in shared intellectual property and profits, generating significant added value for the NIMSB and its industry partners. This model goes

beyond financial gain; it drives the NIMSB´s research into new areas of clinical trial innovation and contributes to developing more efficient and effective trial methods. Overall, this engagement represents a revenue stream and a platform for the NIMSB to apply its research in the real world and increase the impact and reach of its clinical trial work.

4.3. Enhancing Patient Outcomes and Credibility (Group Part)

Involvement in clinical trials offers the NIMSB a unique opportunity to enhance patient outcomes and solidify its credibility in the scientific community while accelerating its impact in healthcare. By actively participating in clinical trials, the NIMSB can directly contribute to improved patient care by applying its innovative technologies or community initiatives s.a. patient engagement workshops. This participation enables the validation and practical application of the NIMSB´s research and enhances its reputation as a well-respected and influential institution in the medical science community. The data collection and insights gained through the use of the NIMSB´s technologies in clinical trials provide valuable contributions to the field, advanced understanding, and new avenues for medical research. Additionally, the NIMSB can effectively bridge the gap between fundamental research and practical clinical applications by focusing its preclinical research towards transitioning to clinical trials. It represents a strategic move for the NIMSB to transition from basic research to product development, which is crucial for tangible health benefits (Bertero, interview, November 7, 2023). This progression showcases the NIMSB's commitment to advancing medical science and strengthens its role as a health-related research and innovation leader.

5. Practical Recommendations (Group Part)

In the strategic context of the NIMSB's involvement in clinical trials, it is evident that managing a CTU to conduct clinical trials directly is not feasible for the NIMSB. Instead, the NIMSB should leverage its strengths through strategic partnerships and high-impact, collaborative research efforts. This approach is in line with the NIMSB´s broader objectives

that are mentioned in the overall introduction chapter about the NIMSB. Given the vital role of clinical trials for testing and validating new therapeutic strategies for patients, the NIMSB´s commitment to clinical trials positions it to contribute significantly to developing and validating innovative health solutions. For the NIMSB to make a meaningful impact, a detailed roadmap outlining timelines and steps for clinical application is essential, aligning its capabilities with the evolving market needs and positioning it at the forefront of innovation in clinical trials. Key milestones of this roadmap are depicted in Figure 8 in Appendix 20. This forward-looking approach is vital to harnessing the full potential of the NIMSB´s technological advancements in the dynamic medical research landscape.

To reach the first milestone of such a roadmap and establish the NIMSB as a key player in clinical trials, the NIMSB´s focus must be preparing its technologies for clinical use. This is crucial for meeting the current and future demands of the clinical trials market, particularly in precision medicine and the integration of advanced technology. Thus, the NIMSB should prioritize ***(1) the development and analytical validation of its cutting-edge technologies***, especially single-cell multi-omics and AI. The NIMSB can refer to established guidelines like the “Guideline on bioanalytical method validation” (https://bit.ly/3tlaMZw) for a comprehensive understanding of necessary validation criteria. Subsequent collaboration with biobanks, or leveraging its own biobank for sample testing and validation, is essential to ensure the technologies´ clinical applicability.

For reaching a further milestone of said roadmap, after successful analytical validation, the NIMSB should start concentrating on addressing local clinical trial needs by offering holistic solutions encompassing both basic research and clinical applications to local entities, s.a. hospitals (CUF or Hospital da Luz) and pharmaceutical companies. This strategic local engagement will not only showcase the NIMSB´s capabilities and strengthen its industry credibility but also lay the groundwork for its ***(2) contributions to translational research by***

offering accompanying research. Once this local foundation is established, the NIMSB´s validated, cutting-edge technologies can be applied to clinical trial samples, offering in-depth analyses that enhance understanding of patient responses and complex biological pathways.

To reach the last milestone of said roadmap, the NIMSB can effectively address shortcomings in patient recruitment and patient retention for clinical trials by ***(3) developing companion diagnostics for stratifying patients***. By leveraging its technological strengths, particularly in single-cell multi-omics and artificial intelligence, the NIMSB can more accurately categorize patients - a process that requires complicated and lengthy developments. This approach can improve treatment outcomes and streamline patient recruitment by identifying specific patient subgroups who would benefit most from targeted therapies. This long-term focus reflects the evolving role of the NIMSB´s technologies, which are expected to become increasingly important in patient stratification.

In addition to offering single-cell multi-omics and AI data analysis, the NIMSB should address local challenges of technology integration and talent shortages in clinical environments. Collaborating with hospitals like CUF or Hospital da Luz, who expressed a need for AI and single-cell multi-omics expertise, the NIMSB can help integrate these technologies effectively. By providing educational training programs, the NIMSB can increase scientific capabilities and technology adoption in medicine. Furthermore, by working closely with clinicians, the NIMSB can align its preclinical research with clinical applications, enhancing the practical impact and relevance of its findings.

Following the path outlined above will give rise to a series of interesting new opportunities and generate synergies with potential partners. However, it is important to acknowledge that this represents a relatively uncharted area, even for other research institutes. As NIMSB ventures into this new domain, several challenges must be carefully considered and addressed, incl. factors s.a. regulatory hurdles, talent shortages, and rising costs.

In conclusion, the NIMSB's strategic focus on advancing precision medicine through cutting-edge technology and strong healthcare collaborations will position the institute to make essential contributions to clinical trials. The NIMSB has great potential to significantly improve medical science and patient well-being by merging innovative research with practical healthcare applications. This will be an important step forward in the NIMSB's efforts to redefine clinical trial methodology and enhance healthcare progress.

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Appendices

Appendix 1: List of Abbreviations

AI	Artificial Intelligence
BBMRI	Biobanking and BioMolecular resources Research Infrastructure
BRC	Biological Resource Centers
CAGR	Compound Annual Growth Rate
CEDOC	Centro de Estudos de Doenças Crónicas
CEIC	Ethics Committee in Portugal
CEO	Chief Executive Officer
CF	Champalimaud Foundation
CHRC	Comprehensive Health Research Centre
CINTESIS	Center for Health Technology and Services Research
CNPD	Comissão Nacional de Proteção de Dados
CRG	Centre for Genomic Regulation
CRO	Contract Research Organization
CTIS	Clinical Trials Information System
CTO	Career, Education, and Training Office
CTU	Clinical Trials Unit
DCT	Decentralized Clinical Trials
DNA	Deoxyribonucleic acid
EBI	European Bioinformatic Institute
EEA	European Economic Area
ELSI	Ethical, Legal, Social Issues
ERIC	European Research Infrastructure Consortium
ESBB	European, Middle Eastern & African Society for Biopreservation and Biobanking
EU	European Union
FFPE	Formalin-fixation and paraffin-embedding
FIMM	Finnish Institute for Molecular Medicine
GDPR	General Regulation on Protection of Personal Data
HR	Human Resources
HUB	Hannover Unified Biobank
IARC	International Agency for Research on Cancer
iBET	Institute of Experimental and Technological Biology
IEC	Independent Ethics Committee
IGC	Instituto Gulbenkian de Ciencia
ILP	Industry Liaison Program
IMM	Institute of Molecular Medicine

IMP	Research Institute of Molecular Pathology
IP	Intellectual Property
IPM	Industry Partnership Model
IPO	Instituto Português de Oncologia
IRB	Institutional Review Board
IRB	Institute for Research in Biomedicine in Barcelona
ISB	Institute for Systems Biology
ISBER	International Society for Biological and Environmental Repositories
ISO	International Organization for Standardization
ISPUP	Instituto de Saúde Pública da Universidade do Porto
IT	Information technology
ITQB	Instituto de Tecnologia Química Biológica António Xavier
KI	Karolinska Institute
KOL	Key Opinion Leader
KPI	Key Performance Indicator
MBA	Master of Business Administration
MDC	Max Dellbrück Center
MHH	Hannover Medical School
MIT	Massachusetts Institute of Technology
MoU	Memorandum of Understanding
MTA	Material Transfer Agreement
NISMB	Nova Institute for Medical Systems Biology
NMS	Nova Medical School
OECD	Organization for Economic Cooperation and Development
R&D	Research & Development
RNA	Ribonucleic acid
RWD	Real-World Data
RWE	Real-World Evidence
TRL	Technology Readiness Level
TT	Technology Transfer
TTO	Technology Transfer Office
UCD	University College Dublin
UK	United Kingdom
VIB	Vlaams Institute voor Biotechnologie
WHO	World Health Organization

Appendix 2: Definitions

(1) Retrospective research: Retrospective research involves the analysis of pre-existing data and/or biological samples (Junod 2010, 1).

(2) Omics data: Omics data refers to data conceived in scientific disciplines, called "omics", which is related to the high-throughput measurement of biological molecules. Various fields of study can be categorized as omics. Examples encompass proteomics, transcriptomics, genomics, metabolomics, lipidomics, and epigenomics. These terms refer to comprehensive investigations of proteins, RNA, genes, metabolites, lipids, and methylated DNA or changed histone proteins in chromosomes, respectively (Micheel CM, Nass SJ, Omenn GS 2012, 1)

(3) FFPE (formalin-fixation and paraffin-embedding): Formalin fixation and paraffin embedding (FFPE) are commonly used techniques to preserve tissue specimens for diagnostic pathology. However, formalin fixation causes significant fragmentation of nucleic acids (Berrino et al. 2020, 173).

(4) Retrospective studies: A retrospective study is a clinical study that empirically examines the effectiveness of a medical treatment procedure or the factors leading to a disease, starting from the outcome identified at the beginning of the study (DocCheck 2014).

(5) Biomarkers: A biomarker is an objective and measurable indicator of a physiological or pathological process or a response to a therapeutic intervention (European Medicine Agency, n.d.).

(6) Companion diagnostic: A companion diagnostic is a medical device, usually an in vitro diagnostic (IVD), that is critical to the safe and effective use of a corresponding drug or biological product. Its functions include identifying patients who will benefit most from a particular therapy, detecting patients at higher risk for serious adverse

events, and monitoring treatment responses to adjust safety and efficacy (Food and Drug Administration 2023b).

(7) Technology Transfer (TT): is formally described as the movement of scientific and technological research outcomes to the marketplace and broader society, incl. the relevant skills and methods (European Commission 2012)

Appendix 3: Method

A total of 44 qualitative semi-structured interviews were conducted with professionals from various sectors, incl. research- and academic institutes, hospitals, biobanks, pharmaceutical companies, and governmental institutions. The objective of these interviews was to gain a comprehensive understanding from a diverse range of experts in these fields. A list of all conducted interviews, incl. interviewee names, company/institutional names, job roles, and contact information (i.e., LinkedIn profile link and email address), is attached in Appendix 4.

Identification and Recruitment of Participants

Participants were recruited through a rigorous, independent process, primarily utilizing LinkedIn and direct email contact. Our selection strategy ensured a diverse pool of interviewees, encompassing roles, s.a. Principal Investigators, Senior Researchers, Vice Presidents, Heads of Partnerships, and Clinical Research Coordinators. The selection and recruiting was made with minimal reliance on the NIMSB's and our supervisor's network to avoid self-selection bias and ensure a broad representation of perspectives.

Interview Structure and Process

Interviews were conducted between October 10th and December 13th, 2023, each lasting approximately 30 to 90 minutes. The integrated transcription tool of Microsoft Teams was utilized to accurately document the interviews. Handwritten note-taking was additionally used when deemed essential. The interviews were semi-structured to provide flexibility in delving into the expertise of each participant. Thereby, questions could be modified dynamically, honing in on the topics where the interviewee demonstrated the highest level of expertise and reliability. This method reduced response bias by limiting participants' likelihood of delivering replies based on what they believed was desired.

Appendix 4: Conducted Interviews

No.	Current Organization	Name	Current Position	Date of Interview	Contact
1	AccelBio	Barbara Gomes	CEO	October 27, 2023	**LinkedIn:** https://www.linkedin.com/in/barbaraslgomes/ **Mail:** barbaragomes@accelbio.pt
2	Almac Group	Richard Kennedy	Global Vice President and Medical Director	October 12, 2023	**LinkedIn:** https://www.linkedin.com/in/profkennedy/ **Mail:** richard.kennedy@almacgroup.com
3	Ascenion	Esther Lange	Industry Liaison & Technology Manager	November 27, 2023	**LinkedIn:** https://www.linkedin.com/in/esther-maria-lange-1069a112/ **Mail:** lange@ascenion.de
4	Ascenion	Céline Christiansen-Mensch	Technology Scout	November 27, 2023	**LinkedIn**: https://www.linkedin.com/in/cechri/ **Mail:** lange@ascenion.de
5	AstraZeneca	Jacopo Biasetti	Associate Director - Systems Medicine	December 16, 2023	**LinkedIn**: https://www.linkedin.com/in/jacopo-biasetti-ph-d-5a660a65/ **Mail:**
6	Bayer	Theresa Kolben	Global Head Early Clinical Development Oncology	October 17, 2023	**LinkedIn:** https://www.linkedin.com/in/theresa-kolben-prof-dr-med-0278a811b/ **Mail:** theresa.kolben@bayer.com
7	Bayer Pharmaceuticals	Marina Penney	Vice President, Global Head of Oncology Precision Medicine	November 27, 2023	**LinkedIn:** https://www.linkedin.com/in/marina-penney-aa2b9a6/ **Mail:** christiansen-mensch@ascenion.de
8	BBMRI-ERIC	Saba Abdulghani	Head of Biobanking Development	November 22, 2023	**LinkedIn:** https://www.linkedin.com/in/dr-saba-abdulghani-38139bb/ **Mail:** saba.abdulghani@bbmri-eric.eu
9	BIMSB	Ashley Sanders	Group Leader	December 13, 2023	**LinkedIn**: https://www.linkedin.com/in/ashleydsanders/ **Mail**: ashley.sanders@mdc-berlin.de
10	Casa di Cura	Melania	Biobanker	December	**LinkedIn:**

	Privata del Policlinico	Filareti		4, 2023	https://www.linkedin.com/in/melania-filareti-880bb9109/?originalSubdomain=it **Mail:** m.filareti@casadicuraigea.it
11	Centre for Genomic Regulation (CRG)	Diana Dominguez	New Ventures Manager	November 8, 2023	**LinkedIn:** https://www.linkedin.com/in/diana-dom%C3%ADnguez-rodr%C3%ADguez-phd-7a349b192/ **Mail:** diana.dominguez@crg.eu
12	Champalimaud Foundation (Biobank)	Mireia Castillo	Responsible for Biobank	November 22, 2023	**LinkedIn:** **Mail:** mireia.castillo@research.fchampalimau
13	Champaulimaund Foundation	Joana Lamego	Head of Strategic Research Development	November 22, 2023	**LinkedIn:** https://www.linkedin.com/in/joana-lamego-10741a26/ **Mail:** joana.lamego@research.fchampalimaud.org
14	Charité	Verena Benz	Head of Match&Connect	October 13, 2023	**LinkedIn:** https://www.linkedin.com/in/dr-verena-benz-b018a756/ **Mail:** verena.benz@bih-charite.de
15	Charité	Alexandra Stege	Operational Manager	December 12, 2023	**LinkedIn**: https://www.linkedin.com/in/alexandra-eva-stege/?originalSubdomain=de **Mail**: alexandra.stege@charite.de
16	Charité BIH	Tim Huse	Head of BIH Digital Labs with Digital Health Accelerator	November 17, 2023	**LinkedIn:** https://www.linkedin.com/in/timhuse/ **Email:** tim.huse@bih-charite.de
17	CUF	Ingrid Gouveia	Group Lead - Clinical Research Coordinator	November 14, 2023	**LinkedIn:** https://www.linkedin.com/in/ingridgouveia/?originalSubdomain=pt **Mail:** ingrid.gouveia@jmellosaude.pt
18	CUF Academic Center	Maria Barros	Director	October 31, 2023	**LinkedIn:** https://www.linkedin.com/in/maria-barros-387803a/?originalSubdomain=pt **Mail:** maria.jose.barros@jmellosaude.pt
19	EU Life	Marta Dias Agostinho	Executive Director	October 24, 2023	**LinkedIn:** **Mail:** marta.agostinho@eu-life.eu
20	Hospital da Luz	Francisca Leite	Executive Director	October 18, 2023	**LinkedIn:** https://www.linkedin.com/in/francisca-leite-217505/ **Mail:** francisca.leite@luzsaude.pt

21	IDIBAPS	Michela Bertero	Strategy Director	November 7, 2023	**LinkedIn:** https://www.linkedin.com/in/michela-bertero-23a2584/?originalSubdomain=es **Mail:** BERTERO@recerca.clinic.cat
22	Innovation & Incubation Center Leuven	Michael De Blauwe	Chairman of the Board	November 21, 2023	**LinkedIn:** https://www.linkedin.com/in/michaeldeblauwe/ **Mail:** deblauwemichael@gmail.com
23	Institute for Molecular Medicine Finland (FIMM)	Mari Anneli Kaunisto	Senior Researcher	November 10, 2023	**LinkedIn:** https://www.linkedin.com/in/mari-kaunisto/ **Mail:** mari.kaunisto@helsinki.fi
24	Instituto de Medicina Molecular // Biobanco IMM	Sergio Dias	Principal Investigator	October 12, 2023	**LinkedIn:** https://www.linkedin.com/in/s%C3%A9rgio-dias-9903352/?originalSubdomain=pt **Mail:** sergiodias@medicina.ulisboa.pt
25	ITBQ	João Crespo	Dean	October 10, 2023	**LinkedIn:** **Mail:** jgc@fct.unl.pt
26	ITQB NOVA	Miguel Santos	Invited Principal Investigator - StartUp Research Coordinator	November 14, 2023	**LinkedIn:** https://www.linkedin.com/in/miguel-santos-1755295/ **Mail:** miguel.santos@unl.pt
27	Karolina Institute Biobank	Mark Divers	Retired Director	November 15, 2023	**LinkedIn:** https://www.linkedin.com/in/mark-divers-61761711/ **Mail:** mark.divers@ki.se
28	Massachusetts Institute of Technology (MIT)	John C. Roberts	Executive Director, MIT Corporate Relations (Interim)	December 4, 2023	**LinkedIn:** https://www.linkedin.com/in/john-roberts-97b8b06/ **Mail:** roberts5@mit.edu
29	Max Delbrück Center (MDC)	Stan Gorski	Science Strategy	October 11, 2023	**LinkedIn:** https://www.linkedin.com/in/stan-gorski-8913ab248/ **Mail:** stan.gorski@mdc-berlin.de
30	Max Delbrück Center (MDC)	Marie Vidal	Industry and innovation Manager	December 12, 2023	**LinkedIn:** https://www.linkedin.com/in/marie-vidal-phd-mba-14892643/?originalSubdomain=de **Mail:** Marie.Vidal@mdc-berlin.de
31	Max Delbrück Center (MDC)	Antonia Klein	Innovation and Technology Manager	December 13, 2023	**LinkedIn:** https://www.linkedin.com/in/antonianicoleklein/ **Mail:**

					Antonia.Klein@mdc-berlin.de
32	Max Delbrück Center (MDC)	Uta Elisabeth Höpken	Group Leader; PhD at Max Delbrueck Center for Molecular Medicine	November 28, 2023	**LinkedIn:** https://www.linkedin.com/in/priv-doz-dr-uta-elisabeth-h%C3%B6pken-7a89106a/ **Mail:** Uta.Hoepken@mdc-berlin.de
33	Medical University of Bialystok // ISBER	Anna Michalska-Falkowska	Deputy Director of Quality Management in Biobank & Clinical Trial Coordinator	October 17, 2023	**LinkedIn:** https://www.linkedin.com/in/anna-michalska-falkowska/?originalSubdomain=pl **Mail:** anna.michalska-falkowska@umb.edu.pl
34	Nova Medical School	Antonio Jacinto	Future Director of NIMSB	September 30, 2023	**LinkedIn:** https://www.linkedin.com/in/antonio-jacinto-a584509/ **Mail:** antonio.jacinto@nms.unl.pt
35	Nova Medical School	Patricia Calado & Mariana CC Silva	Vice Dean for Research	October 26, 2023	**LinkedIn:** https://www.linkedin.com/in/patriciacalado/ **Mail:** patricia.calado@nms.unl.pt
36	Oeiras City	Elisabete Baiôa Brigadeiro	Administration	October 18, 2023	**LinkedIn:** **Mail:** elisabete.brigadeiro@oeiras.pt
37	Ophiomics	Jose Leal	CEO	October 19, 2023	**LinkedIn:** https://www.linkedin.com/in/pereiraleal/ **Mail:** jleal@ophiomics.com
38	Ophiomics	C. Gaspar	Business Development	November 1, 2023	**LinkedIn:** **Mail:** cgaspar@ophiomics.com
39	Roche	Joao Mouta	Principal Global Medical Leader - Breast and Gynecological Cancers	November 3, 2023	**LinkedIn:** https://www.linkedin.com/in/jo%C3%A3o-mouta-60050a57/ **Mail:** joao.mouta@roche.com
40	Universidade Nova de Lisboa (Lisbon New University)	Rui Manuel Silva	Innovation, Knowledge Valorisation, and Intellectual Property Officer	November 8, 2023	**LinkedIn:** https://www.linkedin.com/in/ruimrsilva/ **Mail:** rui.silva@unl.pt
41	University College Dublin (UCD)	Ciaran O'Beirne	Manager, Knowledge Transfer	November 16, 2023	**LinkedIn:** https://www.linkedin.com/in/ciaran-o-beirne-52b42141/ **Email**: ciaran.obeirne@ucd.ie
42	Victorian Cancer Biobank / ISBER	Wayne Ng	Director at Large	October 25, 2023	**LinkedIn:** https://www.linkedin.com/in/wayne-ng-844654a8/?originalSubdomain=au **Mail:**

					Wayne.Ng@cancervic.org.au
43	Virtuleap/ VectorB2B	Bebiana Moura	Head of Partnerships	October 18, 2023	**LinkedIn:** https://www.linkedin.com/in/bebiana-moura/?originalSubdomain=pt **Mail:** bebianamoura@gmail.com
44	Vlaams Instituut voor Biotechnologie (VIB)	Erwin Sablon	Head of Business Development	October 19, 2023	**LinkedIn:** https://www.linkedin.com/in/erwin-sablon-27b4115/ **Mail:** erwin.sablon@vib.be
45	Vlaams Instituut voor Biotechnologie (VIB)	Sofie Coleus	Business Development Manager	November 16, 2023	**LinkedIn:** https://www.linkedin.com/in/sofie-coelus-7476a628/ **Mail:** sofie.coelus@vib.be

Appendix 14: Combined Biobanking Model Recommendation

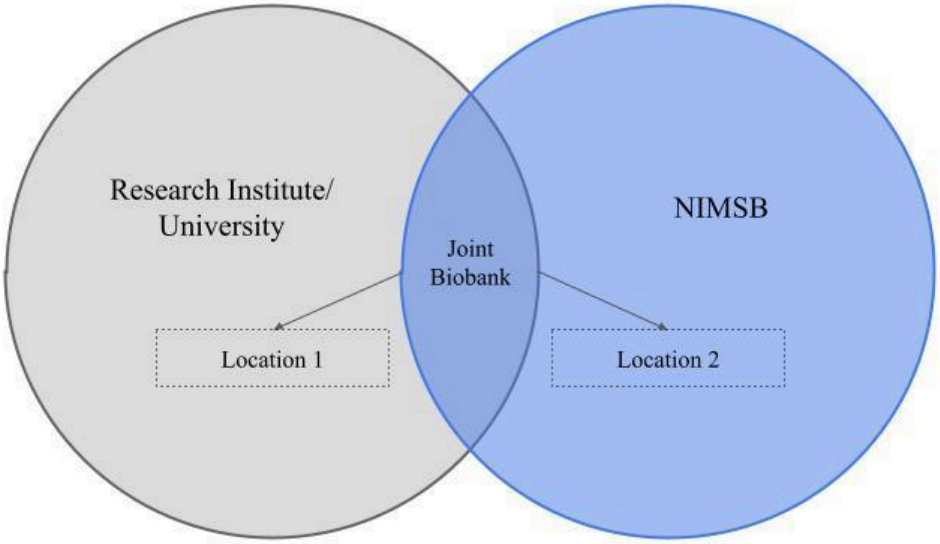

Figure 6: Combined Biobanking Model for the NIMSB

Appendix 15: The Drug Development Process

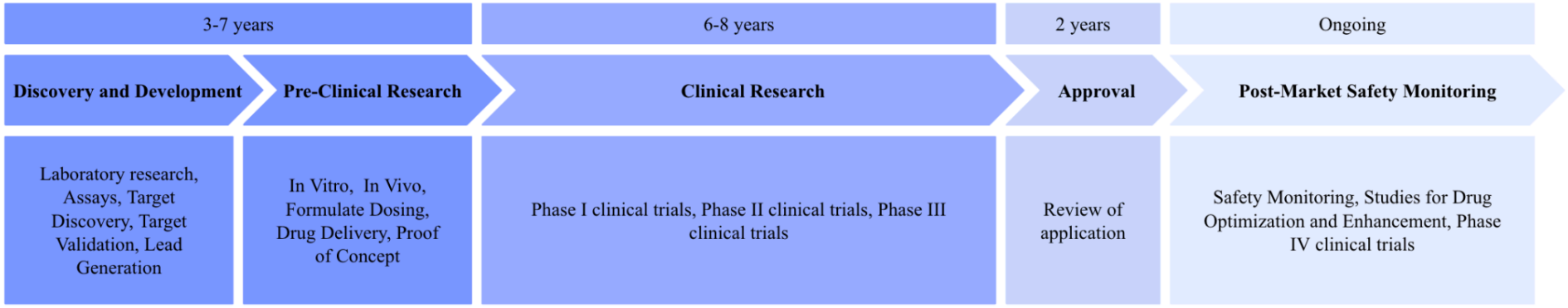

Figure 7: The Drug Development Process

Appendix 16: The Clinical Trial Phases

Table 2. *Detailed Description of the Clinical Trial Phases*

Phase	Description
Phase 0 (exploratory)	- Investigates significantly lower drug concentrations (1/100th of standard dosing), known as micro-dosing, over a shorter duration - Aims to study pharmacokinetics and establish appropriate dosing levels for Phase I trials - Historically conducted in animal models, but currently shifting towards human-based studies - Microdosing studies: previously done in animals but now in human volunteers to understand dose tolerability before being administered as a part of the phase I trial
Phase I (non-therapeutic phase)	- Recruits approximately <50 healthy subjects - Establishes safe dose range and Maximum Tolerated Dose (MTD) - Focuses on pharmacokinetics and pharmacodynamics - Typically single-center studies - **Phase Ia** includes Single Ascending Dose (SAD) studies, with durations ranging from one week to several months, involving 6-8 groups of 3-6 participants each - **Phase Ib** involves Multiple Ascending Dose (MAD) studies, with dose refinement across three groups of 8 individuals each
Phase II (exploratory)	- Enrolls around 5-100 patients of either sex - Evaluates effective dosage and therapeutic effects on patients - Determines therapeutic regimen and potential drug-drug interactions - Usually conducted as multicenter studies - **Phase IIa** focuses on deciding drug dosage, involves 20-30 patients, and lasts weeks to months - **Phase IIb** examines dose-response relationships, drug-drug interactions, and includes a placebo comparison
Phase III (therapeutic confirmatory)	- Involves more than 300 to 3000 patients of either sex, in multicentric trials - Pre-marketing phase to assess drug efficacy and safety - Compares test drug with placebo or standard medication - Notes any adverse drug reactions/events - Begins the process for New Drug Application (NDA) with regulatory bodies like the FDA.
Phase IV (post-approval /marketing surveillance)	- Conducted post-approval/licensure and for post-marketing surveillance - Involves long-term patient follow-up to monitor potential adverse reactions and drug-drug interactions

Source: (Kandi and Vadakedath 2023)

Appendix 17: Real-World Data and Real-World Evidence

The global RWE solutions market, valued at USD 2.6 billion in 2023, is expected to witness a CAGR of 8.4 percent from 2024 to 2030. Factors influencing this growth include regulatory support for RWE solutions, increased R&D investment, and the transition from volume-based to value-based healthcare models (Grand View Research 2022b). RWE, derived from real-world data (RWD) outside of traditional clinical trials, is increasingly enriching clinical research. By leveraging data sources like electronic health records and patient registries, RWE is revolutionizing clinical trial design. This wealth of data not only improves recruitment strategies by identifying patient cohorts likely to adhere to study protocols but also helps in reducing study variability by excluding groups less likely to benefit from the intervention. It enables researchers to categorize patients, better track the disease, and assess the efficacy of the treatment. RWE represents a significant advancement over traditional methods by bridging the gap between controlled research environments and the complexity of the real world (Baumfeld Andre et al. 2020, 1201-12; Swift et al. 2018, 450-60; Viedoc Technologies 2023).

However, accessing RWD in clinical trials presents significant challenges. Key issues include the fragmentation of data across different sources, complicating the identification of high-quality data, and the process of de-identifying patient data for privacy, alongside the necessity to clean and enrich different data components (Miseta 2022). Mouta expects that analyzing RWD through AI will be the most groundbreaking application in clinical research in the next decade, which in turn addresses the challenges of handling RWD and represents a potential opportunity for the NIMSB to establish its presence in the AI segment.

Appendix 18: Decentralized Clinical Trials

The global market for DCT was valued at approximately USD 4.48 billion in 2022 and is projected to grow at a CAGR of 15.42 percent, reaching around USD 10.58 billion by 2028 (Market Research Guru 2023). DCTs are transforming the clinical trials paradigm, moving from conventional methods to a model that utilizes innovative digital health technologies. This evolution facilitates the expansion of clinical trial activities beyond traditional settings, reaching directly into participants' homes and local healthcare facilities. Integrating digital health technologies, s.a. telemedicine, electronic data capture systems, and mobile health devices, enables real-time health data collection. This shift broadens participant access, promoting inclusivity and diversity in clinical research (Cohadzic 2023; Food and Drug Administration 2023a).

However, the shift to DCTs also brings key challenges, incl. concerns over investigator oversight and ensuring participant safety in remote settings when physical examinations and face-to-face contact are limited (De Jong et al. 2022, 344-52). Concentrating on AI offers NIMSB a strategic avenue to enhance patient safety monitoring and guarantee the integrity of remote data collection, thus effectively addressing these challenges.

Appendix 19: Translational Research

Translational Research (TR) is a complex and structured process aimed at moving scientific discoveries from researchers´ benches to patient´s bedsides, with the goal of improving the health and well-being of individuals and populations. TR has a dynamic bidirectional characteristic, as it not only converts basic research into clinical practice but also simultaneously integrates clinical observations into laboratory investigations for additional exploration. The exact definition varies slightly among academic and clinical institutions but is generally described as a connection between basic and clinical research following a two-step process. Firstly, it involves the translation of basic research into clinical trials. The initial phase begins with basic scientific research, involving preclinical and animal studies to establish mechanisms, targets, and lead molecules. Following that, the translation to humans occurs, specifically in the proof of concept phase I clinical trials, when new approaches to diagnosis, treatment, and prevention are evaluated. Finally, the translation to patients occurs through Phase II and III clinical trials, which are rigorous evaluations that result in the implementation of effective treatment. Secondly, TR aims to apply the results obtained from clinical trials in the clinical setting and in health-related decision-making processes. The second step involves the translation into practice. Phase IV clinical trials and clinical outcomes research are essential in this context. The goal is to provide appropriate and timely medical care to the right patient. Subsequently, it will be translated into the community via population-level outcomes research. This will guarantee a real benefit to society (UAMS Translational Research Institute, n.d.).

Appendix 20: Roadmap for Clinical Trial Contribution

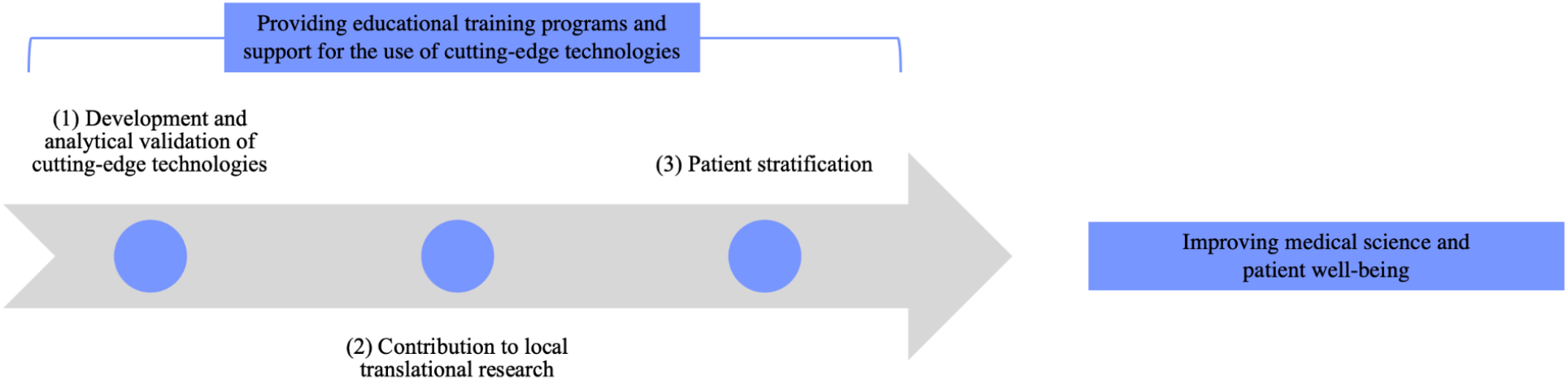

Figure 8: Key milestones of Clinical Trial Contribution

Appendix 21: Technology Readiness Level

Table 3. *Description of the Different Stages and Technology Readiness Levels for Artificial intelligence, Big Data Analysis, IoT's, software development & Bioinformatics.*

Stage	Technology Readiness Level	Definition
Ideation	TRL-1	- Need identified, - Development of basic use, basic properties of software architecture, Mathematical formulations, and general algorithms.
Proof of Principle	TRL-2	- Research ideas developed - Technology concept or application formulated. - To carry out analytics studies and coding starts & comparing competing technologies
Proof of concept demonstrated	TRL-3	- Concept/Pre-alpha script is ready and working draft is created.
Proof of concept established	TRL-4	- Development of limited functionality environments to validate critical properties and analytical predictions using nonintegrated software components and partially representative data - Laboratory results showing validation of critical properties.
Early stage validation	TRL-5	- Developed Software technologies to integrate with different aspects of the existing system - Developed Software technologies implementations conform to target environment/interfaces. Experiments with realistic problems - Rigorous alpha testing
	TRL-6	- Feasibility of the software technology is demonstrated on full-scale realistic problems - Technology validation in a relevant end-to-end environment. - Rigorous Beta testing
Late stage Validation	TRL-7	- Rigorous testing & validation by third parties
Pre-commercialization	TRL-8	- ISO/IEC 9126 software quality as per the international standards - Data Privacy & Protection as per international standards (may be complied as per HIPAA Norms) - Launch of the software
Commercialization and post-market studies	TRL-9	- Continuous improvement (New versions) as per user demand and feedbacks. - Continuous incorporation of new features as per user demand and feedback.

Source: Biotechnology Industry Research Assistance Council (BIRAC)

Appendix 26: Events and Conferences

Building and maintaining relationships with industry partners, without doubt, comes with a lot of presence and conversations stemming from events hosted by other parties and, in the best case, by the NIMSB itself. As highlighted in section A, events are one driver of becoming a place of fostering exchange and technology transfer in an innovative and inspiring research environment.

Moreover, some conferences should be attended by the responsible teams within the NIMSB that will allow for relevant industrial interaction. Conferences that were considered relevant for the NIMSB and its research by nearly all interview partners were the Bio conferences held in many locations globally.

Appendix 27: Outlook and Practical Recommendations for Forging Ties with Industry

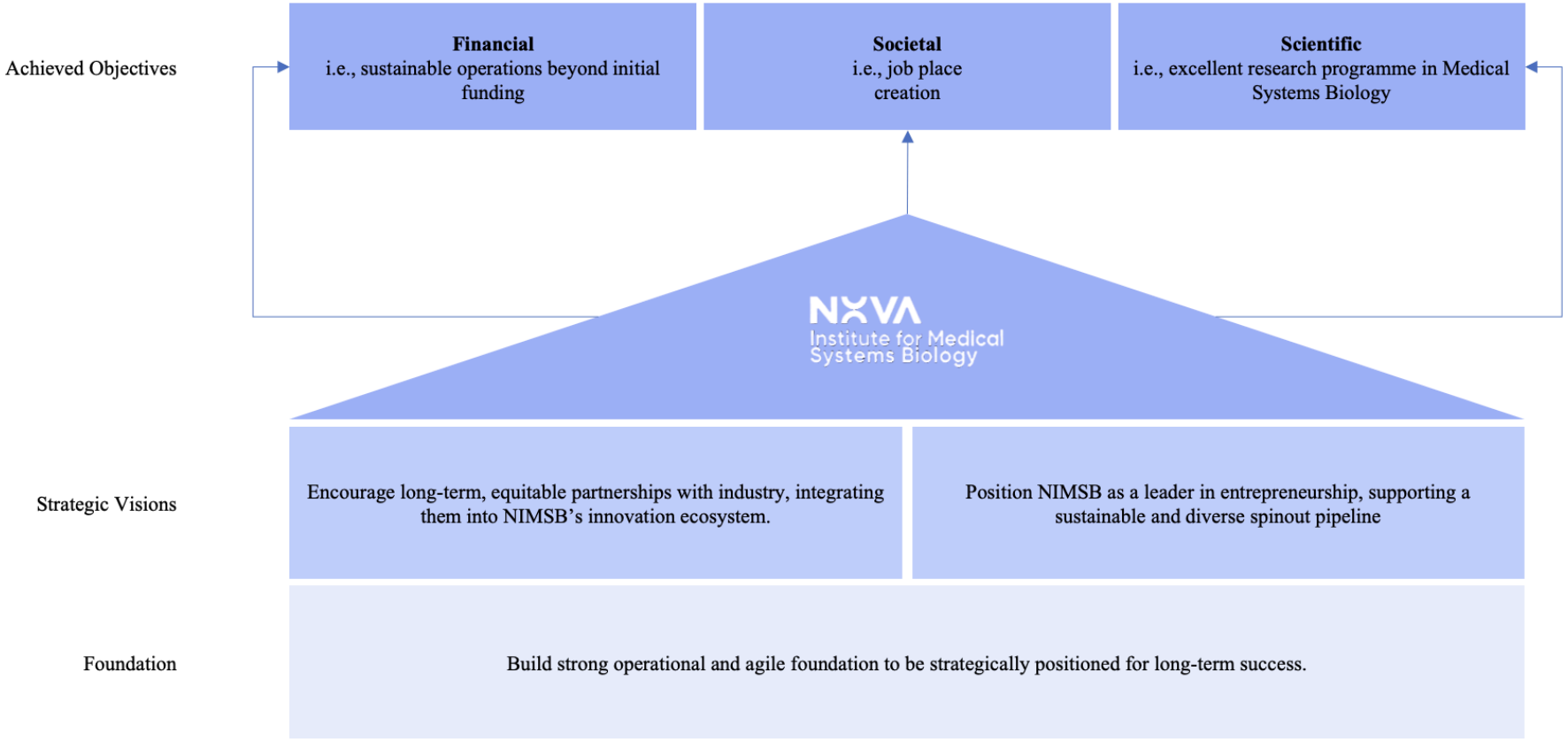

Figure 9: Illustration of the Outlook and Practical Recommendation for Forging Ties with Industry

Appendix 28: The House of NIMSB

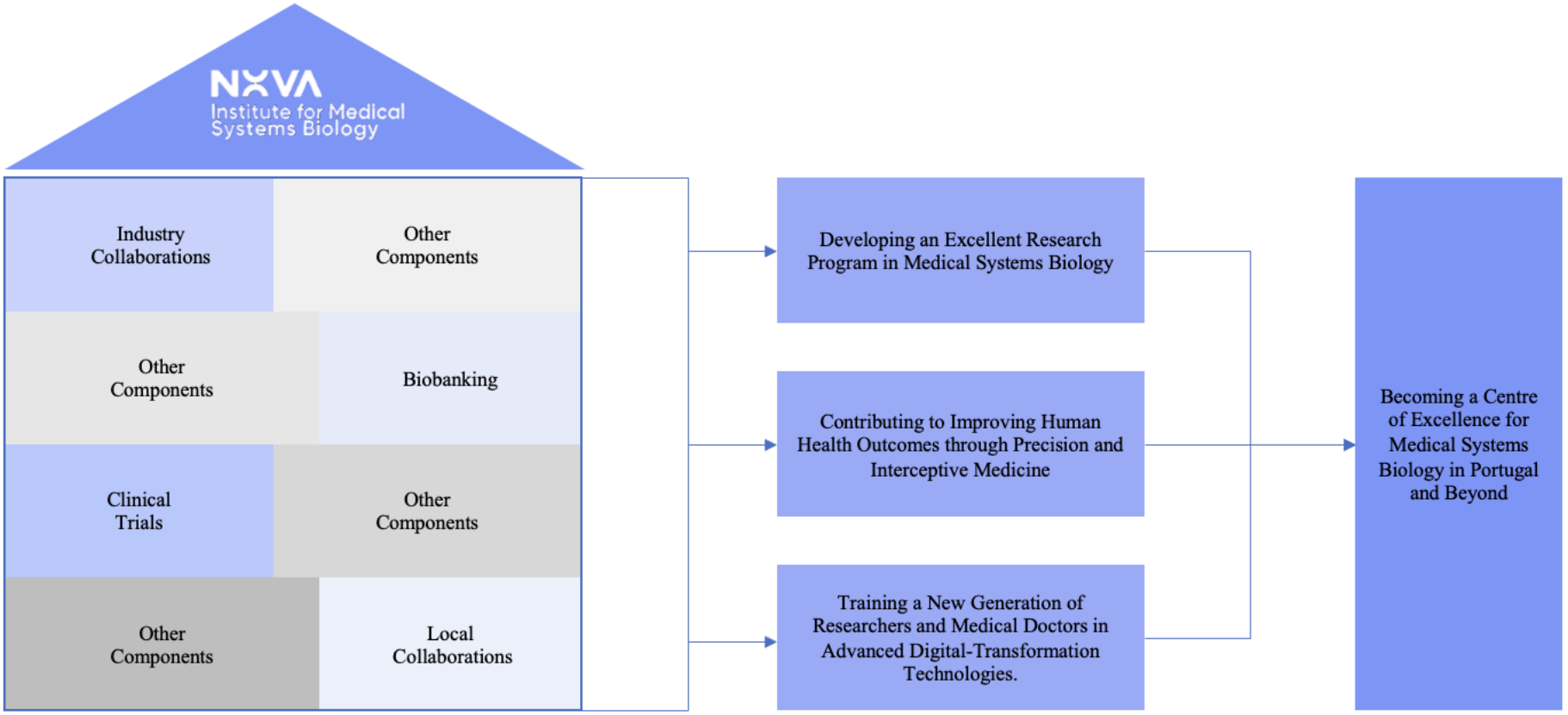

Figure 10: Illustration of The Cohesive Force of The Different Building Blocks of NIMSB House