

AMICARE

Aachen – Maastricht Institute for CardioRenal Disease

Heart-kidney interaction - from knowledge to therapy

Aachen and Maastricht combine their cardiorenal research to develop new therapeutic options to reduce cardiovascular disease in patients with chronic kidney disease



RWTH AACHEN
UNIVERSITY

UNIKLINIK
RWTH AACHEN



Maastricht University



Maastricht UMC+

To the interested readers,



Rector of RWTH Aachen

Prof. Dr. Dr. Ulrich Rüdiger



President of Maastricht University

Prof. Dr. Martin Paul

As a rector or president of a university, you are called upon to prioritize research that addresses the challenges of today's world and aims to meet these challenges. Health protection is a particularly important issue here. While progress in medicine and better living conditions have considerably improved our life expectancy over the last decades, at the same time chronic illness, such as cardiovascular diseases, is becoming more and more relevant.

At RWTH Aachen University and Maastricht University, we are proud to address this clinically and socially highly relevant health issue with AMICARE as a joint international institute of our universities. This cooperation is a great added value and is especially interesting for industrial partners, but also for patients. The location on the RWTH campus leads to an excellent cooperation between clinic, science and industry and follows the goal of developing innovative approaches in diagnostics and therapy to improve the quality and expectancy of life of patients with cardiorenal disease, which remains a worldwide problem.

In order to be able to tackle such global challenges in a targeted manner, a strong network with international partners is required. AMICARE as a direct result of the many years of close and successful cooperation between RWTH Aachen University and Maastricht University combines two institutions of excellence in cardiovascular and cardiorenal research.

We would like to emphasize AMICARE's unique approach to combine basic research, a patient study center with phenotyping of cardiorenal patients and clinical studies. In addition, active public-private-partnerships in one building will ensure cutting-edge, industry-relevant and patient-oriented research with effective clinical translation. Furthermore, education and training are promoted, with a focus on education of a healthy life style to combat the devastating impact of cardiorenal disease and its comorbidities.

AMICARE demonstrates that joining forces and expertise on an international level between clinicians, basic researchers and private partners pays off: Together, we will achieve our mission to fight against chronic kidney and cardiovascular disease, to the benefit of the cardiorenal patient and the aging population in general.

Within AMICARE, we look forward to an even closer and more intensive cooperation between RWTH Aachen University and Maastricht University and we would be very happy to broaden our network and welcome you as an industry partner. Diseases do not stop at a national border, so research and education shouldn't either: With close cooperation and building on each other, we can jointly achieve more!

We hope you enjoy reading this brochure and learning more about this initiative!



THE CHALLENGES

► The cardiorenal research gap

Cardiovascular disease (CVD) is the leading cause of death worldwide [1]. In Europe, CVD accounts for 43% of deaths [2], which exceeds the global average by 11% [1]. Also, the prevalence of chronic kidney disease (CKD) in Europe exceeds with 18% the global average of 13% [3]. Annually, 1.2M people die from CKD worldwide [4]. However, almost 45% of CKD patients also suffer from CVD [5], with CVD being the leading cause of death in CKD [6]. Globally, 1.4M annual CVD-related deaths are attributable to impaired kidney function [4].

Taking the ageing population and changing lifestyle into account, the incidence and impact of cardiorenal diseases are expected to grow. By 2040, CKD deaths are expected to increase in number by 83% in best case and up to 233% in worst case [7]. While the global age-standardised mortality rate decreased by 30.4% for CVD in the last 30 years, for CKD only a 2.8% decline was

observed [1], demonstrating the urgent need for the development of new therapeutics specifically for the cardiorenal patient.

However, the mechanisms underlying the effects of CKD on the cardiovascular system are still largely unexplored. Until now, the complex heart-kidney interplay has largely been neglected and both organs have mainly been considered as separate entities. Although CKD has been identified as an independent risk factor for CVD, cardiorenal patients are currently underrepresented in scientific and clinical studies, and therapeutic options to reduce cardiovascular risk in patients with CKD are only available to a very limited extent. This is associated with a high socio-economic burden in addition to the individual limitation of quality of life and reduced life expectancy of these patients.

These alarming numbers and the cardiorenal research gap highlight the urgency of in-depth understanding of the complex heart-kidney interplay and calls for an increased focus on the cardiorenal patient. Also, it underlines the need of interdisciplinary research, combining the expertise of cardiologists, nephrologists and pathologists, basic researchers in the field of biochemistry, molecular biology and biomedical engineering, as well as private partners in the field of pharmaceuticals, biomedical applications and medical and digital device development. Only by actively joining forces, innovative diagnostic and therapeutic approaches focusing on the cardiorenal patient can be identified and translation of research results into clinical practice will be met.

[1] GBD Study 2017 - Cause of death, Lancet, 2018 [2] WHO, Deaths by cause and region, 2000-2016 [3] Hill et al., PLoS One, 2016
[4] GBD study 2017 - CKD, Lancet, 2020 [5] Stevens et al., Kidney Int, 2007 [6] Thompson et al., J Am Soc Nephrol, 2015 [7] Foreman et al., Lancet, 2018

18%

of the population in Europe suffer from CKD

45%

of CKD patients stage 4-5 suffer from CVD, with CVD being the No.1 cause of death

1,4M

people die annually from cardiorenal disease

► The application gap

Valorisation of research results becomes applicable through the identification of disease markers and interventional targets, the development of medical and digital devices, as well as the development of bioassays, bio-based products and technologies.

However, valorisation of research results is often failing, since it requires a direct and interdisciplinary interaction of basic researchers, clinicians and private partners as pharmaceutical companies, medical and digital device companies as well as biotech companies.

Only close proximity and interdisciplinary interaction of researchers, clinicians and private partners can accelerate application-driven and patient-relevant research and translation thereof.

► The education gap

A low education level has been linked with an increased presence of cardiovascular risk factors, such as obesity, in the western world. Furthermore, both the North Rhine-Westphalia region of Germany and the Limburg province of the Netherlands show elevated prevalence of childhood obesity and lifestyle-related CVD [8, 9]. Risk analyses of the Robert-Koch Institute showed that low social status and low educational achievement lead to an increased risk of obesity. Especially if both parents are also obese, this is associated with a significantly increased risk for their children [10].

Public health education and raising awareness of diet-induced obesity, hyperlipidemia, diabetes, hypertension and other risk factors are essential in combatting cardiorenal disease in a sustainable manner.

[8] Bartelink et al., BMJ Open, 2019

[9] Hilbert, V., Ruhr Nachrichten, 2018 [10] RKI, 2008

by 2040

CKD deaths are expected to increase in number by

83 - 233%

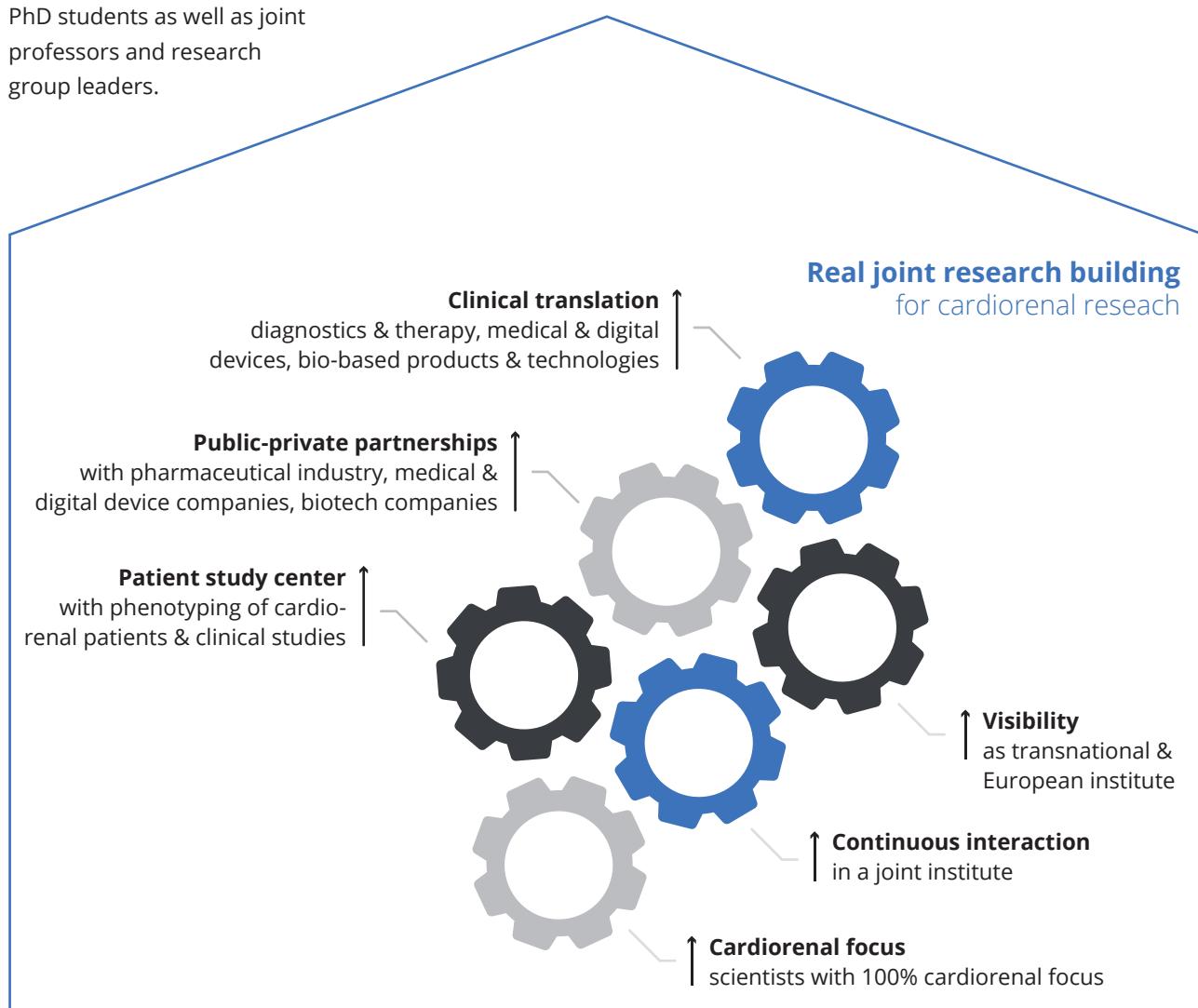
THE SOLUTION

Pioneering into the field of cardio-renal research, the RWTH Aachen and Maastricht University (UM) have established a strong and successful cross-border collaboration over the past 10 years, bringing cardiovascular and renal research of both institutes closely together.

This has resulted in a common cross-border research platform (IMCARIM), multiple collaborative Aachen-Maastricht cardiovascular and cardiorenal projects and jointly acquired third-party funding, joint high-impact publications, patents, PhD students as well as joint professors and research group leaders.

Extending on this successful collaboration, AMICARE as Aachen-Maastricht Institute for CardioRenal Disease is being erected to further promote innovation and dedication in the field of cardiorenal research.

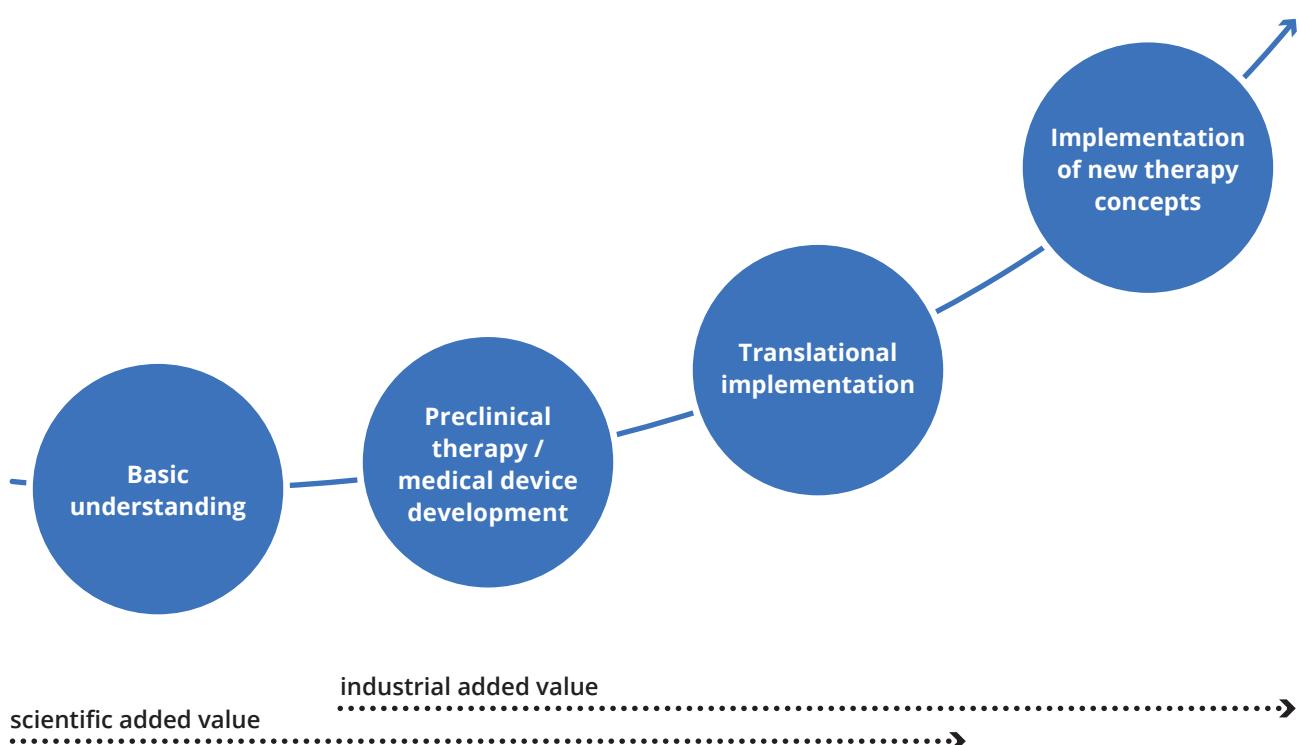
AMICARE, as a joint international institute between the RWTH Aachen and Maastricht University, brings the cooperation between Aachen and Maastricht in the field of cardiorenal research to the highest level: The full potential in the development of innovative diagnostic and therapeutic approaches, international visibility as well as industry-relevant research is being exploited.



Operating at the forefront of science, AMICARE will fully support translational, cardiorenal patient-oriented research and cutting-edge innovation in the cardiorenal field by joint research & development of clinic, science and industry. In this way, university research and patient care will proceed hand in hand with the pharmaceutical, biotech and medical device industry to simultaneously prepare the ground for clinical progress as well as industrial value creation.

AMICARE: The Aachen-Maastricht Institute for CardioRenal Disease has devoted itself to establish and continuously improve cardiorenal patient care by patient-oriented, innovative research and prompt translation of research findings to the clinic.

Clinical need



AMICARE AS AACHEN-MAASTRICHT INSTITUTE FOR CARDIORENAL DISEASE

► History towards development of AMICARE

As pioneers in the field, the Medical Faculty of the RWTH Aachen and the Faculty of Health, Medicine and Life Sciences of the Maastricht University have successfully performed collaborative research projects focusing on the cardiorenal patient: Amongst others, the DFG SFB/TRR219 consortium, the joint EU- Marie Skłodowska Curie-ITN- Consortia CaReSyAn and INTRICARE as well as the joint Euregio Interreg project EURLipids have revealed the advantage of collaborative approaches in closing the cardiorenal research gap. In fact, more than 33.5 M€ of third-party funding was acquired for this transnational Aachen-Maastricht collaboration in cardiovascular and renal research since 2016. In addition, of all joint European H2020 projects acquired by the medical faculties of the RWTH Aachen and Maastricht University, 25% are related to cardiorenal research. Furthermore, 45% of all joint Aachen-Maastricht

publications are of cardiovascular or cardiorenal topic since the start of EuCAR as first joint research consortium in 2008, demonstrating the scientific strength of the cardiorenal Aachen-Maastricht axis.

The previous and ongoing collaborations between the RWTH Aachen and the University of Maastricht have successfully established a common language on cardiovascular and renal research.

Building on this successful Aachen-Maastricht collaboration and under impulse of both the RWTH Aachen and the Maastricht University, AMICARE as real transnational institute focusing on cardiorenal disease was launched in 2017 to stimulate cutting-edge innovation and research valorisation in the field.

Lead of DFG SFB/TRR219 consortium
www.SFB-TRR219.de

Lead of joint EU- Marie Skłodowska Curie-ITN CaReSyAn
www.CaReSyAn.eu

Lead of joint EU- Marie Skłodowska Curie-ITN INTRICARE
www.intricare.eu

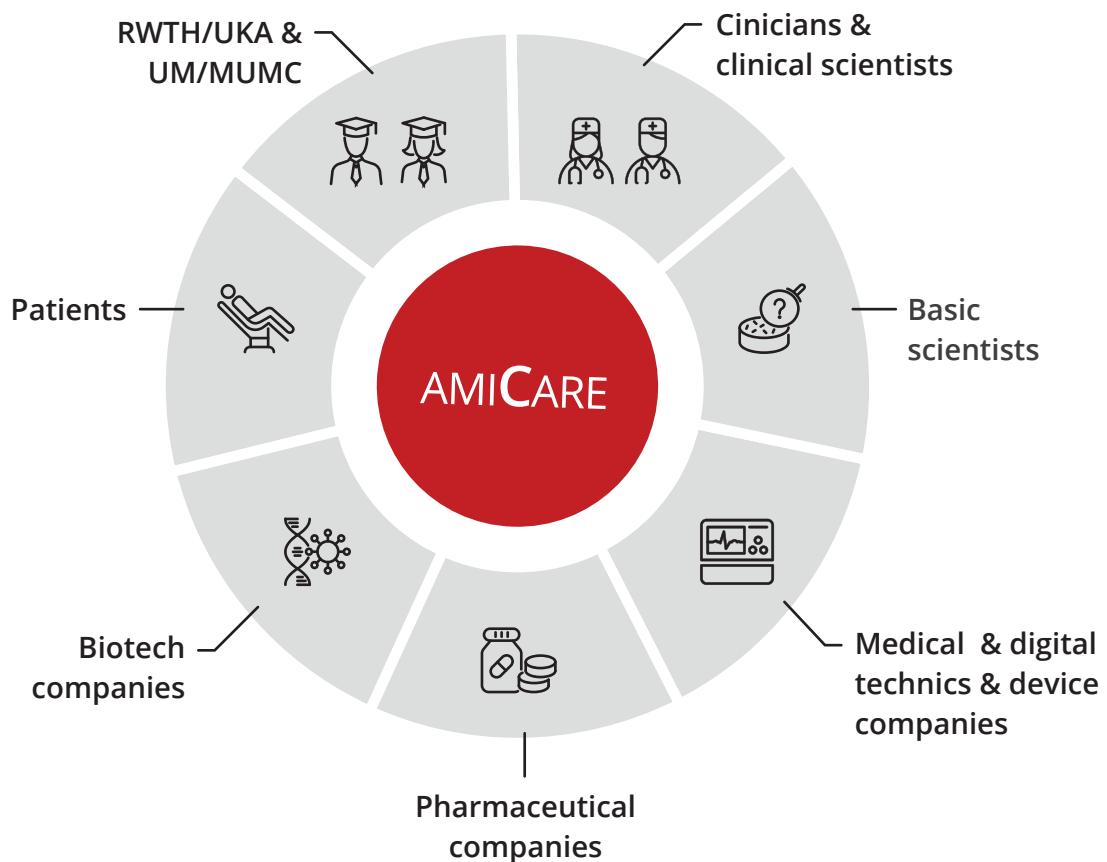
► Vision of AMICARE

AMICARE strives to be a cross-border, internationally leading research centre for innovation and translational research, dedicated to sustainable improvement of the cardiorenal patient's life.

As a reply to the identified gaps and urgency in relation to cardiorenal disease, AMICARE's mission is to establish and continuously improve

cardiorenal patient care by patient-oriented, innovative research and translation of research findings into the clinic. This is promoted by close, interdisciplinary collaboration of clinicians and scientists, the integration of a study center for patient phenotyping & clinical trials as well as active public-private partnerships within

AMICARE. The latter includes close interactions with pharmaceutical companies in the development and testing of new drugs, medical and digital device manufacturers, e.g. for optimisation of dialysis machines, as well as with biotech companies in the field of diagnostics, biologicals and regenerative medicine.



Patient-oriented and industry-relevant research

Interdisciplinary research with scientists and clinicians from two excellent universities as well as with renowned private partners

Application-oriented research through an integrated study centre for phenotyping of cardiorenal patients and clinical studies

Research, development and market launch of innovative diagnostics and therapeutic approaches

► Strategy of AMICARE

Building on 4 scientific pillars

Four scientific pillars will be driven by dedicated young as well as established investigators from both the RWTH Aachen and the Maastricht University with focus on clinical as well as basic cardiorenal research.

Together, these research teams will bring cardiorenal research forward in AMICARE, exploiting the full potential of close collaboration and

combining expertise. As such, they will establish a working life cycle for AMICARE going from patient characterisation over clinical and basic cardiorenal research to clinical translation and valorisation of research results through close private partnerships collaboration, hand in hand with academic, clinical and public health education.

			
Early detection	Understanding & interference	Therapy & regenerative medicine	Prevention & education

- | | | | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> ▶ Identification of early detection markers ▶ Development of diagnostic & predictive tests | <ul style="list-style-type: none"> ▶ Identification of disease mechanisms & risk factors ▶ Derivation of therapeutic candidates ▶ Artificial intelligence for the analysis of complex systems | <ul style="list-style-type: none"> ▶ Development & testing of target-oriented drugs & therapy approaches ▶ Development of approaches for organ repair ▶ Innovative, interdisciplinary forms of care | <ul style="list-style-type: none"> ▶ Public health education ▶ Clinical & scientific education and training |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|

Strategy of AMICARE: Each of the research topic areas offers extensive added value for pharmaceutical companies, biotech companies and medical device manufacturers, thus to jointly drive forward clinical translation to improve the life quality of cardiorenal patients.

► Innovation model



Clinical and translation-driven research:

AMICARE integrates a study center for phenotyping of cardiorenal patients and clinical studies, as well as harbors active public-private partnerships in one institute. Thereby, AMICARE works from bedside (patient material) to bench-side (research bench) and back to the patient. With this approach, AMICARE acts as a dedicated translational research institute, centered around the cardiorenal patient.

Research platforms, integrating cross-border interdisciplinary expertise:

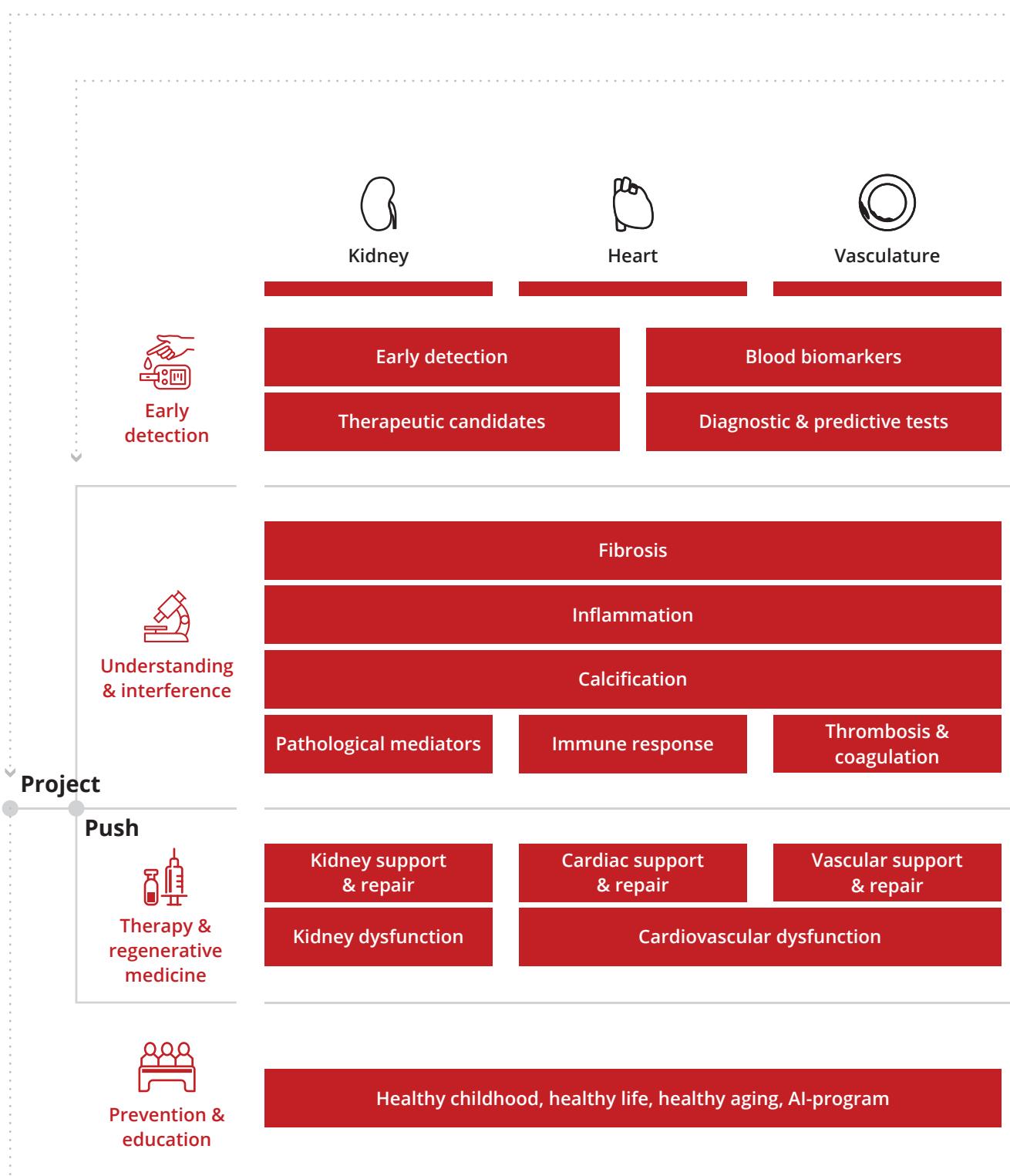
AMICARE actively integrates research platforms from dedicated research groups with interdisciplinary expertise as well as public-private partnerships. This ensures innovation and further development of cutting-edge technologies and applications, as being essential for competitive research. Furthermore, for optimal knowledge and technique exchange, AMICARE is devoted to intensively collaborate with its mother institutes within the RWTH Aachen and Maastricht University, as well as with external partners from Germany, the Netherlands and internationally.

Public-private partnerships, technology push and market pull:

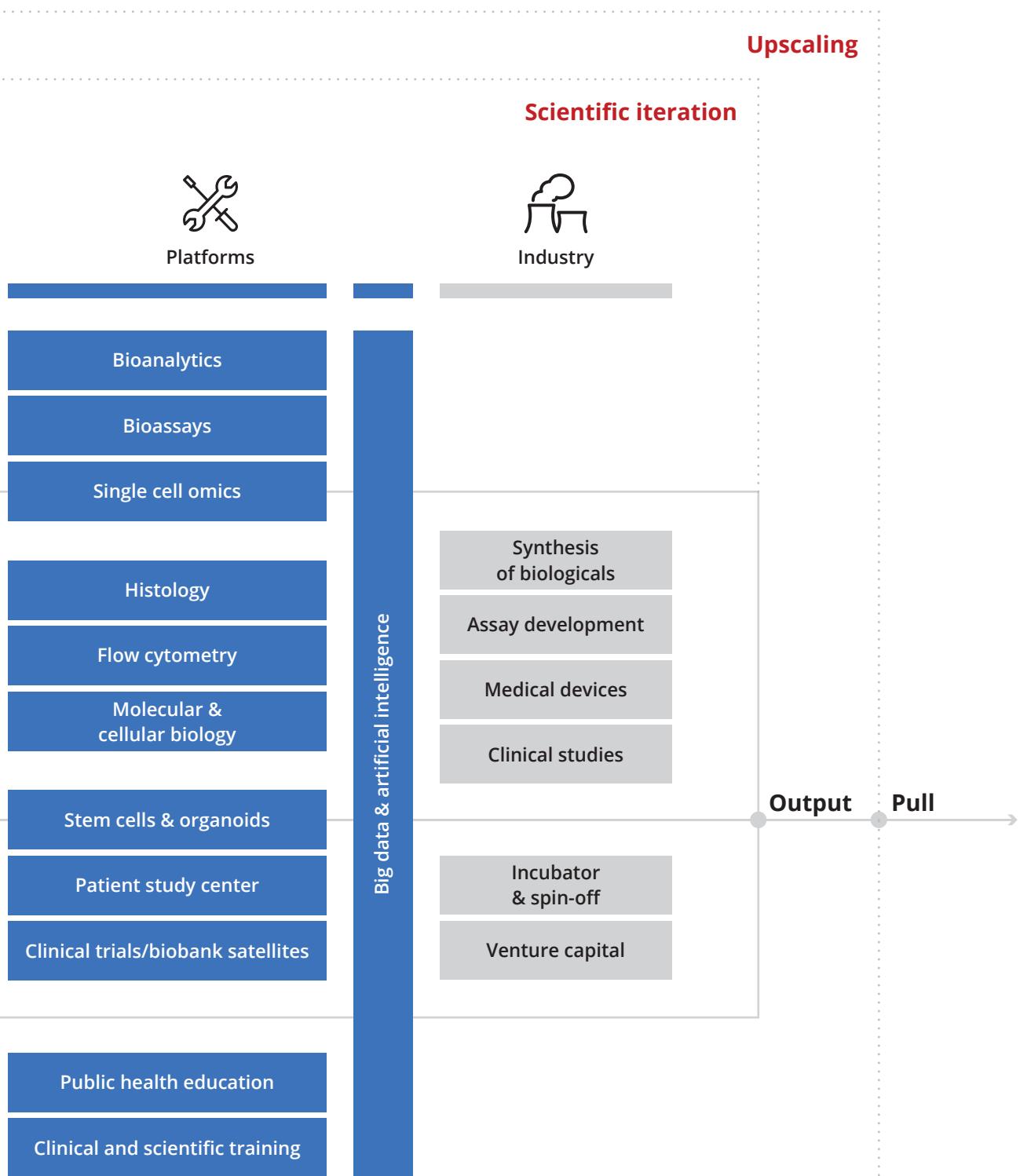
With the cardiorenal patient as center point of AMICARE, clinical translation and valorisation of research results is essential for AMICARE's mission.

To this end, AMICARE integrates international, interdisciplinary project-driven research and cutting-edge technology (technology push) with in-house private partner-driven and market-focused research, mainly dictated by the patient itself as well as the private partners (market pull).

Close collaboration between the different disciplines will create internal feedback loops between technological possibilities and medical needs as well as product applications at the market. These feedback loops ensure relevant and targeted innovation, at the benefit of the patient.



The innovation model: Dedicated research teams are working on selected scientific topics in alignment with the scientific pillars (red boxes). Research platforms covering main required technologies are integrated through dedicated research groups at the institute (in blue boxes). Application domains and translation fields are indicated in light grey.



► How AMICARE can overcome current hurdles of research translation and valorisation

01

Solution

Researchers investigate independently of clinicians, and thereby often do not address the real challenges that the patient and clinicians are confronted with.

In AMICARE, researchers work intensively together with clinicians to jointly identify the most valuable topics that best address the clinical and patient's need.

02

Solution

Researchers mostly perform their research independently of private partners: Universities file patents, but companies are not aware or are not interested in them, because the results and patents are not advantageous from exploitation point of view.

In AMICARE, researchers and clinicians work intensively together with private partners to jointly identify the most promising topics for research translation and valorisation, and then work them out and patent together. Only such approach can result in high valorisation, since projects are selected based on valorisation and exploitation potential together with the exploitation partners, taking into account economic and feasibility factors.

Summary

In summary, the unique, direct and interdisciplinary interaction of basic researchers, clinicians and private partners (pharmaceutical companies, biotech and medical device companies) in AMICARE offers exactly what is needed to increase research valorisation.

► Why AMICARE is interesting to private partners

01

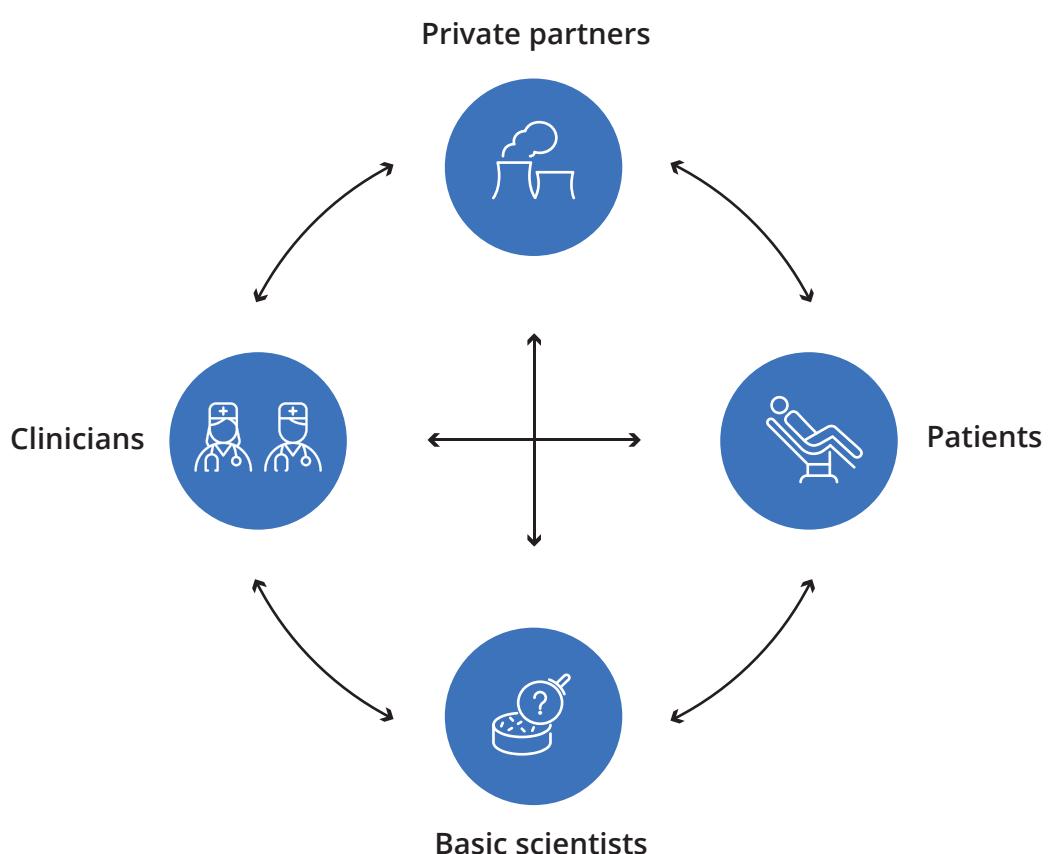
Direct contact with clinicians as well as basic researchers for the identification and development of diagnostics, novel therapeutic strategies as well as medical devices

02

Direct contact with patients as well as clinicians for clinical studies

03

Interdisciplinary expert knowledge to enable research, therapy and product development as well as valorisation in one institute by integrating basic researchers, clinicians as well as private partners with interdisciplinary expertise.



► Why **AMICARE** is interesting to patients

A statement of Bundesverband Niere e.V.

Almost half of the patients suffering from chronic kidney disease develop cardiovascular disease in an advanced stage kidney insufficiency. The quality of life of those affected is thus severely restricted and life expectancy is considerably shortened. Effective treatment options are hardly available and the success of treatment for simultaneous kidney and cardiovascular disease ("cardiorenal patients") is significantly reduced. The self-help network Bundesverband Niere e. V. wants to achieve that these patients and their relatives live better and longer with the disease.

In our opinion, the exploration of the underlying causes of the significantly increased mortality of patients with chronic kidney disease from cardiovascular diseases will lead to a sustained improvement in the quality of life and a reduction in this cause of death. With AMICARE, the first international research center focusing on cardiorenal patients will be established and contribute to improving quality of life and life expectancy. In addition to interdisciplinary cooperation between clinicians and basic researchers, the active involvement of public-private partnerships and kidney patients is a key element of AMICARE's successful concept. Patient-oriented research as well as the development of innovative diagnostics and therapeutic approaches is guaranteed by a prompt clinical translation.

It is clear that the active participation of patients and their organisations in basic research up to drug and medical device research and development is a qualified enrichment for all involved parties and will improve the results.

The direct contact between researchers, clinicians, companies and kidney patients structures the communication, and the latest discoveries and developments are immediately implemented into practice. This feedback carries the research results and ensures a secure path into the future. This also enables patients to work out a responsible treatment concept together with the treating physician ("Shared-Decision-Making"). This is likely to become a crucial factor in the adherence of the agreed treatment strategies and the resulting treatment successes.



Peter Gilmer

President of
Bundesverband Niere e.V.
(Federal Association of
Kidney Diseases e.V.)

President of
Patientenstiftung Aktion
Niere (Patient Foundation
Action Kidney)

On the other hand, active patient participation in research and therapy development can identify and understand unmet needs. The involvement of kidney patients in AMICARE's study center allows to identify relevant biomarkers and mediators of kidney and heart disease and to learn how to deduce or improve diagnosis and treatment options.

The cooperation between AMICARE and us, the kidney patients, is therefore a lucky win-win situation: The patients are "authorized" and the research and industry gets to know the "other side" in order to balance therapy approaches optimally in accordance to the patients and their living environment.

EMBEDDING OF AMICARE



Within the Medical Faculty of the RWTH Aachen and the University Hospital (UKA), AMICARE represents a direct extension of the Institute for Molecular Cardiovascular Research (IMCAR), the Department Cardiology, Nephrology and Pathology, as well as the Helmholtz Institute for Biomedical Engineering. Together, their clinicians and researchers strive for scientific excellence in the field of cardiovascular and renal disease.

With an outstanding track record in the identification and characterisation of pathological mechanisms and mediators underlying CKD and CVD, the availability of a broad range of techniques including molecular and cellular analyses tools, histology and high-end mass spectrometry combined with well-characterized patient samples, these partners have evolved together into a translation-oriented research group for cardiorenal disease.



Maastricht University



Maastricht UMC+

Similarly, AMICARE represents a direct extension of portfolio for the Faculty of Health, Medicine and Life Sciences of the Maastricht University and the Maastricht University Medical Center (MUMC). The Cardiovascular Research Institute Maastricht (CARIM) comprises a multitude of cardiovascular-oriented basic and clinical research groups and is one of the largest cardiovascular research institutes in Europe.

CARIM focuses on three main spear points: blood, vessels and the heart. CARIM offers a broad range of facilities covering the entire field of translational cardiovascular research.



► AMICARE in relation to the RWTH Aachen University and the Maastricht University

AMICARE as joint international institute of the RWTH Aachen University and the Maastricht University

Building on and extending the successful cooperation between Aachen and Maastricht over the past years, AMICARE as joint international institute of the RWTH Aachen University and the Maastricht University will provide the required innovation breeding place for fruitful exploitation of the established collaboration.

Within AMICARE, basic researchers and clinicians from both Aachen and Maastricht will combine expertise and efforts.

Within its patient study center, phenotyping of cardiorenal patients and clinical studies will be performed and active public-private-partnerships within AMICARE will ensure cutting-edge, industry-relevant and patient-oriented research with effective clinical translation.

AMICARE installed on RWTH Aachen University location

RWTH Aachen location

All partners will actively work together in the international AMICARE institute, with its offices and laboratory spaces installed on the RWTH Aachen location nearby the University Hospital Aachen. This guarantees the close interaction of patients, clinicians and researchers. Additionally, private partners will be actively involved.

Nucleation site

The Center for Bio-Medical Technology (ZBMT) currently offers space for the nucleation of AMICARE and its public-private partnerships. This building is located on the "Campus Melaten" at a ca. 200 meter distance from the University Hospital Aachen and is specifically tailored to the needs of public-private partnerships focussing on biotechnology and medical technology companies.

Building plan

Furthermore, initial steps towards a building plan for our AMICARE institute have been taken with regard to building content and requirements, and are currently being further worked out.



- 7500m² rentable area
- 30% of capacity reserved for industrial partners
- ca. 40M € building costs (ex. premises, basic equipment)
- 170 FTE

► Academic and clinical partners of AMICARE

Initiators (*Main appointment):



Prof. Dr. Jankowski
IMCAR
(RWTH/UKA*, UM)



Dr. Noels
(Director)
IMCAR
(RWTH/UKA*, UM)



Prof. Dr. Hackeng
CARIM, Biochemistry
(UM/MUMC*, RWTH/UKA)



Prof. Dr. Marx
Cardiology
(RWTH/UKA*)



Prof. Dr. Crijns
CARIM, Cardiology
(UM/MUMC*)



Prof. Dr. Floege
Nephrology
(RWTH/UKA*)



Prof. Dr. Biessen
CARIM, Pathology
(UM/MUMC*, RWTH/UKA)



Prof. Dr. Schurgers
CARIM, Biochemistry
(UM/MUMC*, RWTH/UKA)



Dr. Ramakers
Business developer
(UM*, RWTH/UKA)

Together with an interdisciplinary team of scientists and clinicians from:

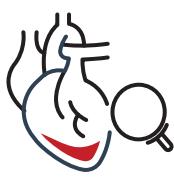
Cardiology
(RWTH/UKA)



Nephrology
(RWTH/UKA)



Institute for Molecular
Cardiovascular
Research (IMCAR)
(RWTH/UKA)



(Helmholtz) Institute
for Biomedical
Engineering
(RWTH/UKA)



Pathology
(RWTH/UKA)



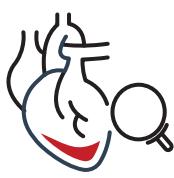
Cardiology
(UM/MUMC)



Nephrology
(UM/MUMC)



Cardiovascular
Research Institute
Maastricht (CARIM)
(UM/MUMC)



Biochemistry
(UM/MUMC)



Pathology
(UM/MUMC)



► Private partners of AMICARE

AMICARE offers extensive added value for pharmaceutical companies, biotech companies as well as medical and digital device manufacturers. Companies are being officially enrolled as official member of AMICARE for a period of up to five years.

► ACTIVE AND TIMELY DEVELOPMENT OF AMICARE

Intense and fruitful collaboration

- ▶ between the Maastricht University and the RWTH Aachen
- ▶ initiated by the Aachen-Maastricht Cardiovascular Graduate School "EuCAR" (2008-2011)
- ▶ and extended through research platform "IMCARIM" with shared professors, research group leaders and PhD students



Lead of two Marie Skłodowska Curie International Training Networks on Cardiorenal Disease

INTRICARE (lead in Maastricht by Prof. Hackeng & Prof. Schurgers) & **CaReSyAn** (lead in Aachen by Prof. Jankowski & Dr. Noels)

Lead of German SFB/TRR219 Consortium on Cardiovascular Disease in Aachen

by Prof. Jankowski & Dr. Noels

Scientific content & unique selling points of AMICARE defined

- ▶ Translational focus (diagnostics, therapy, medical devices)
- ▶ "Humanised institute" with study center for patient phenotyping & clinical trials
- ▶ Public-private partnership in one building
- ▶ Artificial intelligence in medicine
- ▶ Active public health education



Q1/2008

Q3/2017

Q1/2018

Q1/2019

Q2/2019

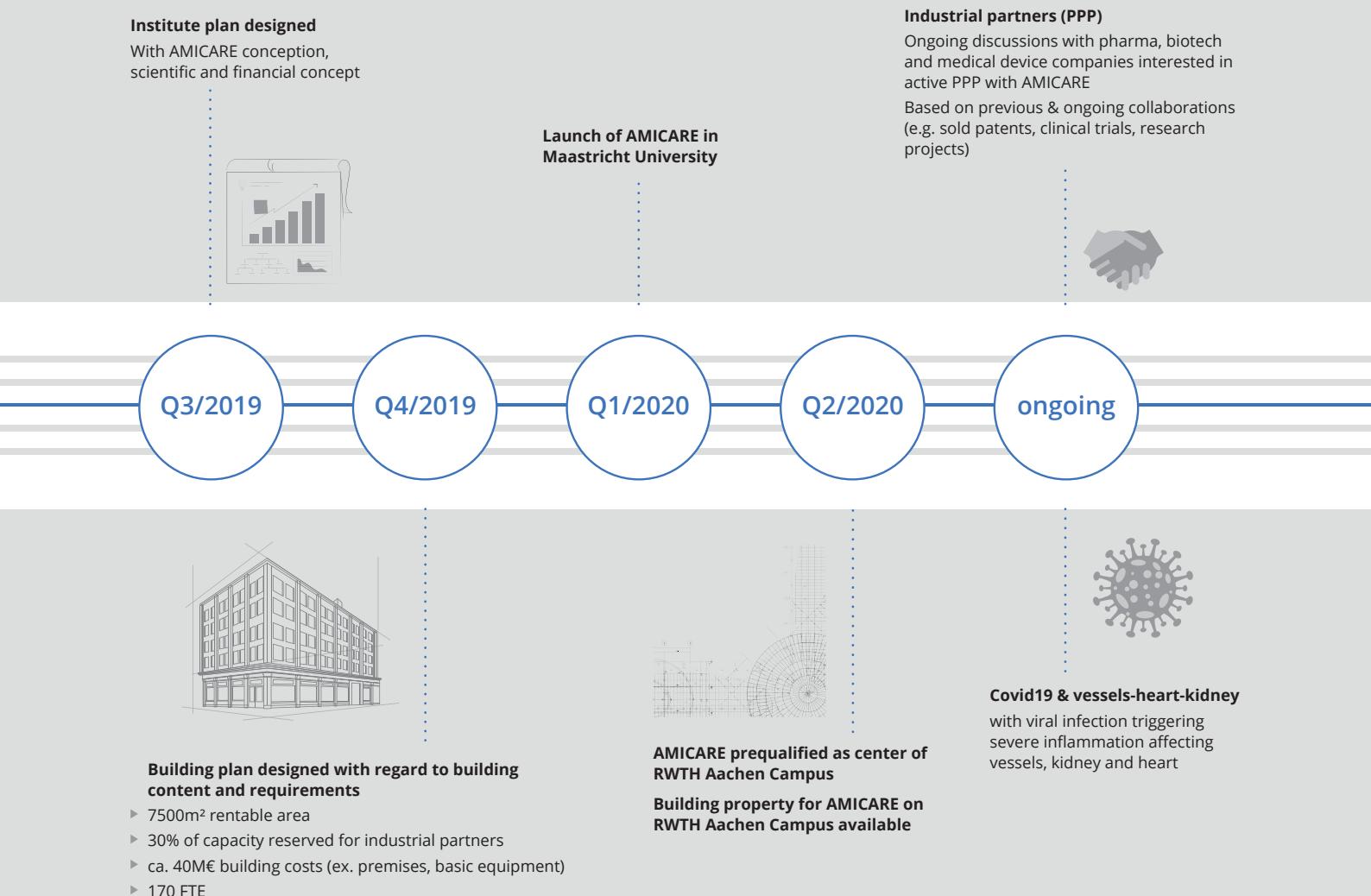


AMICARE as „Aachen-Maastricht Institute for CardioRenal Disease“ launched at RWTH Campus
under impulse of both the RWTH Aachen and the Maastricht University



Active integration of Aachen-Maastricht partners in AMICARE

- ▶ Cardiovascular Research Institute Maastricht (CARIM), UM/MUMC
- ▶ Biochemistry, UM/MUMC
- ▶ Institute for Molecular Cardiovascular Research (IMCAR), RWTH/UKA
- ▶ Cardiology, RWTH/UKA, UM/MUMC
- ▶ Pathology, RWTH/UKA, UM/MUMC
- ▶ Nephrology, RWTH/UKA
- ▶ Nephro-Cardiology, RWTH/UKA
- ▶ Helmholtz Institute for Biomedical Engineering, RWTH/UKA





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Maastricht University



Maastricht UMC+



Contact

Prof. Dr. Joachim Jankowski

jjankowski@ukaachen.de

Pauwelsstraße 17, 52074 Aachen

Dr. Heidi Noels

hnoels@ukaachen.de

+49 (0)241 80 80580

Prof. Dr. Tilman Hackeng

t.hackeng@maastrichtuniversity.nl

www.eu-amicare.eu

www.eu-amicare.de

www.eu-amicare.nl