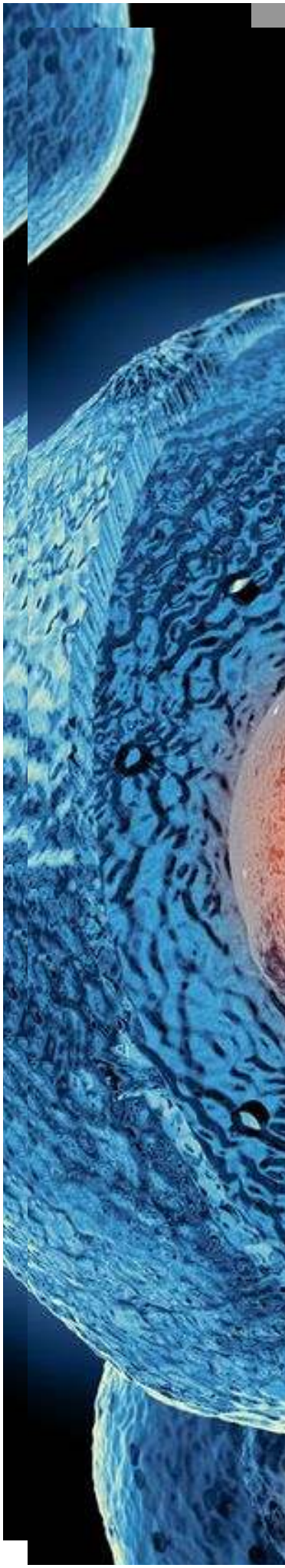
REGMEDXB
FROM CARE TO CURE

Annual Report 2023

Index



CEO's Foreword

Dear reader,

2023 was a transformative year for RegMed XB as we navigated significant milestones in our mission to advance regenerative medicine.

With the successful conclusion of various research programs, Moonshot roadmaps have set the stage for new and ambitious endeavors. Securing necessary funding to support ongoing and future research projects will be pivotal. Our infrastructure expansion, through the RegMed XB Pilot Factory, is driving innovation and collaboration. Despite challenges, we made strides in business development, with new spin-offs and the continued success of the F1RST Fund.

Without the continuous support of our academic partners, industrial participants, health foundations, Health~Holland, and local, regional, and national governments, we could not have achieved what we have today.

As we strengthen our international partnerships and broaden our impact, I am confident that RegMed XB is well-positioned to lead in the regenerative medicine field. Together, we will continue to push the boundaries; together we make the impossible possible!

Bernard Mulder

CEO RegMed XB

Company overview

At RegMed XB, we are determined to change the future of healthcare. Our mission is clear: cure instead of care. We aim to improve the lives of people with chronic diseases through regenerative medicine (RM). To achieve this goal, we are committed to bringing affordable RM solutions to market and fostering a competitive and sustainable RM industry.

RegMed XB: Objectives and activities

The RegMed XB initiative is evolving into a sizeable, internationally leading translational research institute in the field of regenerative medicine. Its primary focus is on centralizing patients' interests, ensuring that their needs and benefits are at the forefront of its research and development efforts.

Ecosystem: regional collaboration
In the involved regions of Limburg, Noord-Brabant, Utrecht, Zuid-Holland, and Flanders (Belgium), RegMed XB's activities are organized in areas and disciplines that reflect the strengths of the regions and its excellence in musculoskeletal and cardiovascular Regenerative Medicine applications and in regenerating (part of) organs, particularly the kidney, eye and pancreas.

Economic contribution
RegMed XB contributes and will contribute towards the regional economies in terms of job creation, new companies and business for existing companies. RegMed XB is convinced that these economic objectives can very well be combined with improved affordability and availability of regenerative medicine solutions for patients and shortening research and development into applications for patients.

Pilot Factory
With RegMed XB's Pilot Factory, thanks to the grant of the National Growth Fund, access to manufacturing infrastructure for the production of RM solutions has become available in the coming years, helping to achieve the goals of RegMed XB: bringing RM solutions to patients at affordable cost and creating a new industrial sector in the participating regions.

Statutory aims of Foundation RegMed XB

- **combine resources of academic partners, business, provinces and health foundations, due to which researchers and entrepreneurs can perform fundamental, applied and translational research on regenerative medicine and as a result will contribute to affordable healthcare;**
- **provide services regarding project and programme management, including support, control and reporting;**
- **carrying out any further activities, which may be beneficial to all mentioned above, in the broadest sense;**
- **the Foundation explicitly does not seek to make profit and/or represent commercial interests.**

Organisational structure – governance

The governance model of RegMed XB is as follows: The Board of Directors consists of a Statutory General Director (GD), a Medical Scientific Director (MSD), a Director of Operations (DoO), a New Business Development Director (NBDD) and a Patient Advocate, reports to the Supervisory Board and is advised by a Scientific Advisory Board.

Board of directors

The Board of Directors, consisting of Bernard Mulder (GD), Frank Luyten (MSD), Erik Eijrond (DoO) and Marianne van der Steen (NBDD – until the end of August 2023), has been responsible for the daily operational management during the year 2023. Tom Oostrom holds the position of Patient Advocate as non-executive member or the Board of Directors. The Board of Directors is supported by a Funding & Finance Manager, two Project Managers, two Impact Officers, a Legal Counsel, a Communications Manager and a Management Assistant.

During 2023 the Supervisory Board and Scientific Advisory Board consisted of the following members:

Supervisory Board

Prof. dr. Louise Gunning-Schepers
(until May 1, 2023)

Prof. dr. Koenraad Debackere

Drs. Wim van der Meeren

Drs. Luc Keltjens

Dr. Rob van Leen

Jopie Nooren, MSc

Board of Directors

Bernard Mulder, MD, MBA
General Director

Prof. dr. Frank Luyten, MD, PhD
Medical Scientific Director

Erik Eijrond, MBA
Director of Business Operations

Prof. dr. Marianne van der Steen
New Business Development Director
(until September 1, 2023)

Drs. Tom Oostrom
Patient advocate

Scientific Advisory Board

Prof. dr. Clemens A. van Blitterswijk
University of Maastricht

Prof. dr. Katja Schenke-Layland
Eberhard Karls University

Prof. dr. Philippe Menasché
University of Paris Descartes

Prof. dr. René Bindels
Radboud Institute for Molecular Life Sciences

Prof. dr. Thierry Berney
University of Geneva

Prof. Dr. Alicia El Haj
University of Birmingham

Prof. Dr. Maurilio Sampaolesi
University of Leuven

System of Quality Control

RegMed XB's research is performed at the labs of the participating universities, university medical centers and within the participating companies using the local systems of quality control. Within the RegMed XB project control cycle, the progress of the research program (called "Moonshots") has been changed from a quarterly reporting schedule to a bi-annually reporting schedule. Meanwhile, the progress of the Moonshots was discussed in the Moonshot leadership team meetings and reported to the Scientific Advisory Board. Three times a year, the Scientific Advisory Board monitors and evaluates progress made in the Moonshots.

An International Scientific Advisory Board (ISAB) annually performs a peer review. The ISAB is organized per Moonshot and consists of members selected in close collaboration with the foundations participating in the respective Moonshot. The results of the peer reviews are discussed in a joint meeting of the Moonshot leaders and the Scientific Advisory Board and subsequently reported to the health foundations. The Scientific Advisory Board defines – based on ISAB outcomes – improvements within next years' programming.

Within the RegMed XB office, documentation of all major office processes has been drafted using standardized process protocols. These process protocols will continue to be improved in 2024.

Ambition and Strategy

Foundation RegMed XB aims to become an internationally leading translational research and valorization institute in the field of regenerative medicine focused on patients' needs with strong patient involvement in order to bring regenerative solutions to the market at affordable cost. Secondly, RegMed XB aims to establish a competitive and sustainable Regenerative Medicine industry in The Netherlands and Flanders.

To achieve its ambition, RegMed XB comprises a collaboration of strong regional institutes and bundles their forces with top international research groups. RegMed XB brings together multiple health foundations, top scientists, entrepreneurs and governments to cooperatively integrate research and valorization to shorten the time-to-patient and optimally translate research results into new businesses.

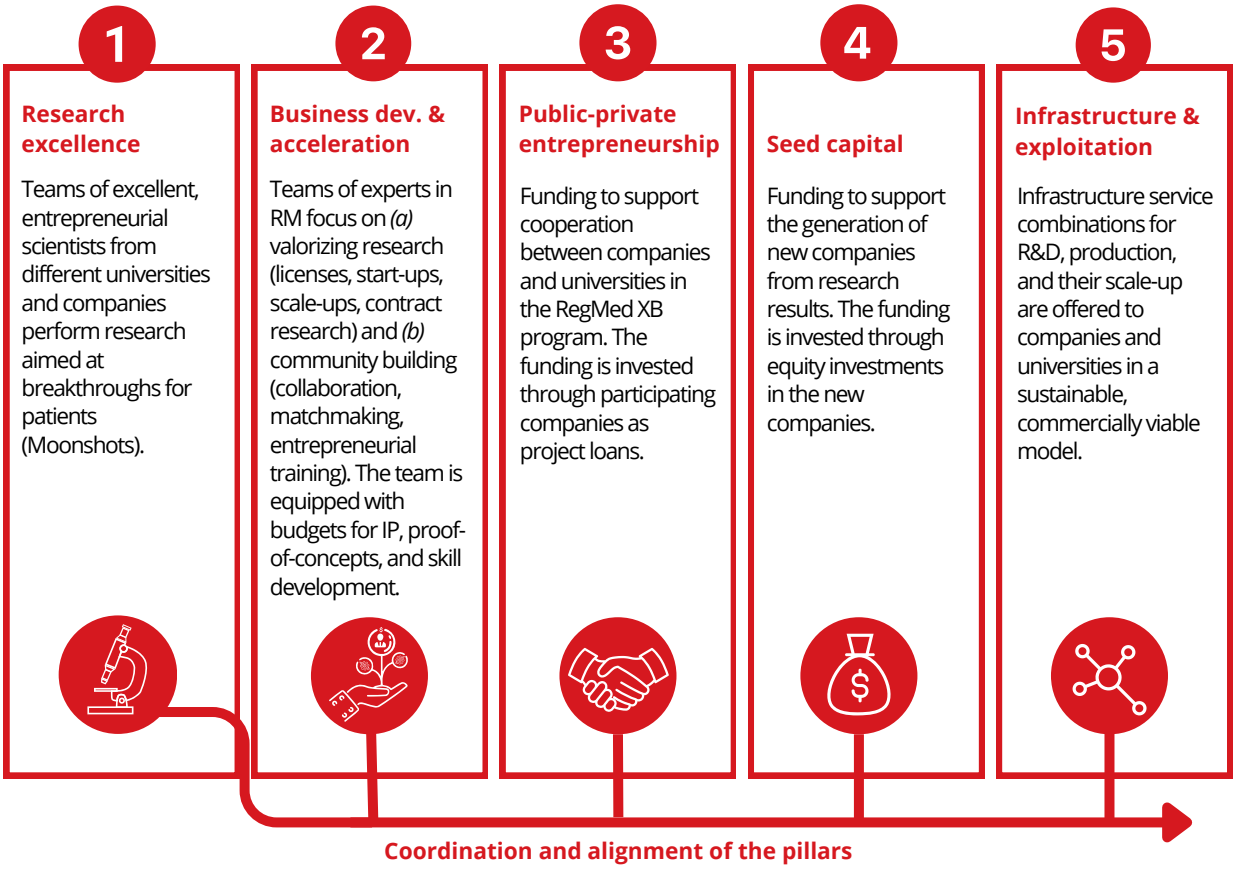


Figure: RegMed XB is based on five strategic activity pillars driving basic research towards solutions for patients

Funding

November 15, 2018, 14 stakeholders of RegMed XB (regional ministers of the relevant provinces, representatives of the ministries EZK and VWS, academic participants and health foundations), assembled in the Stakeholders Steering Committee, committed to an annual fee of € 805.000, for coordination activities provided by the RegMed XB office in the period 2019–2023 thus securing structural funding of RegMed XB's coordination and support activities. In July 2023, discussions with stakeholders regarding an increase in funding for the 2024-2026 period have been concluded in a manner that provides confidence that sufficient funding will be available to realize our objectives and ambitions in the 2024-2026 period.

RegMed XB's research programs ("Phase 1", "Scale-up" and "Scale-up 2") have been fully funded by a consortium of health foundations, Health~Holland, regional governments, academic partners and industry. By the end of 2022, the Phase 1 program was concluded, the Scale-up programme by the end of 2023 and Scale-up 2 will continue till the end of 2024.

RegMed XB and the Dutch CardioVascular Alliance (DCVA) were granted the "Toekomstfonds" grant of the Ministry of Economic Affairs and Climate of in total 8M EUR for the period 2020-2024.
Part of that money, 2.5M EUR, is used for executing valorization activities, comprising of screening and scouting of potential business cases by impact officers in the regenerative medicine and cardiovascular fields, resulting in the creation of spin-offs. Other important valorization activities include setting up business education and a solid RM ecosystem by organizing training programs and network events.
The other 5.5M EUR was used to set up the F1RST fund (Fonds InvesteringRijpe STarters Coöperatief U.A.) which is a pre-seed investment fund focussing on early seed funding of start-ups in the RM and cardiovascular field. Both RegMed XB and DCVA committed to an investment of 2M EUR each, creating an investment fund of 9.5M EUR. The fund is professionally managed by BGV (BioGeneration Ventures) in Naarden (NL).

During 2022 and 2023, the SGF (Vereniging Samenwerkende Gezondheids Fondsen) grant of 1M EUR PPS allowance to RegMed XB for studying two additional Moonshot overarching research areas was used to execute two projects. The first project involves a better understanding of immune responses to stem cell derived organoids and study potential strategies to evade or mitigate this immune response.

The second project is related to cell expansion, providing more insight into how to effectively grow cells in suspension and as such, speeding up the development of RM cures. Both projects are instrumental for the research executed in the Moonshots. These projects are finished now and follow-up projects are under discussion.

Following RegMed XB's September 2020 proposal to the National Growth Fund to build a national RegMed XB Pilot Factory for regenerative medicine, consisting of five pilot lines for the production of RM solutions in Leiden (2), Utrecht, Brabant and Limburg, the Dutch Cabinet awarded this proposal with 56M EUR, consisting of 23M EUR unconditionally and 33M EUR conditionally. In December 2021, the first subsidy of 23M EUR has officially been awarded by the Rijksdienst voor Ondernemend Nederland (RVO), resulting in the first payments to both the five pilotlines (NecstGen, LUMC, UMCU/ICAT, SBMC and ReGEN Biomedical) and to RegMed XB for coordination and reporting ("penvoerder"). In April 2022 the second part became unconditional as well, leading to a positive RVO decision by the end of December 2022. During 2023, the pilotlines continued to build the infrastructure and capabilities and started to work on projects. Of the 56M EUR, only the 1.4M EUR awarded for the "penvoerder" tasks runs through the RegMed XB annual accounts.

In January 2024 the Flemish government has recognized the importance of this cross border collaboration by conditionally awarding a further €15 million to RegMed XB Flanders, spread over a 5 year period, starting with a first €2.88 million in 2024.

Corporate social responsibility and environmental management

RegMed XB is aware of the social impact and ethical aspects of its activities and considers social responsibility therefore of paramount importance. RegMed XB is committed to a research approach in which animal testing is limited to legal and regulatory requirements. ■

Operational performance

At RegMed XB, everything we do is centered around translation: bringing innovations to market and to the patient. We operate on five strategic activity pillars: research excellence, business development & acceleration, public-private entrepreneurship, seed capital, and infrastructure & exploitation. In this section, you'll discover more about our activities and achievements in 2023.

1 Research excellence: Moonshots & Projects

We bring together leading scientists, university medical centers, institutes and a range of companies in these so-called "Moonshots": long-term visions of breakthroughs for patients. In addition we actively conceive and facilitate prime "Projects". These initiatives are designed to cover overarching themes which are highly relevant for all Moonshots.

Conclusion of Phase 1 and Scale-up Projects
With the completion of the Phase 1 and Scale-up projects, our original Moonshots required new follow-up programs. Early in 2023, the RegMed XB office, in collaboration with health foundations, began discussions to continue the Moonshots. Based on insights from previous years, the health foundations requested detailed Roadmaps before committing to fund follow-up research. These Roadmaps were to include feedback from both the International Scientific Advisory Board and the Scientific Advisory Board. This marked the beginning of the next phase for our Moonshots.

Roadmap Diabetes Moonshot
The roadmap exercise for the Diabetes Moonshot was highly successful, thanks to many partners including Diabetes Fonds en Stichting DON. We established clear short-term and long-term Roadmaps (1 and 2) and secured funding for Roadmap 1 projects. These projects focus on the preclinical development and early clinical validation of a delivery device for beta cells.

Roadmap Osteoarthritis (OA) Moonshot
For the Osteoarthritis Moonshot, the roadmap exercise is ongoing. External consultants, sponsored by Reuma-NL and RegMed XB, developed a business plan with support from RegMed XB's business developers. The positive outcome of this business evaluation supports further product development. Although future support from Reuma-NL is pending, we secured funding from Flanders until 2026 (Department Economie, Wetenschap & Innovatie = EWI).

Roadmaps Kidney and Cardiovascular Moonshots
Roadmap discussions for the Kidney and Cardiovascular Moonshots were initiated and emphasized translational research, a key strength of RegMed XB. Both Moonshots received TKI funding for short-term transition projects (2 years), supported by the health foundations Nierstichting and Hartstichting.

New Moonshot: Eye-Cornea
In 2023, in collaboration with the Eye Foundation, a new Moonshot came to fruition, focusing on developing a corneal replacement. The official kick-off for this Moonshot is planned for Q2 2024, featuring cross-border research groups from Flemish universities and universities from the Netherlands. Funding for the Flemish part has been secured through EWI-Flanders funding until 2028 (EWI = Departement Economie, Wetenschap & Innovatie).

These developments in our Moonshot programs demonstrate RegMed XB's ongoing commitment to pioneering regenerative medicine and achieving impactful results for patients.

- Cardiovascular
- Diabetes
- Eye - Cornea
- Kidney
- Osteoarthritis

2 Business development and acceleration

We foster valorization within the field of regenerative medicine by supporting the development of translational strategies for early-stage innovations to attract investments and progress towards the clinical phase. Collaborating closely with the Dutch CardioVascular Alliance and BGV's F!RST Fund within a Thematic Tech Transfer (TTT) program, RegMed XB facilitates academic research with high valorization potential at an early stage.

Through vouchers worth up to €25,000, researchers are assisted in taking the next step towards spin-off creation. Our business developers provide guidance and networking opportunities to determine which activities would add the most value to a project, thereby increasing the likelihood of securing additional investments.

Identifying Promising Projects

In 2023, our impact officers, working under the 'Impact Versnellen' program, identified 49 new promising academic projects. This was achieved through extensive networking, screening of scientific publications, and accessing project databases from hospitals and health foundations. Since the start of the program, 28 vouchers have been granted, with 11 of those awarded in 2023. Currently, 98 projects are being monitored for potential voucher awards.

Spin-off companies

The success of the voucher program is evident, with four spin-off companies established in 2023 based on previously supported projects: Genewity B.V., Orgonex B.V. (RegMed XB), InSteps, and PrecorDx (DCVA).

3 Public Private Entrepreneurship

During 2023 RegMed XB continued to lobby for the Public Private Entrepreneurship Fund (PPE fund). Resources of the Ministry of Economic Affairs and Climate remained limited, resulting in the handing-over of the dossier several times to different civil servants in 2023, not helping progress. However, the fruits of this work resulted in the announcement of the PPE fund of €30 million in May 2024. The PPE fund was renamed and is now called: the SRGO subsidy (Subsidie Regeneratief Geneeskundig Onderzoek).

READ MORE

4 Seed Capital

F1RST Fund Activities

The F1RST fund evaluated 105 new deal opportunities during 2023, of which 14 are still being pursued. Notably, 25% of these opportunities emerged from the voucher pipeline. Although the F1RST fund did not invest in new companies in 2023, portfolio companies Phlox Therapeutics and River Biomedics successfully obtained follow-on investments of €900,000 and €2 million, respectively.

Investment Impact

Since the start of the 'Impact Versnellen' program, approximately €3.98 million has been invested through two main channels: grants via voucher awards and pre-seed investments via the F1RST Fund.

These initial investments have supported promising cardiovascular and regenerative medicine concepts, attracting additional funding totalling €59.8 million and achieving a 14.5x multiple on the initial investments.

These results highlight the significant impact of our valorization and business development efforts in fostering innovation and accelerating the development of new healthcare solutions.

5 Infrastructure: RegMed XB Pilot Factory

The RegMed XB Pilot Factory is a major infrastructure initiative dedicated to the production of regenerative medicine products. Funded by a €56.3 million grant from the Dutch National Growth Fund (NGF), the Pilot Factory consolidates expertise and infrastructure to bring regenerative medicine products to market.

Facilities

The Pilot Factory includes facilities or Pilot Lines that span the entire spectrum of development and production processes for stem cells, Organ-on-Chip systems, micro- and macro-tissues, and smart biomaterials. These lines are situated in five locations: Leiden (2x), Utrecht, Eindhoven, and Maastricht. These Pilot Lines foster collaborative efforts between companies and a to develop clinical applications through public-private partnerships.

Objectives by 2028

- Serve approximately 250 users/customers (academic institutions and companies).
- Generate around €75 million in revenue from capacity, services, and equipment sales/rentals.
- Create approximately 120 new direct jobs within the production lines.
- Establish roughly 25 spinout ventures from research conducted on the production lines and developed production technology.
- Achieve a reduction of approximately 90% in production costs per micro-tissue.

RegMed XB Responsibilities

- Facilitate collaboration and coordination among the Pilot Lines.
- Develop and promote joint national and international business propositions.
- Achieve the Key Performance Indicators (KPIs) defined at the national RG Pilot Factory level.
- Integrate the RG Pilot Factory into the broader RegMed XB ecosystem.
- Monitor, evaluate, and report on collective and individual progress.

Of the €56.3 million awarded, €54.9 million went directly to the Pilot Lines, and €1.4 million was allocated to Stichting RegMed XB for facilitation and coordination. The subsidies directly awarded to the Pilot Lines are not included in Stichting RegMed XB's Annual Reports.

Progress and Challenges

The initial phase of delivering the physical infrastructure is largely complete. The official openings of the Leiden locations (LUMC and NecstGen) and SBMC in Eindhoven occurred in 2022. On September 21, 2023, Governor Emile Roemer inaugurated the Maastricht Pilot Line, ReGEN Biomedical. SBMC in Eindhoven also announced a second location for producing medical implants and combination products. ICAT (UMCU) in Utrecht began construction on a Zeist location, set to open in May 2024. In 2023, ReGEN Biomedical engaged Demcon as a strategic development partner to expedite the construction of large-scale manufacturing lines.

Despite progress, several lines faced delays in construction and setup due to various factors, including prolonged processes in location selection and financial challenges from price increases and higher salary costs. Conversion of leads into contracts was slower than expected, prompting increased business development activities across all lines. In 2023, a process to secure a strategic partner for NecstGen commenced.

Collaborative Efforts and International Activities

Throughout 2023, significant efforts were made to refine joint and individual propositions, staff organizations, and foster collaboration. The Pilot Factory and its lines were prominently featured during the Annual Conference RegMed XB in June 2023. Initial steps were taken to establish regional ecosystems and initiate projects with both internal and external clients.

Internationally, the Pilot Factory and its lines participated in various activities, including visits to Japan and presentations in Leuven and Heidelberg. Business developers from the Pilot Lines engaged in numerous national and international conferences and symposia. Employment and Revenue In 2023, approximately 64 full-time equivalents (FTEs) were employed within the Pilot Factory, generating a total revenue of around €1 million.

Coordination and Planning

The Focusgroup, consisting of operational representatives from all five Pilot Lines and led by RegMed XB, met every three weeks to review progress. Executives held four meetings in 2023 to discuss propositions, business development, human capital, the Annual Conference, 2022 reporting, strategic collaborations, and 2024 plans. Additionally, business developers regularly convened to coordinate activities.

Challenges and Outlook

The report submitted to the National Growth Fund highlighted the new infrastructure and organization available within the five Pilot Lines two years after inception. However, challenges in converting leads to contracts persisted, primarily due to market conditions, necessitating the implementation of additional measures while maintaining a positive outlook. ■

RegMed XB Pilot Factory

Microtissue pilot line
» ICAT

iPSC and OoC pilot line
» LUMC

Stem cells pilot line
» NecstGen

Macrotissue pilot line
» ReGEN

Biomaterials pilot line
» SBMC

Organisation and communication

In 2023, RegMed XB placed significant emphasis on strengthening its organizational structure and enhancing communication strategies. This focus was pivotal in ensuring that our mission and activities were effectively coordinated and communicated to all stakeholders, including our partners, researchers, and the broader public.

Governance

During 2023, the Supervisory Board met in 4 meetings with the Board of Directors of RegMed XB. The main topics of discussion were the research activities, valorization, the Pilot Factory, the collaboration with Flanders and the roadmap for RegMed XB.
The Scientific Advisory Board met three times in 2023. The Moonshots were evaluated based on the scientific progress, ISAB reports, health foundations input and discussions with the Moonshot Leaders. As a result of these discussions, Milestone 0 plans were adapted for 2023.

Support office

The office supports management and Moonshot leaders, and coordinates interim and annual reporting. In 2023, personnel changes took place. Three members of the team left (New Business Development Director, Project Manager and Impact officer) and three new persons joined RegMed XB: in April 2023 a new project manager joined (1.0 FTE). In September 2023, two Impact Officers joint RegMed XB for the TTT program. In order to help develop the organisation into the next phase and build the team, a consultant (the Scale-Up company) continued during 2023 to help improving business processes and adapt the way of working.

International Cooperation

International cooperation is of growing importance for the RegMed XB ambition. RegMed XB, where the XB stands for crossing borders, requires focussed collaboration with world-leading institutes in regenerative medicine. The cooperation with Flanders, initiated in 2017, is developing in a solid way, which led to the initiation of the cross-border Eye Moonshot. The 2020 Memorandum of Understanding between Flanders and the Netherlands helps to drive this development. Not only is the contribution of Prof. Luyten (former KU Leuven) as Medical and Scientific Director instrumental to the RegMed XB ambition, also the membership of the Supervisory Board of Prof. Debackere (KBC and KU Leuven) underscores the tied connection.

In the course of 2022, the outcome of fruitful discussions between the KU Leuven, VIB and RegMed XB resulted in the establishment of the non-profit organisation called RegMed XB Flanders VZW, providing the “boots on the ground” in Flanders as well as creating the roadmap for Flanders in close collaboration with the development of the overarching roadmap of RegMed XB. In the course of 2023, this collaboration was strengthened by regular meetings on the roadmap, governance and role of the RegMed XB office in both NL and FL. In the course of 2024, the Chair of RegMed XB Flanders joint the management team and joins strategic meetings. In January 2024 the Flemish government has recognized the importance of this cross border collaboration by conditionally awarding a further €15 million to RegMed XB Flanders, spread over a 5 year period, starting with a first €2.88 million in 2024.
Next to the collaboration with Flanders, RegMed XB maintains strong connections with the main innovation hubs for regenerative medicine. The collaboration with important hubs in the US was maintained, however with the departure of the New Business Development Director in August, these ties need attention since the contacts were maintained by this officer. Next to these contacts, also interest from the Netherlands Innovation Network (“innovatie attachés”) of the Ministry of Economic Affairs and Climate, resulting in contacts with Switzerland and Japan. During 2023, two online meeting with Japan were organised as well as a visit to Japan in October. Further visits were initiated in 2023, resulting in visits to Switzerland, UK and Germany in 2024. These are important steps to make international collaboration possible in the future. The increased international interest is also mirrored by the statistics from Linkedin, showing that of all visits to the RegMed XB company page, 55% is from outside the Netherlands.

Communication and publications

Communication is of crucial importance within a virtual institute and community building is key in a patient-oriented research organisation. In June 2023, the first Annual Conference was held in Leiden, the main activity of the year. The Conference was open for participation from outside the RegMed XB community, leading to new participants from both the academic and industrial world. Several companies from outside the Netherlands showed interest as well. The Conference was well received by the participants and several important stakeholders took a role in the program, such as the Mayor of the city of Leiden.

Representatives of the Provinces and Flanders participated as well. It was the first time the RegMed XB Pilot Factory had a booth at the conference. The Pilot Factory presented itself by presentation of the different pilot lines followed by a panel discussion. Feedback was positive and the meeting was well attended (> 200 participants). RegMed XB pays much attention to external and internal communication. Especially communication via the social media platform LinkedIn became more prominent. The number of followers of RegMed XB on LinkedIn increased with 666 to 1981, posts generated 53,642 unique impressions and the engagement rate was 9.275% (average healthcare industry rate 1.49%). At the end of the year, RegMed XB published the Highlights 2023, providing an overall impression of the activities of RegMed XB.

Financial results

Thanks to the investment and collaboration of our partners, Regmed XB can fulfill its crucial role within the regenerative medicine ecosystem. Their contributions enable us to effectively coordinate efforts, strengthen the regenerative medicine chain. This collective commitment is essential for the success and impact of our initiatives.

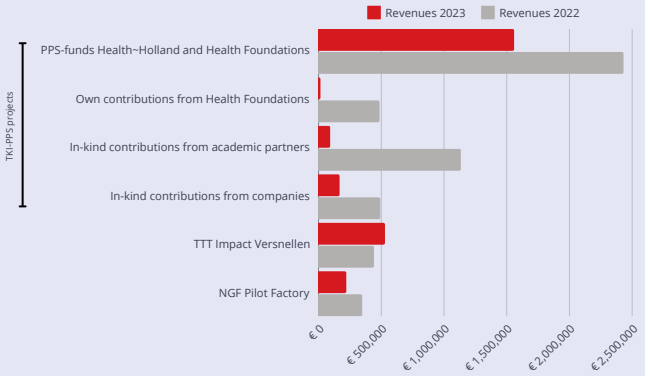
This year, we received funding for projects and the operational costs of our office. Project funding primarily came from Health~Holland, various health foundations, contributions from academic partners and companies, and subsidies for the TTT program and NGF Pilot Factory.

It is important to note that total project revenues (and expenses) in 2023 are lower compared to 2022. Additionally, office expenses appear relatively high compared to last year. This is due to 2023 being a transitional year: projects from RegMed XB's first phase were completed or nearing completion, while new follow-up projects had not yet fully started. This has temporarily skewed the ratio between project costs and office expenses.

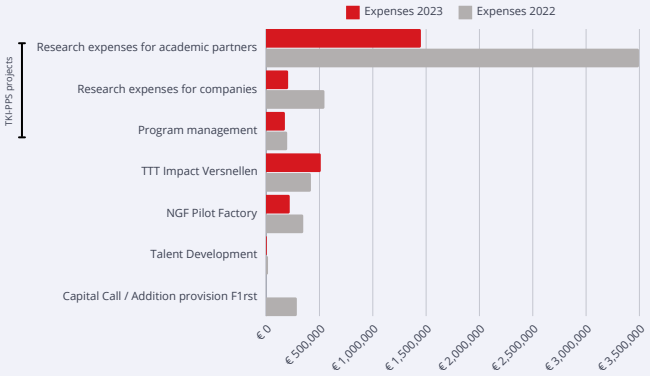
National Growth Fund and the Pilot Factory
In addition to this overview, it is important to highlight that the National Growth Fund (NGF) has allocated €37 million from 2021 to 2023, along with €61.5 million in co-financing. In total, approximately €98.5 million has been invested in the NGF Pilot Factory. This significant investment has been used to establish and expand the infrastructure of the regenerative medicine sector in the Netherlands, including the development of facilities and workforce. Please note that the costs associated with the pilot lines within the NGF Pilot Factory are not included in this overview.

BALANCE SHEET (€ x 1)	**2023**	**2022**
ASSETS		
Tangible fixed assets	7.672	8.424
Current assets	1.631.885	2.303.051
Cash and banks	1.911.419	2.183.452
Total	**3.550.975**	**4.494.927**
EQUITY AND LIABILITIES		
Current liabilities	3.550.975	4.494.927
Total	**3.550.975**	**4.494.927**

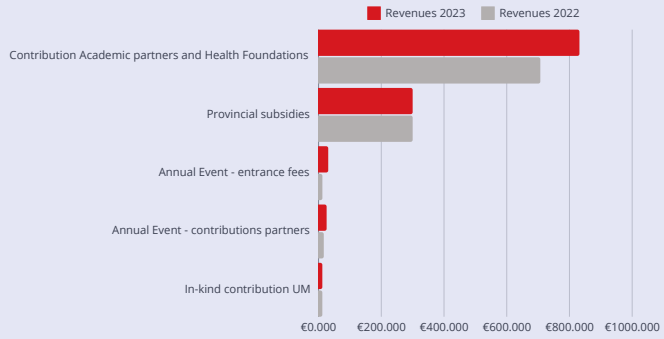
Project Revenues 2023 vs 2022



Project Expenses 2023 vs 2022



Revenues Office RegMed XB 2023 vs 2022



Expenses Office RegMed XB 2023 vs 2022

Outlook 2024

As we look ahead to 2024, RegMed XB is prepared to build on its successes and navigate new opportunities in regenerative medicine. Our strategic focus for the coming year encompasses a multifaceted approach designed to advance our mission and expand our impact. Key areas of focus include:

Key areas of focus 2024

Further Developing and Applying for Funding for the "Translatiemotor": With the expert process support from consultant Roland Berger, we aim to drive this initiative forward, enhancing our capabilities in translating scientific research into practical medical applications.

Securing Interim Research Funding (Pillar 1): Reaffirming the status of Strategic Partner with Health~Holland will be pivotal in securing necessary funding to support ongoing and future research projects, ensuring continuity and progress in our scientific endeavors.

Screening, Scouting, and Funding Promising Technologies and Projects (Pillar 2): We will intensify our efforts in identifying and supporting innovative technologies and projects that hold potential for significant advancements in regenerative medicine.

Starting the SRGO Fund (Pillar 3): The launch of the SRGO fund will mark a significant milestone, providing crucial financial support for groundbreaking research and development initiatives within our ecosystem.

Advancing the RegMed XB Pilot Factory (Pillar 5): Continued development and optimization of the Pilot Factory will remain a top priority, focusing on expanding its capacity and capabilities to support the production of cutting-edge regenerative products.

Strengthening Cooperation with Flanders and Exploring International Opportunities: Enhancing our collaboration with Flanders and seeking new international partnerships will be essential in fostering a global network of innovation and expertise in regenerative medicine.

Roadmap RegMed XB

The Board of Directors decided in December 2021 to draw up a new ambitious plan for RegMed XB in order to cope with the challenges RegMed XB faces. Since the Moonshots are progressing, translational research becomes more and more important and the funding becomes more challenging as significant amounts of money are needed to execute this research. Private parties (such as private equity or big pharma) might provide the funding, but then the RegMed XB goal of "affordable RM solutions for patients" will be difficult to achieve. Additional funding streams need to be identified. Next, in order to collaborate better and more with partners, new ways of working together need to be explored. It calls for disruptive thinking. And last but not least, RegMed XB needs to become a centre of expertise on several topics related to the development of RM products. An example is in-depth knowledge on regulatory aspects. Together with key players from institutions, health foundations and the Board of Directors, with process support from consultant Roland Berger, a plan was developed called the "Translatiemotor" to provide the vision and framework for the translational goals of RegMed XB, from mice to men. In 2023, RegMed XB continued building on this plan and started to prepare a submission of this plan to the National Growth Fund, fourth round. Although the Dutch Government fell in the summer of 2023, preparation for the fourth round of the NGF continued from the governmental side as well as from the RegMed XB side.

In December 2023, a Quickscan of the plan was submitted to RVO which was positively reviewed in January 2024. RegMed XB initiated the further development of the NGF plan by hiring Roland Berger for further process support, forming working groups and detailing the plan. Unfortunately, in March 2024, the Minister of Economic Affairs and Climate decided to pause the activities of the NGF fourth round and on 16th of May 2024, the coalition parties of the new government decided not to continue with new rounds of the NGF. Meanwhile, RegMed XB continued finalising the "Translatiemotor" plan, as it is the strategic plan for the future for RegMed XB. Funding for the plan needs to be sought for. Contacts with the Ministry of Economic Affairs and Climate and the Directorate of the NGF remain strong, giving opportunities for the future.

Strategic pillar 1: research excellence
RegMed XB program management in support of research excellence matured further and the activities within the Moonshots were increasingly focusing on translation and building consensus on clear Roadmaps, both short and long term.

For the Diabetes Moonshot, major progress was achieved both for the manufacturing of stem cell derived functional beta cells, and for the development of a delivery device for these cells. Delays were encountered for assembling the device preclinical dossier, as this appeared to be quite challenging both in content and financing as several parts needed to be outsourced to industrial/private partners including the validation of Quality Management Systems and Manufacturing. A first clinical trial to establish safety and tolerability for the device is now planned for 2026.

For the OA Moonshot, Roadmap discussions were initiated and overall the way forward on building a living osteochondral implant for large and deep osteochondral defects was agreed upon. Also, in the longer term, the goal of building large living joint replacement parts, including a total joint replacement for the relatively young patient (below 60 years), was defined.Several candidate implants were further explored in relevant model systems. Uncertainty with regard to future funding and support by ReumaNL was responsible for the delays encountered, although financing in Flanders was obtained till 2026.

For the Cardio Moonshot, increased focus goes to the ex vivo perfusion technology, allowing longer term survival (8-24 h) and functional assessment of a heart ex vivo, to turn heart (donor hearts) transplantation from an emergency to an elective procedure. Furthermore, the ex vivo model will be used to explore the efficiency of gene transfer. The Kidney Moonshot continues the preclinical studies on the production of stem cell derived tubuloids, including in depth functional characterisation and scaling. Tubuloids as part of an organ-on-a-chip model and vascularisation will be explored together with Mimetas using the organoplate platform. A long term Roadmap is being discussed.

A new Eye Moonshot has been set up with as first goal to build a corneal transplant for patients with keratitis bullosa. The official announcement of this Moonshot with kick off meeting will be in early summer 2024. The Moonshot goal is to develop a combination product with iPS derived endothelial corneal cells seeded on an unfoldable membrane. The timelines are anticipating a first-in-man in 2029.

Importantly, the new initiative funded by extra SGF funds on technology platforms relevant across Moonshots will be explored for further funding, in particular the transplant immunology platform. Indeed, experiments were successfully performed and coordinated in 3 centres to assess the expression of immune markers on cells derived from embryonic stem cell derived beta cell organoids, iPS derived kidney organoids, adult stem cell derived tubuloids and adult stem cell derived cartilage organoids. The results indicated that expression levels of molecules associated with an alloimmune response are comparable yet distinct depending on the organoids. In the presence of interferon gamma or IL-1 beta, mimicking inflammatory conditions, a modest upregulation of some markers is detected. Further functional assessment are required providing also more insights on underlying mechanisms of immune response by the host.
For the expansion scaling studies, substantial progress was made to obtain the growth and differentiation at scale and in suspension of a number of organoids, including cartilage, betacell and liver organoids. Further funding to be investigated with respective companies involved, possibly through the new PPE funding.
The ambition of RegMed XB to cure chronic diseases with regenerative medicine solutions and explore the potential in early exploratory trials in patients will require substantial additional funding.

Finally, further integration with RegMed XB Flanders is planned : 1) to focus additional power on topics needing attention (e.g. regulatory affairs, large animal models, the manufacturing platforms, business development), 2) to better integrate our talent pool within the organization, and 3) to develop talent looking towards the next generation of leaders.

Strategic pillar 2, 3 and 4 – valorization, SRGO subsidy and seed capital
The focus of 2024 will be on continuing to build the valorization structure and associated activities. As the TTT subsidy will end by the end of the 2024, new opportunities are explored to continue the program. Contacts are initiated with Biotech Booster and PharmaNL (other NGF programs) to look for potential collaborations. Next, due to the success of the TTT subsidy, we lobby for a new TTT program, allowing for renewed investments.
The funding of the PPE fund was uncertain in 2023, but was secured in May 2024 (SRGO subsidy). It means that companies can apply for a loan while working with an academic partner. The academic partner receives a subsidy for their work. The subsidy will be directly granted to the applicants. RegMed XB does not receive any money from this subsidy.

Strategic pillar 5 – Infrastructure
2024 will be an important year for the Pilot Factory of RegMed XB, as the infrastructure has been built and business needs to be generated. Activities need to be intensified and expanded by the individual pilot lines and RegMed XB helps building the Pilot Factory as a whole. This involves:

- Strengthening the cooperation and coordination between the pilot lines:
- Further development and marketing of joint national and international (business) propositions;
- Strengthening business development activities;
- Integrating the RegMed XB Pilot Factory into the entire RegMed XB ecosystem – connecting to the other pillars of RegMed XB;
- Monitoring, evaluating and reporting on joint and individual progress (coordinatorship);
- Continuation of realizing the infrastructures and strengthening the organizations.

International collaboration

RegMed XB will continue exploring international opportunities for collaboration. With the help of the Innovation Counsels of the Embassies abroad, the NFIA and RVO, innovation missions will continue to be planned to foster international collaboration. As RegMed XB has a relatively small office, choices have to be made where to invest. For sure, the collaboration with Flanders will only be strengthened. The activities in the US need to be reassessed.

For the upcoming World Expo 2025 in Osaka, Japan, preparations will be made. For 2024, visits were planned (and executed) to Switzerland, UK and Germany. Follow-up will take place during the course of 2024.

Community building

Another cornerstone of RegMed XB is to cross the borders of disciplines, academic, industry, and regions. To be really successful in research and valorization it is of crucial importance to boost interaction between researchers (in both academia and companies) and to establish a close connection to the target patients. This is where RegMed XB has an opportunity to differentiate itself from other initiatives. When scientist see the potential impact of their work in real life, meet with patients and see the need and urgency for solutions, it will boost the spirit in which research is performed. The major event in 2024 is the Second RegMed XB Annual Conference, which took place in Maastricht. For the second time, the Conference was open for participants outside the RegMed XB consortium. The Annual Conference did not only focus on research, but also on valorization and the Pilot Factory. The extensive program covered all elements of the RegMed XB platform and created the possibility of interaction between all disciplines present. Interaction that is needed to achieve the goals for RegMed XB: bringing RM solutions to patients at affordable prices! ■

Thanks to all partners

Academic partners

- Academic Hospital Maastricht (MUMC+)
- Eindhoven University of Technology (TUe)
- Ghent University (UGent)
- KU Leuven
- Leiden University Medical Centre (LUMC)
- Maastricht University (UM)
- University Medical Center Utrecht (UMCU)
- University Utrecht (UU)
- University of Antwerp (UAntwerp)
- Vrije Universiteit Brussel (VUB)

Industrial partners

- 300MICRONS
- Access2Bone
- Axion BioSystems
- CiMaas B.V.
- Coagulation Profile
- ETB-BISLIFE
- FUJIFILM Visualsonics
- Genome Diagnostics (GenDx)
- HCM Medical
- Interflow
- Kuros Biosciences
- Leiden Regenerative Medicine Platform (LRMP)
- Mimetas
- Ncardia
- NecstGen
- Ntrans Technologies
- Quality Assistance
- ReGEN Biomedical
- SBMC
- Scannexus
- Scinus Cell Expansion Netherlands
- Single Cell Discoveries
- STENTiT
- Suprapolix
- U-CyTech biosciences
- Veldlaser
- Xeltis

Health Foundations

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- Hartstichting
- Nierstichting
- Oogfonds
- ReumaNederland

Governmental partners

- Government of Flanders
- Health~Holland
- Ministry of Economic Affairs
- Ministry of Education, Culture and Science
- Ministry of Health, Welfare and Sport
- National Growth Fund
- Provincie Limburg
- Provincie Noord-Brabant
- Provincie Utrecht
- Provincie Zuid-Holland


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possible
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