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**GBi5S: Ein auf Flüssigbiopsie basierender Biomarker zur  
Unterstützung der Frühdiagnose von Krebs und Immundefekten  
(SWIBRID)**

„Das diesem Bericht zugrundeliegende Vorhaben wurde  
mit Mitteln des Bundesministeriums für Forschung,  
Technologie und Raumfahrt unter dem  
Förderkennzeichen SWIBRID gefördert. Die  
Verantwortung für den Inhalt dieser Veröffentlichung liegt  
bei der Autorin.“

**Forschungsvorhaben:** XXXXX | **Projektleitung:** Clara Vázquez García, Ph.D.

**GBi5S:** Ein auf Flüssigbiopsie basierender Biomarker zur Unterstützung der Frühdiagnose von Krebs und Immundefekten (SWIBRID)

## **Teil I - Kurzbericht**

### **Ursprüngliche Aufgaben zu Beginn des Projekts:**

Der Antrag für die Go-Bio Initiale Sondierungsphase 5 (GBi5S) sah die folgenden Meilensteine vor, die im Rahmen des Projekts erreicht werden sollten:

- Meilenstein 1: Durchführung einer Freedom-to-Operate-(FTO)-Analyse
- Meilenstein 2: Identifikation der dringendsten medizinischen Anwendung
- Meilenstein 3: Aufbau einer Strategie für den zukünftigen regulatorischen Weg
- Meilenstein 4: Erstellung eines Entwurfs der Investigator's Brochure
- Meilenstein 5: Erwerb von Business-Erfahrung und Soft Skills für die nächsten Schritte der Start-up-Entwicklung

### **Ablauf des Vorhabens:**

Meilenstein 1 wurde durch die Beauftragung einer FTO-Analyse bei Kroher & Strobel erreicht, der Patentanwaltskanzlei, die für das Patent unserer Technologie verantwortlich ist.

Die Identifikation der dringendsten medizinischen Anwendung (Meilenstein 2) erfolgte durch vier zentrale Aufgaben: i) Durchführung einer Marktanalyse durch Ascenion zu drei unterschiedlichen medizinischen Bedarfen, ii) Analyse der regulatorischen Anforderungen für jede dieser medizinischen Anwendungen gemeinsam mit der CSG mbH, iii) Validierung des identifizierten medizinischen Bedarfs durch Patientenbefragungen und Interviews mit Klinikern sowie iv) Analyse von Proben der dringendsten medizinischen Anwendung.

Die Grundlagen einer regulatorischen Strategie (Meilenstein 3) wurden durch die Beauftragung der Beratungsunternehmen CSG mbH und LSCN GmbH erarbeitet.

Meilenstein 4 wurde durch die Beschaffung der ersten Dokumente erreicht, die für die Erstellung der Investigator's Brochure im Rahmen der CE-Zertifizierung erforderlich sind.

Schließlich wurde Meilenstein 5 durch die Teilnahme an zwei Kursen der IPI Academy sowie durch die Teilnahme an translationalen Veranstaltungen wie der BIONNALE 2025, Nucleate-Events und dem Berlin Bio Innovation Day erreicht.

### **Die wesentlichen Ergebnisse sowie ggf. die Zusammenarbeit mit anderen Forschungseinrichtungen:**

Im Rahmen von Meilenstein 1 zeigte die von Kroher & Strobel durchgeführte FTO-Analyse, dass die Kerntechnologie von SWIBRID (Patentanmeldung WO2024194255A1) keine bestehenden Schutzrechte verletzt. Dies gilt sowohl für die Laborpipeline als auch für die Identifikation von DNA-Reparaturdefekten mittels B-Zellen. Auch eine Kollision mit Schutzrechten von Myriad Genetics, einem führenden Anbieter im Bereich der Krebsrisikobewertung, wurde ausgeschlossen. Potenzielle Einschränkungen durch noch nicht erteilte Patentanmeldungen wurden identifiziert, deren Relevanz jedoch als begrenzt eingeschätzt wird.

Im Rahmen von Meilenstein 2 identifizierten wir die „Identifikation der Anfälligkeit für Gürtelrose (Herpes Zoster)“ als eine der dringendsten medizinischen Anwendungen mit hohem Marktpotenzial. In der von Ascenion durchgeführten vorläufigen Marktanalyse auf Basis der Literatur wurde zunächst die „Identifikation von Immundefizienzen“ als Indikation mit dem größten Markt identifiziert. Die Beratungen mit der CSG mbH zu regulatorischen und Erstattungsstrategien führten jedoch zur Auswahl von „Gürtelrose“ als initiale Indikation für SWIBRID. Ausschlaggebend war, dass es sich hierbei um die einzige Indikation mit einer unmittelbaren Handlungsmöglichkeit (Impfung nach Diagnostik) und einem vergleichsweise kurzen regulatorischen Weg handelt. Entsprechend wurden Interviews mit Klinikern sowie Patientenbefragungen durchgeführt, um den hohen medizinischen Bedarf und die Akzeptanz dieser Indikation zu belegen. In den Interviews mit den Klinikern Dr. Baumgarten, Dr. Grunwald, Dr. Lais und Dr. Schultheiß vom ZFI – Zentrum für Infektiologie in Berlin zeigte sich, dass sie diese Indikation als sehr vielversprechend einschätzen, da sie regelmäßig Patienten mit Interesse an ihrer individuellen Infektanfälligkeit betreuen. Zudem ergaben 70 Patientenbefragungen, dass 60,3 % ein hohes Interesse am Thema Impfdringlichkeit haben und 22,4 % bereit wären, einen solchen Test selbst zu bezahlen, insbesondere um unnötige Impfungen zu vermeiden (45,7 %). Diese Ergebnisse waren entscheidend für die Identifikation potenzieller Kunden, die Vorbereitung der Marketingstrategie sowie den Nachweis der Akzeptanz bei Nutzern und Kunden für die gewählte Indikation.

Im Rahmen von Meilenstein 3 wurde die Geschäftsstrategie unter Berücksichtigung der regulatorischen Beratung durch die CSG mbH und der finanziellen Beratung durch die LSCN GmbH entwickelt. Die regulatorischen Aspekte der diagnostischen CE-Zertifizierung lieferten wichtige Einblicke für die Planung der nächsten Schritte. In diesem Zusammenhang nahmen wir Kontakt mit der benannten Stelle TÜV Rheinland auf und sammelten Informationen zu spezifischen ISO-Anforderungen, die für die Durchführung der Experimente zur klinischen und analytischen Validierung erforderlich sind. Die LSCN GmbH beriet uns beim Aufbau eines Businessplans und stellte Werkzeuge zur Strukturierung eines Pitch Decks mit dem Ziel der Kapitalakquise zur Verfügung.

Im Rahmen von Meilenstein 4 stellten die regulatorischen Beratungen mit der CSG mbH die ersten für die CE-Zertifizierung des diagnostischen Tests erforderlichen Dokumente (Investigator's Brochure) bereit. Dazu zählen: ein Dokumentenpaket für die Produktentwicklung, ein Dokumentenpaket für die Softwareentwicklung sowie ein Dokumentenpaket für die Leistungsbewertung. Diese Dokumente enthalten grundlegende Informationen, mit deren Erfüllung bereits begonnen wurde.

Schließlich führte Meilenstein 5 zur Entwicklung von Soft Skills, die im Prozess des Venture Building genutzt werden können. Ich nahm am Kurs „Reviewing and Negotiating Technology Transfer and Licensing Agreements“ teil, in dem wir die EU-Wettbewerbsgesetze und -richtlinien kennenlernten und ein praxisnahes Training zur Verhandlung von Lizenzverträgen erhielten. Zudem absolvierte ich den Kurs „MBA Strategic Thinking for Pharma and Biopharma Professionals“, in dem ich strategisches Projektmanagement in pharmazeutischen Unternehmen erlernte, unter anderem durch Wettbewerbsanalysen, die Analyse realer Unternehmenssanierungen sowie Kulturveränderungen zur Verbesserung des Unternehmensmanagements.

Zusammenfassend hat uns die GBi5S dabei geholfen, einen ersten Markteintritt für unser Diagnostiktool zu definieren und mich gezielt auf die für die Ausgründung erforderlichen Soft Skills vorzubereiten.

**GBi5S:** Ein auf Flüssigbiopsie basierender Biomarker zur Unterstützung der Frühdiagnose von Krebs und Immundefekten (SWIBRID)

## **Teil II: Detailed description**

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### **1.- Most important items of the numerical evidence:**

The main cost items comprised external consulting services for:

- IP: FTO analysis
- Market analysis: Preliminary market assessment, interviews to clinicians and polls to patients.
- Business strategy analysis with respect to our potential venture
- Regulatory: workshops about in-vitro diagnostic (IVD) regulatory requirements with an additional perspective on the reimbursement institutions as well as, the obtention of the initial documents for a draft of the investigator's brochure.
- Training: Reviewing and Negotiating Technology Transfer and Licensing Agreements & MBA Strategic Thinking for Pharma and Biopharma Professionals

Details are provided in the "zahlenmäßiger Nachweis".

### **2.- Necessity and appropriateness of the GBi5S project: SWIBRID**

The Go-Bio Initial Sondierungsphase 5 (GBi5S) application was granted to develop the diagnostic test called SWIBRID in a commercial way. At the beginning of the grant, the technology had a patent application, the method was completed and the analysis of immunodeficient samples was ongoing. Clara Vázquez García, Ph.D. (CVG) started her entrepreneurial career at the start of this grant. Thus, the GBi5S was needed to identify the most pressing medical need for the technology and to allow CVG gaining soft skills for the near future.

As part of the GBi5S we had a set of work packages necessary for the completion of the project:

- Work package 1: Freedom-to-operate (FTO) analysis
- Work package 2: Market analysis
- Work package 3: Identification of the most pressing medical need
- Work package 4: Workshop in in-vitro diagnostics (IVD) regulation requirements
- Work package 5: Gap analysis draft
- Work package 6: Soft skills training

The work package 1 consisted in performing an FTO analysis. This was necessary to mitigate the risk before commercialising the patent application of the technology. An FTO analysis identifies if the commercialization of our technology infringes active patents, or patent applications submitted before ours. Results of an FTO analysis can indicate use cases, methodologies or even material of our technology that we cannot use when commercialising

it, allowing us to adjust the technology without infringing other intellectual property (IP). An FTO analysis protects our ability to use our technology.

The work package 2 was to perform a market analysis. This was necessary to find a use case that is relevant and worth investing in, beyond being scientifically interesting. CVG as a scientist needed a market's view on the most interesting scientific use cases. The market analysis would validate the real unmet medical need, confirming that the problem exists and that the current solutions are insufficient. This exploration would differentiate the use cases where there is an existent market and the ones where the market needs to be created, which is a more complicated scenario. Assessment of the market potential would show the market size and growth, the willingness to pay and the reimbursement or purchasing pathways. In the context of market analysis, we opted to approach it in different levels. The first one was to perform a preliminary market assessment and the second, which came later, was to perform a set of interviews to clinicians and patients on the selected indication. The different approaches were necessary to start working with the preliminary market assessment to get a brief idea of the use cases and the second at the end, to question the potential clients and users about the selected use case.

Work package 3 was to identify the most pressing medical need for our diagnostic tool. This process was necessary to obtain a clear idea of in which direction we would need to pivot the technology. Identification of a medical need for a versatile tool is mandatory to focus the work towards one main idea that aligns with the market, regulatory and science. This work package did not have a unique work to be done, but several that will be discussed below.

The work package 4, exploration of IVD regulation requirements, was needed to define the clauses in which our diagnostic assay could legally reach the market. There are aspects that can change the commercial development of the IVD, for example, the class, which dictates the clinical evidence requirements and timelines. The necessity of this also lies in the generation of a credible IVD regulation pathway for potential stakeholders.

On the same lines, work package 5 was focused on identifying gaps of documents, information and knowledge to develop an investigator's brochure. IVD development can start from the moment the method is done. There are a set of documents that we can start doing and we needed to identify them. Therefore, we needed to perform a gap analysis.

Last, work package 6 was focused on the training of CVG's soft skills on entrepreneurship matters. This was necessary because the education and career of CVG have been focused on the academic career and back then, she was starting to shift towards translation. Soft skills such as business strategic management or negotiation skills, can make a positive difference at the time of talking to future stakeholders.

The funds were spent in accordance with the project plan. € XXX.XX was spent on materials. The expenditure for travel costs amounted to € XXX,XX. Other costs, including third party services and courses amounted to € XX,XXX. In addition, administrative costs of € XXX.XX were claimed.

All work packages were designed and carried out in an appropriate step-wise approach, in which the outcomes of each work package informed and guided the subsequent steps. The objectives were well defined and realistic within the scope of the grant and were fully achieved. The services required for specific work packages were outsourced to companies with outstanding expertise in the respective subject areas. Overall, the project design, resource allocation, and choice of external partners were well aligned with the project objectives and ensured efficient and goal-oriented implementation.

### **3.- Description of the work outcomes and expected benefits:**

The GBi5S project comprised several work packages, the outcomes of which have already provided benefits and are expected to continue doing so in the near future.

The performance of the **FTO analysis (WP1)** was highly important to reduce the risk of infringing previously filed intellectual property (IP). The analysis focused on (i) potential infringements related to the technological pipeline, (ii) existing IP concerning the diagnosis of DNA repair deficiencies and cancer, and (iii) IP owned by Myriad Genetics, a company with a broad portfolio in cancer risk diagnostics. No IP infringement was identified for SWIBRID's laboratory pipeline, the prediction of DNA repair deficiencies using B cells, or the patents owned by Myriad Genetics. Potential and partial IP risks were identified only in relation to not-yet-granted patent applications in the field of cancer diagnostics. In conclusion, there is no immediate threat to the freedom to operate of SWIBRID. We will regularly monitor the above-mentioned patent applications that are still in examination procedures and avoid IP infringement by adapting the SWIBRID technology if necessary.

This analysis increases our legal certainty for its commercialization, and made sure that our laboratory pipeline does not infringe any IP. In the future, we will use the obtained results to perform an extra FTO analysis on specific use cases and will follow up some patent applications with wide claims that could limit our freedom to operate if granted. The FTO analysis was crucial to evaluate the feasibility and attractiveness of developing a commercial pipeline for SWIBRID.

One of our biggest work packages that involved the performance of other was to identify the **most pressing medical need for our diagnostic tool SWIBRID (WP3)**. SWIBRID can identify immune and DNA repair defects as a consequence of antibody diversification. The tool analyses the phenotypical consequences of these defects directly at the DNA level in the antibody gene in B cells. This makes it possible to identify defects by signs of the defect. This tool has the potential to serve as a diagnostic for several diseases: primary immunodeficiency, DNA repair defect-related cancers, specific infection susceptibility, radiation intolerance or wound healing efficiency. In order to develop the tool that would sell best as an initial market, we needed to identify the most pressing medical need and avoid spiralling around different indications as a consequence of the versatility of the product.

The performance of a **market analysis (WP2)** was performed by Ascenion GmbH for early, medium and long SWIBRID indications; being identification of shingles susceptibility, diagnosis of PID and colorectal cancer companion diagnostic, respectively. Regarding our shingles susceptibility as our first indication for market access, the estimated accumulated market potential is 787,261,080 EUR. Also, they found no tests in the market or in active development that assesses the risk of shingles development, so SWIBRID would be considered a "first mover".

Then, included in the understanding of **IVD regulation requirements (WP4)** we learned that our strategy should also consider the steps into CE-certification, the acceptance for reimbursement by the statutory (GKV) and private (PKV) health insurance, and the payment by self-payers (Selbstzahler) or hospitals via the inpatient care Diagnosis-Related Groups (DRG) system. Under these circumstances, we decided to focus on an indication where SWIBRID diagnosis will trigger an immediate clinical action, expecting to accelerate the clinical validation process required by the CE-certification and boost appeal to doctors, users, and insurance companies. Consistent with this approach, we selected the identification of susceptibility to infections for diseases with available reimbursed vaccines. Specifically, the identification of shingles susceptibility.



the analysis of use cases of SWIBRID, since they provided an idea and pipeline on how a use case should be thought and sold.

Developing new soft skills (WP6) was a very important step to take during the course of the GBi5S. The practical use of the courses that CVG attended on i) negotiation skills and ii) the strategies used by pharmaceutical companies to succeed is both immediate and long term. CVG was able to put in practice some of the strategist skills to build up pitch deck in pitch competitions. Also, negotiations skills were used during preliminary negotiations on future shares of the spin-off. However, this will become more relevant in the near future upon exclusive licensing negotiations.

In the course of the GBi5S, the strategic focus on “shingles susceptibility” as the initial market entry and the development of a business strategy for competitive pitching facilitated the establishment of new collaborations and contacts:

- Medical University of Hannover (MHH): We started collaborating the Prof. XXXXX Werfel to test the ability of SWIBRID to identify shingles susceptibility using their 250 patient RESIST ZOSTER cohort
- Charité – Cardiovascular Department: We started a collaboration with Dr. XXXXX XXXXXX to follow his lead on identifying left heart disease using an immunological biomarker like SWIBRID
- We got selected to take part on the Nucleate Activator Cohort 2026 to improve on the assets necessary for spinning-off and increase our network

#### **4.- Relevant external developments during the course of the GBi5S:**

During GBi5S, notable advances in immune fitness assessment were observed in both academic and industrial contexts. Academic progress was directly related to the immune system, while industrial developments were more indirectly linked; nonetheless, they are worth highlighting. There are two important academic publications to highlight:

- Short after the GBi5S ended, a very relevant article was published in Nature: “*Multi-omic profiling reveals age-related immune dynamics in healthy adults*”. They performed a longitudinal analysis on 300 healthy individuals from ages ranging 25-290 years old. They performed single-cell RNA-seq and found that there is an age-related reprogramming in T cell subsets that make vaccine booster less efficient due to a dysregulation of B cells. This method is very powerful, since they can find and link set of biomarkers to this finding, potentially relating individual vaccine responsiveness to biomarker analysis (<https://www.nature.com/articles/s41586-025-09686-5>).

- A new method with diagnostic potential for the identification of immune status was published. They created the “Machine Learning for Immunological Diagnosis (Mal-ID)” by using the repertoire composition of B cell and T cell receptors. With it, they were able to identify diseases like lupus with a 95% of accuracy (<https://www.science.org/doi/10.1126/science.adp2407>).

On the industrial side, two startups are directly or indirectly advancing on the immunological status diagnosis:

- The startup Inflammatrix receives FDA clearance for first-in-class TriVerity™ Test (<https://inflammatrix.com/inflammatrix-receives-fda-clearance-for-first-in-class-triverity-test/>). The TriVerity™ Test is a diagnostic tool that uses whole blood to help triage by indicating if an individual is suffering from a bacterial or viral infection and its degree of severity. This diagnostic is fast and reliably acting on the immune response on an individual. While the diagnostic is not preventive it is actionable.

- Quantune Technologies GmbH was awarded with an EIC-Pathfinder grant, which is still running, on the development of a wearable mid-infrared spectrometer measuring blood parameters involved in the metabolic state (MiWear). The metabolic state of an individual is tightly related to the immune fitness; therefore, we consider this technology as a potential tool to be assess indirectly immune fitness in the future. <https://cordis.europa.eu/project/id/101115476/reporting> - <https://doi.org/10.3030/101115476>.

Last, it is worth highlighting that Europe has launched flagship initiatives to enable countries to build national whole-genome reference cohorts and the associated infrastructures. For example, as part of France's national strategy, the French Genomic Medicine Initiative (PFMG2025; <https://pfmq2025.fr/en/>) was launched in 2025. This program focuses on rare diseases and cancer predisposition and includes large-scale genome sequencing, development of capacity to manage big datasets, and integration of genomic data into patient care through comprehensive disease exploration. These initiatives are highly beneficial for the field of genomic diagnostics, as they establish public infrastructure for genomic analysis and make genomic diagnosis a standard component of the healthcare system.

While these advances can aid in identifying immunodeficiencies and infection susceptibility, SWIBRID represents a complementary and accessible approach, particularly due to its PCR-based methodology and adaptability to specific clinical questions. Like the other academic advances mentioned, SWIBRID is highly versatile and can be tailored to specific medical needs, allowing it to occupy a distinct niche among existing methods.

#### **5.- Publication of results of the GBi5S:**

During the GBi5S project, preliminary results related to shingles susceptibility were generated. However, these results are exploratory and preliminary in nature, therefore currently we do not have sufficient data for a standalone scientific publication. At this stage, the dissemination activities during the funding period were limited to non-public presentations and pitch decks prepared for funding and innovation competitions. No public disclosure of projects was made in order to safeguard intellectual property and future commercialization.