

A man with grey hair, wearing a blue checkered shirt and khaki shorts, is sitting on a large, mossy rock. He is looking out over a body of water towards a bright sunset. The sun is a large, glowing orb on the horizon, casting a warm orange glow across the sky and water. The man's back is to the camera, and his legs are crossed at the ankles.

# Improving Quality of Life for People with Neurodegenerative Diseases

Stockholm Researchers and Health Tech Companies

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## Executive summary: Stockholm Uppsala – a world leader in the field of healthy ageing



PHOTO: SINA GRANFORS / JOHNER

Improved health of people in later life is a global success but it also represents a societal challenge as more retired people need to be supported in order to live dignified and meaningful lives.

It is estimated that the number of people with dementia will increase from 50 million today to 150 million in 2050. Alzheimer's disease is the most common form of dementia and is a major cause of disability and dependency among old people worldwide. The cost to society of Alzheimer's disease is greater than that of cancer and cardiovascular disease combined. But despite alarming projections for the number of cases, R&D funding for this condition is still only around one twentieth of the funding for oncology.

Parkinson's disease is another progressive neurodegenerative condition that can have a devastating impact on quality of life. Around 10 million people currently have Parkinson's disease – although four percent of those affected are diagnosed before the age of 50, the incidence increases significantly with age and it is the fastest growing neurological condition globally.

Universities and research institutes in the greater Stockholm region are carrying out vital research into these diseases, which will help to achieve early diagnosis and reduce the impact of neurodegenerative conditions on people's lives. The universities are working closely with health tech companies to develop new technologies which can facilitate research and support people in old age. As Stockholm is established as a global leader in the field of healthy ageing, its scientists and business community are keen to transfer their knowledge and experience to the rest of the world, and to welcome new companies to the region.

In this brochure, Miia Kivipelto discusses FINGERS model for lifestyle interventions which can improve brain health and reduce the risk of cognitive impairment. Professor Kivipelto is leading a large number of international projects and has recently been awarded The Ryman Prize for the best work carried out anywhere in the world that has enhanced quality of life for older people. She is Professor in Clinical Geriatrics at Karolinska Institutet's Center for Alzheimer Research in Stockholm and Director of Research and Development, Theme Aging, Karolinska University Hospital.

Pharmtech company Alzecure is also working in close collaboration with the Karolinska Institute to develop targeted drug therapies for the treatment of Alzheimer's disease, other diseases of the central nervous system, and pain.

Leading neurological experts from Stockholm's universities are currently involved in important research projects to investigate Parkinson's disease, in collaboration with other major European institutions. The EU Joint Programme on Neurodegenerative Disease Research has recently awarded funding to a project on the dynamic modelling of deep brain stimulation (DBS) to enhance the outcome of DBS in Parkinson's patients, which relies on the patient-specific modelling platform developed in a long-term collaboration between Professor Dag Nyholm at Uppsala University Hospital and Professor Alexander Medvedev at Uppsala University. Professor Nyholm's clinical research group has contributed to the development of three new, levodopa-based therapies for Parkinson's disease that have gained international recognition.

Stockholm's success in this field is actively promoted by a number of institutions devoted to healthy ageing and the investigation of neurodegenerative diseases. These include the FINGERS Brain Health Institute, the Ageing Research Centre (ARC), Swedish Brain Power, the Swedish Neuroscience Institute and the Centre for the Advancement of Integrated Medical and Engineering Sciences (AIMES). Collaborations between these institutions, the universities, health care providers and startup companies are helping to make the latest technology in lifestyle support available to more people both locally and overseas. Widespread digitisation in Sweden promotes innovation, and recent advances are resulting in the implementation of new technologies that couldn't have been imagined a decade ago.

**Brief profiles are provided for four such companies:**

**Stardots** – which is developing a digital health platform for Parkinson's disease

**Pilloxa** – which has produced a smart pill box to improve medical adherence and patient retention in clinical trials

**Minnity** – which is promoting a personalised approach for carers

**Geras Solutions** – which is revolutionising the diagnostics of cognitive diseases such as Alzheimer's.

The development of new technologies represents a huge market that will be further expanded as the number of older people increases and more scientific breakthroughs are realised. The Stockholm region's success is driven by its world leading research base, a diverse talent pool and a readily accessible testing environment. This is already attracting health tech companies from overseas, helped by targeted government support, a strong financial community and a wide range of professional services, in addition to the welcoming attitudes and exceptional lifestyle that can be enjoyed in Stockholm.

We at Invest Stockholm are doing all we can to promote the sector – so if you are interested in what's on offer, whether to invest, collaborate or set up, we are here for you.

**Ylva Hultman**

Head of Life Science, Invest Stockholm

## How the FINGERS model for lifestyle interventions can improve brain health and reduce the risk of cognitive impairment



Miia Kivipelto is Professor of Clinical Geriatrics at the Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm

Miia Kivipelto is originally from Finland. She studied medicine at the University of Kuopio and gained her PhD with a thesis on vascular risk factors for Alzheimer's Disease (AD) in 2002. Since 2009 she has led the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) clinical trial, which demonstrated that a multidomain intervention of diet, exercise, cognitive training, social activities, and vascular risk monitoring can preserve cognitive functioning in elderly people with elevated dementia risk. Her research is world leading, practical and influential, and has helped improve the lives of older people around the world.

She is currently Professor in Clinical Geriatrics at Karolinska Institutet's Center for Alzheimer Research in Stockholm and Director of Research and Development, Theme Aging, Karolinska University Hospital. Her Nordic-UK Brain Network team includes over 100 research and clinical staff and is also based at the University of Eastern Finland, the Finnish National Institute for Health and Welfare, and Imperial College, London, UK. Prof. Kivipelto leads the World-Wide FINGERS initiative, which aims to test, adapt and optimise multi-domain dementia prevention trials based on the FINGER model and share data internationally. WW-FINGERS currently includes

over 30 countries from all continents. In addition, she is co-founder of the FINGERS Brain Health Institute in Stockholm.

Miia Kivipelto has been the recipient of numerous prizes. In December 2020 she was awarded The Ryman Prize by New Zealand Prime Minister Jacinda Ardern, in recognition of her research into the prevention, diagnosis and treatment of cognitive impairment, AD and dementia. The Ryman Prize is an annual \$250,000 international award for the best work carried out anywhere in the world that has enhanced quality of life for older people. It is the richest prize of its kind in the world.

### Could you briefly describe your research area

Dementia is one of the major causes of disability and dependency among old people worldwide. It is estimated that the number of people with dementia will increase from 50 million today to around 150 million by 2050. The World Health Organization has designated dementia a "global priority for health".

The brain is often the weakest link as we get older, and the challenge is that there are no effective disease modifying drugs for AD. The failure rate in AD drugs under development has been 99.6% and no new drugs have been approved since 2002. Our main progress is in understanding risk and developing prevention strategies. This has been the area in which so much has been achieved, especially with our research in Sweden and the Nordic countries.

The FINGER study started 10 years ago and involved 1,260 elderly people from the general population. It yielded fantastic data from a randomised controlled trial highlighting the role of modifiable risk factors. This was the crucial step, allowing us to move from observation to action.

There are two important FINGER concepts:

1. The first is multidomain intervention, in which we put together different risk factors. It's like five fingers, with physical activity, cognitive training, social activities, healthy balanced diet, and taking care of all vascular and metabolic risk factors like blood pressure, type 2 diabetes, cholesterol and obesity. What is good for the

heart is also good for the brain. The whole multidomain concept comes together with the understanding that dementia and AD are multifactorial disorders, so it is not enough to target a single risk factor – we need to look at several risk factors at the same time to get the optimal preventive effect. FINGER was the first large scale trial to show that a multidomain intervention can prevent cognitive decline.

2. This also nicely links with the concept of brain plasticity. Neuroscience studies show that everything that we do can affect the structure and function of the brain. This provides a great opportunity for lifestyle interventions that can improve brain health and reduce the risks of cognitive impairment.

I think these two important concepts were there in the FINGER study and show that we can prevent or reduce the risk of dementia. Recent studies show that at least 40% of dementia is related to factors that can be influenced, including blood pressure, type 2 diabetes, depression, education and physical activity. There are also several new risk factors so this may be a conservative estimate.

#### **How did World-Wide FINGERS come about?**

These strong results from the FINGERS study were why we got so much attention when we published our findings in *The Lancet* in 2015. After that there was huge interest globally and we launched the World-Wide FINGERS in 2017 to support harmonisation of international prevention studies, focussing on at risk people and patients at the early stages of AD. I'm very happy that at the end of 2020 we have over 30 countries from all continents which are participating in the World-Wide FINGERS.

Unfortunately, there is no miracle cure for dementia and AD – our research focuses on identifying who is at risk, early diagnosis and finding ways in which risk factors can be reduced in order to delay the onset of the disease. We now have population-based studies with more than 30 years' follow-up data, which demonstrate that there are several modifiable risk and protective factors during the whole lifetime. We have developed a tool that can score dementia risk, and this has been widely adopted to target the interventions for those most at risk.

World-Wide FINGERS is a great opportunity to get big data which will help us to optimise the FINGER model in different settings and in different cultures. We understand that although we developed a model, one size doesn't fit all – we all have different risk profiles and we're aiming to optimise the model for different groups and settings.

#### **What's happening with FINGERS 2.0?**

World-Wide FINGERS led us to the new concept of FINGERS 2.0. This is a more individualised, more

personalised FINGER model which will be combined with possible disease modifying drugs. It's not simply lifestyle or drugs – we think that if we combine them, we can get an even better effect.

The initial study will be a combination trial involving multimodal lifestyle interventions and the drug Metformin. Metformin is used in many countries as the first-line medication for the treatment of type 2 diabetes. Vascular dementia occurs due to brain damage that is often caused by reduced or blocked blood flow to the brain, and many people with type 2 diabetes exhibit brain changes that are typical for both Alzheimer's and vascular dementia.

The official title of the trial is "MET-FINGER-ApoE: A randomised controlled trial of multimodal lifestyle intervention and metformin to prevent cognitive impairment and disability in a cognitively healthy APOE4 enriched at-risk population". It will involve around 600 subjects and will be carried out in Sweden, Finland and the UK. We hope it can get underway in the second quarter of 2021.

I think that the drug repurposing approach is very interesting because we do not yet have any specific AD modifying drug that we could easily combine with lifestyle interventions. Using this model, we may be able to develop a next generation of clinical trials for the precision prevention of dementia and AD. I think that this concept is getting very important in complex disorders like late-onset AD.

#### **What has been the impact of COVID-19 and what are the latest developments?**

In the middle of the pandemic, I'm happy that we have been able to move on with our research and that the interest is still really strong. Because we have the FINGER studies and the WW-FINGERS Scientific Helpdesk here in Stockholm, we find that we are getting international researchers and companies coming to us. We're also seeing more collaborations with different stakeholders and public-private partnerships, which are developing and testing new technology and solutions to put our research into practice.

In fact, the COVID-19 pandemic has been speeding up this process because we can't carry out our studies and implementation as we used to do. We can't have the face-to-face meetings or ask people to go to the gym or do the cognitive testing in our centres, which means that we need to use more new technology. For this reason, we've started collaborations with companies using technology for testing and remote monitoring.

We are trialling some online cognitive testing and dementia risk score tools. We try to cover the whole



patient journey from risk reduction to early detection to post diagnostic support, which I think is very important.

We're also studying new risk factors like sleeping disturbances. We know that physical activity is good for the brain, and that stress and sleep disturbances are risk factors that are becoming more common in modern societies. But these have been difficult to study because measuring stress or monitoring sleep patterns is not as easy as measuring blood pressure or blood glucose. So here we see a lot of interest from different companies, which are looking at how it may be possible to develop and use devices to measure these types of parameters in a more objective way.

#### **Which are the main institutes that you're working with nowadays?**

My main position now is at Karolinska Institutet and we also have the FINGERS Brain Health Institute in Stockholm which I set up with Professor Maris Hartmanis in 2019. This is our main hub but part of my research team, the Nordic-UK network, is based at the University of Eastern Finland's Centre for Neuroscience, the Finnish National Institute for Health and Welfare (which has wonderful population-based registers and is the coordinating centre for FINGER study) and Imperial College London.

I would say that through World-Wide FINGERS we're connected with more or less all the leading universities in our field. As an example, I'm leading the Euro-FINGERS consortium that is funded by the Joint Programme of Neurodegenerative Disorders (JPND).

[www.neurodegenerationresearch.eu/wp-content/uploads/2020/06/PROJECT-EU-Fingers.pdf](http://www.neurodegenerationresearch.eu/wp-content/uploads/2020/06/PROJECT-EU-Fingers.pdf)

I am coordinating the consortium from KI in Stockholm and other partners include institutes from Finland, the Netherlands, Germany, Spain, Luxemburg and Hungary.

In addition, we're working with patient organisations and companies, including a company focusing on IT solutions and tools for clinical decision support and a company working with medical food for AD. I think that the Euro FINGERS is a nice example of how we are bringing together leading research institutes, patient organisations and industry.

#### **How can the Stockholm ecosystem in the field of neurodegenerative diseases help to advance the science and improve quality of life for patients?**

There is a great sense of working together here in Stockholm and we feel very much part of the local community. Stockholm is a big city, but it's not a mega city, so we have a critical mass (I'm thinking Karolinska Institutet and Karolinska University Hospital, the Sci Life Lab, the FINGERS Brain Health Institute etc) and we also have a very effective infrastructure to promote cooperation.

I'm the director for research and development for Theme Aging at Karolinska University Hospital, and we have been working to create the infrastructure which allows us to integrate research, development and clinical care. The patients visiting our memory clinics are asked if they want to give informed consent that we can use their clinical data for research, and I think it's quite unique that almost all of the patients say yes. That is also the nice thing in Nordic countries, that that patients and participants are very positive about helping research.

We're also involved in a major collaboration with Gates Ventures, as they are keen to use the big data that is generated by World-Wide FINGERS. We've been looking at data sharing and harmonisation, and we need the appropriate infrastructure in place. There's big challenge in research now with the regulations over data sharing, so we're working with a federated database which would allow us to do joint analyses without sending the data. This is another nice example where we have collaboration with new stakeholders, and I think it's great that Gates Ventures approached us here in Sweden.

#### **Where would you like to go from here?**

We are keen to be involved in joint initiatives between academia and industry. There is a risk that academia is doing one thing and industry another. If we can combine our efforts, and I think we can, it will be better for everyone.

In Sweden, people have the mindset that we want to work together. Organisations like Invest Stockholm can facilitate the process so that we can find the right people to talk to. We are able to present ideas in an open way and move forward.

We currently have a great amount of interest in biomarkers which may be involved in the mediating pathways behind successful interventions. There is also a lot of promise for blood-based biomarkers in AD, which it may be possible to use as an early diagnostic tool in the future. Many of these studies involve several academic partners, pharma companies and also, more and more, IT companies.

It can take a lot of time to get new studies started so it's good to start discussing and brainstorming at an early stage to develop ideas for future collaborations. This could include data analyses, innovative technologies, novel biomarkers, and intervention strategies. I'm certainly open to new ideas!

MET-FINGER Trial is financed by both Alzheimer's Drug Discovery Foundation, ADDF ([www.alzdiscovery.org](http://www.alzdiscovery.org)) and Part The Cloud ([www.alz.org/partthecloud/overview.asp](http://www.alz.org/partthecloud/overview.asp))

## How leading researchers in Stockholm are driving innovation in patient care

Sweden is a world leader in the field of healthy ageing. Its population enjoys the highest number of 'healthy life years' of any European country, and also leads the UN/EU's Healthy Ageing Index<sup>1)</sup>. Research institutes, healthcare providers and the business community in the Greater Stockholm Area provide an ideal ecosystem to foster innovation and develop new treatments, technologies and lifestyle support systems which have the potential to dramatically improve the quality of life for patients with neurodegenerative diseases such as Alzheimer's and Parkinson's.

The Stockholm area has a very high competence level in geriatrics and various forms of dementia care. There is a huge openness in society for the uptake of digital and mobile ways of working, and the country has faced the challenges of an ageing society for a very long time. Sweden has the goal of being the best in e-health by 2025 and is making good progress towards this goal<sup>2)</sup>.

Stockholm's success in this field is actively promoted by a number of institutions devoted to ageing and the investigation of neurodegenerative diseases. Neurological experts from Stockholm's universities are also currently involved in major research projects in collaboration with other leading European institutions.

1) United Nations Economic Commission for Europe/European Commission (2019) "2018 Active Ageing Index: Analytical Report"

2) [www.government.se/information-material/2016/08/vision-for-ehealth-2025](http://www.government.se/information-material/2016/08/vision-for-ehealth-2025)



PHOTO: THERSE WIMBERG/JOHNER



## Universities – providing a strong R&D base and working with industry



Karolinska Institutet



KTH Royal Institute of Technology



Stockholm University

### The Stockholm trio – Karolinska Institutet, KTH and Stockholm University

Karolinska Institutet, KTH and Stockholm University are prominent universities in their respective fields and form a complete academic environment in the areas of medicine, technology, science, humanities, law and social sciences. Together, the universities have 5,200 doctoral students and a total budget of SEK 17.3 billion. As a unified academic environment, the Stockholm trio is among the strongest in the world.



Presidents of the Stockholm trio signing the alliance.

The trio plays a crucial role for the City of Stockholm and the Stockholm region when it comes to research, innovation and competence supply. With 17,000 employees and 55,000 students, it constitutes one of the region's largest employers and workplaces. The universities' activities are mainly gathered on a cohesive campus attracting many international students, doctoral students, researchers and teachers.

The three universities have a history of cooperation in a number of scientific fields, and in 2019 they formed **The Stockholm trio university alliance**, with the aim of promoting in-depth collaboration and providing new facilitates for university-wide research and education. Through the alliance, the universities will become more competitive globally and foster new international collaborations, helping to recruit leading researchers and attract more international students. The universities will also become a stronger force regionally and nationally by working together to engage decision makers, authorities, businesses and industry.

## Uppsala University

Uppsala University was founded in 1477 and is the Nordic region's oldest university. It is ranked among the top 100 universities in the world and is home to over 40,000 students. It can help municipalities, companies and organisations with skills enhancement for their staff through tailor-made courses.

The university's 5,000 researchers and teachers conduct world-leading research – among the University's alumni there are 15 Nobel laureates.



Uppsala University

### The largest universities in the Stockholm region are:

Stockholm University	44,806 enrolled students
Uppsala University	40,094 enrolled students
Linköping University	24,055 enrolled students
Royal Institute of Technology	15,726 enrolled students
Örebro University	12,851 enrolled students

## There are 29 universities in the Stockholm region



**Stockholm**  
The Capital of Scandinavia

- ✓ Stockholm **#4** university city
- ✓ Among **top 100** world wide:  
Stockholm University, Karolinska Institute  
and Royal Institute of Technology
- ✓ **53%** of Stockholm's population aged  
25-34 have tertiary education
- ✓ For people aged 25-64, **1.8%**  
in Stockholm county and **3.8%**  
in Uppsala are doctoral graduates
- ✓ The region enrolls **46%**  
of all university students in Sweden  
(155 000 students)

Sources: Swedish Higher Education Authority & OECD



## Research institutes

### **The FINGERS Brain Health Institute**

Realising the power of lifestyle changes to transform the lives of at-risk individuals, the Stockholm FINGERS Brain Health Institute was set up in 2019 by Professor Kivipelto and Professor Maris Hartmanis. It hopes to bridge the gap between innovative clinical research on brain health and translating the results into patient value, with a focus on personalised treatment methods.

The activities are focused on three main areas:

#### **Clinical Trial Centre**

This will establish a web-based brain health research platform for recruitment of volunteers for clinical trials. After initial assessment, suitable volunteers will be subjected to tests involving deep pheno- and genotyping, blood sampling, etc. to facilitate a thorough risk assessment prior to the clinical trial.

#### **Centre for Imaging and Diagnostics**

This will investigate tools for early detection of cognitive impairment. The centre will utilise novel technologies and tools such as AI, magnetic resonance imaging, "Big Data", bioinformatics, biomarkers, clinical decision support, etc. and pursue local and international collaborative research projects with other organisations.

#### **Centre for Translational Dementia Research**

Here the activities will be focused on facilitating rapid translation of clinical research results into personalised interventions and clinical practice.

#### **Ageing Research Centre (ARC)**

ARC is a multidisciplinary research centre established in 2000 by Karolinska Institutet and Stockholm University which is devoted to ageing and health. Its mission is to improve the health and wellbeing of older individuals by contributing to the understanding of the ageing process from a biomedical, and psychological and sociological perspective in relation to life-long social and physical contexts.

ARC conducts research and education and spreads research findings within and outside the scientific community. Research conducted at ARC is based on data from large-scale longitudinal studies.

#### **Swedish Brain Power**

This is part of ARC and is a national network of leading researchers in the fields of neurodegenerative diseases such as Alzheimer's, Parkinson's disease, and ALS. The network's overarching goal is to improve early diagnosis, treatment, and care of patients with such diseases.

Specific goals are:

- The development of early diagnosis methods to open possibilities for secondary prevention
- Detecting and evaluating possible treatment, care and preventive strategies in primary care and specialised settings.

#### **The Swedish Neuroscience Institute**

The Swedish Neuroscience Institute is at the forefront of clinical care. Almost all of its physicians perform clinical research to test the safety and effectiveness of new drugs and medical devices for diseases of the nervous system.

#### **The Centre for the Advancement of Integrated Medical and Engineering Sciences (AIMES)**

Established at the end of September 2020, AIMES is a joint initiative by the Karolinska Institutet and KTH, providing an academic environment for interdisciplinary research, education and societal benefits.

The intention is to offer researchers who occupy the borderland between technology and medicine, so-called intrinsically interdisciplinary scientists, twin affiliations. They will either be largely grouped with KTH and build a sub-grouping on the medical side, or vice versa.



## Current major research projects

### **Dynamic modelling of deep brain stimulation**

The EU Joint Programme on Neurodegenerative Disease Research has recently awarded funding to the project "Patient-specific dynamical modelling and optimisation of Deep Brain Stimulation" (DynaSti) to be carried out by a consortium comprising three clinical partners and three universities from four European countries. The project concept relies on the patient-specific modelling platform developed in long-term collaboration between Uppsala University Hospital (Professor Dag Nyholm) and Uppsala University (Professor Alexander Medvedev).

DynaSti aims to enhance the outcome of Deep Brain Stimulation (DBS) in Parkinson's disease through the individualisation and optimisation of stimulation settings. Computational software will replace the current practice of selecting stimulation pulse width, amplitude, and frequency by trial and error with a model-based patient-specific calculation. This will be achieved by incorporating insights from novel clinical studies into individualised mathematical models underpinning clinically relevant DBS programming tools.

Overall, DynaSti will acquire novel experimental data, extract new knowledge from it regarding the biologic mechanisms of DBS, and design model-based algorithms to improve its effectiveness. These algorithms will then be

tested in the participating clinics for improved convergence to optimal DBS parameters and patient benefit in terms of improved motor control, minimised side effects, and battery consumption.

### **Development of new levodopa-based therapies for Parkinson's disease**

Research in the Central Nervous System (CNS) field is broad and at a high scientific level in the Stockholm area. Professor Dag Nyholm's clinical research group has contributed to the development of three new, levodopa-based therapies for Parkinson's disease that have gained international recognition.

The first of these, the levodopa/carbidopa intestinal gel infusion, originally produced at the Uppsala University Hospital pharmacy is now a major product, available worldwide, at the US company Abbvie.

Several clinical trials of new CNS treatments are ongoing or planned, and there is a good collaboration between hospitals, academia and industry, to deliver practical solutions from scientific ideas.

With support from Invest Stockholm it should be possible to strengthen these processes, especially the innovative ideas that have not yet reached the large companies.



PHOTO: JAN TÖVE / JOHNER

## Developing targeted drug therapies for the treatment of diseases of the central nervous system, including Alzheimer's disease and pain

AlzeCure Pharma is based at Novum Science Building, at the Karolinska Institute in Stockholm. The AlzeCure organisation was founded in 2012 and was originally sponsored by the Swedish Alzheimer's Foundation. A commercial company was started in 2016, carrying out R&D to early clinical phase trials, at which stage its projects will be out-licensed. It has been listed on Nasdaq's First North Premier Growth Market since November 2018.

The company is developing a broad portfolio of symptom-relieving and disease-modifying/ preventive drugs for Alzheimer's disease (AD), pain and other serious illnesses of the central nervous system for which there is a great unmet medical need. Their focus is on small molecule drugs which are low cost and can be provided in an oral dose form, allowing them to be taken at home rather than administered at hospital. AlzeCure has three project platforms, each with two drug candidates:

**NeuroRestore®** – a novel first-in-class symptomatic treatment for cognitive disorders, such as AD

**Alzstatin®** – an innovative disease-modifying treatment for AD

**Painless** – two innovative projects for osteoarthritic and neuropathic pain, respectively

In 2020, AlzeCure published positive preclinical and clinical results for their leading NeuroRestore drug candidate, demonstrating improvement in memory and cognition, and a second drug candidate in NeuroRestore proceeded the next stage of development. They also acquired a new project for neuropathic pain, ACD440, for which a Phase Ib study was initiated in December. In 2021, AlzeCure will have study readouts in two of its clinical projects (ACD440 for neuropathic pain and NeuroRestore ACD856 for cognitive disorders in AD) and hope to file for a IIa study for ACD440.



AlzeCure's CEO Martin Jönsson leads an experienced and highly dedicated team

### What's the background to your company?

"We are a group of pharma people and scientists who are really engaged in finding solutions to tough problems. Some members of our team have been working on neurodegenerative diseases for over 20 years, originally at AstraZeneca. When AstraZeneca decided to focus on other indications, they were determined not to give up the fight to find a cure for Alzheimer's, and agreed to work in collaboration with Professor Bengt Winblad and his colleagues at the Karolinska Institute. Professor Winblad is one of the world's most cited researchers in neurodegenerative diseases. The Swedish Alzheimer's Foundation provided funding for the initial research, and AlzeCure rapidly evolved into a commercial company. Stockholm provides an ideal environment which minimises the risks of giving up a secure job in order to become an entrepreneur. There are networks that provide insight, education and, in many cases, access to investment that can help get ideas get off the ground. Here at AlzeCure, we give our employees the freedom to become involved in specific areas of research which spark their interest. Of course, they need to drive the projects that we are focusing on as a listed company, but at the same time we want to stimulate them to drive their passion.



This freedom to follow individual research interests benefits the company, as it motivates people to do a great job on our project plans, and it also stimulates them to go beyond what is required. Studies show that generally only around one of five people feel motivated and committed to their work, but here I can honestly say that 100% of our team are 100% committed – it's amazing to see.

**Could you describe your current research projects?**

We have two main projects focussing on Alzheimer's, one to stop the disease progression and another to help people who already have developed cognitive impairment. We also have two projects to help with pain management.

Alzstatin is aimed at stopping the progression of Alzheimer's disease. It appears that amyloid beta 42 is central to the development of AD, and that when large quantities are produced in the brain they aggregate and create bigger fragments which become toxic to the neurons. Over time they form amyloid plaques which are so characteristic for the disease, and these aggregates destroy the neurons and connections in the brain which become damaged and eroded. In pre-symptomatic Alzheimer's, it is possible to detect the build-up of plaque in the brain 15-20 years before clinical symptoms appear, but currently there are no disease-modifying or preventive treatments for Alzheimer's.

Our project focuses on suppressing the formation of amyloid beta 42 that creates these problems, with novel oral small molecules that target amyloid production by

modulating the enzyme and thereby preventing the formation and aggregation of amyloid. Antibodies currently in clinical testing target/eliminate various amyloid fragments like oligomers, protofibrils and plaques. We have one drug in the pre-clinical phase and another in the research phase.

NeuroRestore is a symptomatic treatment for people who have already developed symptomatic AD, as dysfunctional and dying neurons in the brain result in memory loss and dementia. Once this stage is reached, life expectancy is around 7-10 years. We have compounds that enhance neural signalling through neurotransmitters like BDNF (brain derived neurotrophic factor) and NGF (nerve growth factor) which are central to cognition. In preclinical animal models we have shown that following treatment, older animals with memory impairment and difficulty in learning become as good at learning and remembering things as young animals.

This treatment also involves novel oral small molecules, in this case focussing on improving neuronal function. These compounds act as enhancers of neurotrophins (promoting BDNF/NGF signalling) and the broad effect profile in this specific biological pathway enables multiple possible indications, including AD, Parkinson's disease, traumatic brain injury, sleep apnea, and other sleep disorders. We have recently started a new clinical trial, based on the positive results from May 2020 that supported further clinical development of the drug candidate. In the current Phase I trial, which started last December, we are looking at its safety and tolerability in humans.



Our Painless project is targeting neuropathic pain, osteoarthritic pain and other serious pain conditions. Neuropathic pain affects around 25–30 million people, and osteoarthritis and severe pain conditions affect over 250 million people worldwide. Our two projects target key mechanisms in pain signalling – this includes our TrkA-NAM project which has strong validation in the antibodies currently in clinical development. There is a major medical need for several different severe pain conditions, as only about 50% of patients with neuropathic pain respond to existing treatments, and opiates are generally not recommended as first line treatment because of the risk of abuse, overdose and secondary injuries.

We are now conducting a Phase Ib trial in Germany for one of our drug candidates for neuropathic pain, and we have another project in the research phase.

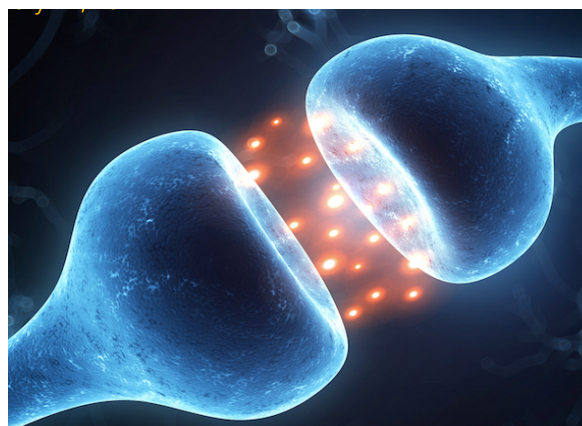
#### **What are the advantages of your approach?**

By working with small molecules instead of biologics, we see a number of benefits including improved penetration of the blood-brain barrier, which means that the drug candidates can reach their target in the brain much more easily than biologics such as antibodies. Small molecules are also much cost-effective than antibodies, which can be very expensive to produce. In addition, the treatment is more convenient for the patient, as small molecules can be taken orally (as a tablet) at home on a daily basis, rather than patients having to go to hospital for treatment every couple of weeks – this further reduces health care costs.

To my knowledge, there is no other Nordic company that has AD projects aimed at preventing the disease as well as treating the symptoms, which makes AlzeCure quite unique.

#### **Why are biomarkers so important to your work?**

Biomarkers are extremely important for us, especially when it comes to the Alzstatin project in AD, as they help to identify which patients should be treated, how the treatment is progressing, and how to regulate the dosing. For example, amyloid beta 42 can be used as a biomarker since it can be measured, and it's possible to monitor the ratio between amyloid beta 40 and 42. Imaging biomarkers such as amyloid-PET are used for inclusion and diagnostic endpoints, and there are also physical biomarkers, such as cognition, speech and movement, which show how the disease is progressing. At the start of a study, it's vital that patients are correctly diagnosed in order to be certain that they have AD, as only around 60 to 70% of people who show symptoms of dementia have Alzheimer's. Failure of the initial diagnosis is part of the reason why many trials have failed in the past, because they included subjects who weren't actually suffering from AD.



We're working with some of the world's most prominent researchers within the field of biological biomarkers connected to Alzheimer's, including Professor Henrik Zetterberg in Gothenburg. Blood-based biomarkers p-tau 217 and p-tau 181 are important because they are predictable, and so they help in patient selection. p-tau 217 has up to 95% predictability for Alzheimer's. As well as being involved in projects in Gothenburg, we continue to work very closely with the Karolinska Institute in Stockholm and publish joint papers. We helped to sponsor a PhD student and she's now a full-time member of our team. We're also working with American thought leaders, including Peter Snyder, who is a leading authority on Alzheimer's.

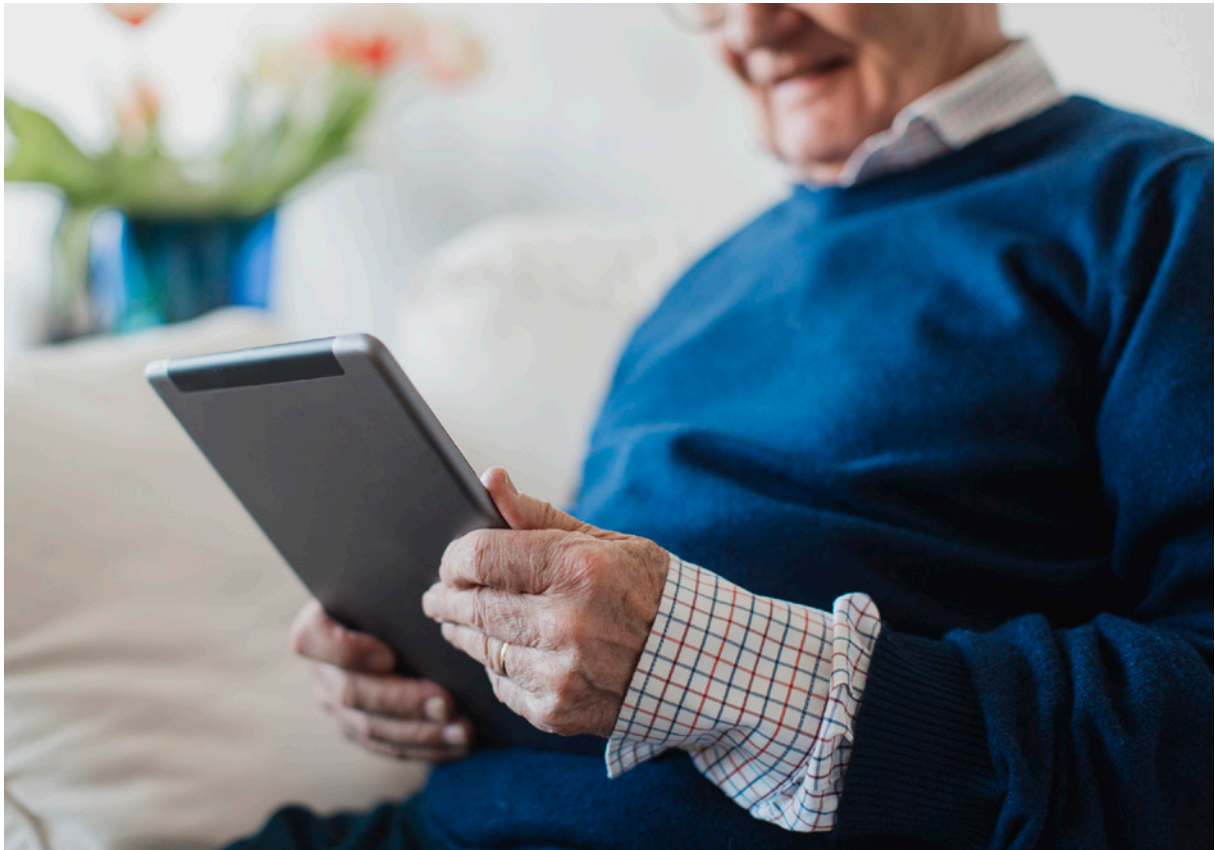
#### **Where do you hope to go from here?**

Fortunately, our trials weren't impacted by COVID-19 in 2020, and we're hopeful that the timelines for our ongoing trials in both Sweden and Germany will proceed according to plan. Our priority is to progress as quickly as possible with NeuroRestore. We're expecting initial results from the SAD (single ascending dose) part of the Phase Ia study this summer, and will immediately proceed to the next study. For neuropathic pain, we should be able to publish the results of the Phase Ib study this summer, and then our goal is to file for a Phase IIa study in autumn, perhaps in the US.

Despite COVID-19, there are signs that society is recognising the importance of tackling Alzheimer's disease. In January 2021, The World Economic Forum noted that it is a potential pandemic which could have a devastating impact not only on individuals but on society around the globe.

With some of our team having dedicated their working lives to researching this disease, we hope that we will be involved in achieving a reduction in the incidence and severity of Alzheimer's in the future, and the anxiety that people feel about how it may affect them and their families in later life.

## Stardots – a digital health platform for Parkinson's disease



Stardots AB, in a joint venture with Uppsala University and Uppsala University Hospital, is developing a revolutionary digital health platform for the treatment of Parkinson's disease. The cloud-based platform will offer a unique opportunity to quantify symptoms and optimise treatment. It will lead to significantly improved quality of life for the estimated 10 million people around the world currently suffering from the disease, and sharply reduced costs to society. The platform will also provide an extremely valuable database of raw data and results, offering unprecedented insights into the disease and opportunities to develop new treatments.

The core ideas were initially developed in response to neurological professionals' need for progressive markers of Parkinson's Disease that would aid decision-making and provide a more objective approach to this complex disease. Unfortunately, costly treatment programmes seldom reach their full potential, and treatment adjustments become more difficult as the disease progresses.

The Stardots platform is built upon many years of R&D and clinical trials at Uppsala University. The patient uploads sensor data to the platform from, for example, tremor, eye-tracking, blink-rate, speech, and gait measurements. The system then allows care to be provided remotely by non-specialist staff, and symptoms can be monitored to gain an understanding of the progression of the disease.

The platform is modular, highly scalable and cost-effective. In addition to quantifying symptoms and classifying subtype of Parkinson's, it will provide guidance for optimised individual treatment programmes. Fewer assessments will be needed, leading to lower associated costs. Also, care will be more objective and equitable, as it will not depend on geographical region, hospitals or neurological professionals.

The project is a true collaboration, combining world-leading scientists in mathematics and neurology with Stardots' development and commercial focus. The core technology and the foundation of the platform is the mathematical modelling of symptoms and treatments by Prof. Alexander Medvedev at Uppsala University.

“

I develop mathematical models and algorithms that help to save time on individualising and optimising advanced treatments of chronic diseases, such as Parkinson's. Caregivers can concentrate on what they do best – planning the treatment and communicating with the patient – and let software quantify measurable symptoms and suggest suitable intervention.”

*Alexander Medvedev*

Dr Dag Nyholm, a world class expert in Parkinson's from Uppsala University Hospital, provided expert neurological insights. He has validated the approach from a market perspective and designed the clinical trials.

“

This digital health platform concept, with objective symptom quantifications coupled with treatment suggestions is very interesting. The initial results are promising, and it is exciting to be part of the development process and as a leader of the clinical trials.”

*Dag Nyholm*

And Stardot's founder and CEO Dr Daniel Petrini has brought the ideas from the lab to the marketplace:

“

We are excited to bring this revolutionising digital health platform to the market. We provide a holistic approach to the care of Parkinson's Disease, and the platform will offer unique possibilities for caregivers and life-science companies to optimise treatments. What really counts is significant improvements in quality of life for the patient – that is our mission and focus.”

*Daniel Petrini*

Stardots has recently expanded to Boston and now has a strong connection and presence in the vibrant life-science community, including the renowned MassBIO organisation.

“

The solution that Stardots is developing is of the utmost importance. It is the only way if we want a state of knowledge that enables us to obtain better treatment methods than those that exist today”

*Lennart Petterson,  
Chairman of The Swedish Parkinson Foundation*

Stardots has already won a number of awards:

**“Game Changer 2019,”** Venture Cup

**“Future Entrepreneur of the year 2019”**  
third place, SvD/Carnegie

**“Attractive Innovation Project 2019”**  
at Uppsala University Innovations



## Improving medical adherence and patient retention in clinical trials



Poor adherence to prescribed medication schedules represents one of the biggest problems in healthcare, resulting in huge personal and financial costs. In the US, approximately 44% of men and 57% of women older than 65 years of age take five or more medications per week, and 12% of people in this age group take 10 or more medications per week.

Of the millions of people around the world who take regular medication, up to half have low adherence to medication. In the EU it is estimated that around 350 people die each day from not taking the right medicines at the right time – this is roughly equal to the number of people who die from a stroke daily. Many people also have a reduced quality of life due to their low adherence to a medication schedule.

Pilloxa started in 2015 when the founders of Pilloxa recognised the need to help people to take their medications while they participated in a Clinical Innovation Fellowship; a joint venture programme run by the KTH Royal Institute of Technology, Karolinska Institute and Stockholm County Council. With mixed backgrounds from medicine, technology and academia – the team set out to use technology to create a solution that can support adherence for people of all ages.

“

We researched and verified the need through hundreds of interviews with patients, relatives, caregivers, pharmacists, researchers and patient organisations, in

addition to a thorough literature study. In the clinical context, we really got to see what poor adherence could lead to: people coming into the emergency department with their medications in large grocery bags and surgeries being aborted due to failure to take the correct medication.

Today, Pilloxa is a patient-centric adherence platform that combines hardware, software and cloud services. Pilloxa provides actionable insights into studies and projects, which enable teams to take direct action, even remotely. It begins with creating a tailored experience for each investigation by combining ready-made modules with custom content to create a standalone app. Alongside the app, our technological platform can communicate in real-time with major Internet-of-Things (IoT) devices with open APIs. This means that our own electronic pillbox can be added to support patients who take oral medication in a pill form. The Pilloxa One smart pillbox has 14 compartments for individual doses with built-in sensors that will track if a medication is taken or not. It won't notify you if you remember your dose, but if you are late with taking your medication then you will receive a notification on the accompanying Pilloxa app.

Working with top pharmaceutical companies and some of the most prominent hospitals in the Nordics, Pilloxa is now being used in several therapeutic areas where adherence is of utmost importance because it optimises the chances of clinical trial and patient support programme success. Furthermore, the cost of monitoring is decreased since no manual data collection is needed.

Recently Pilloxa received €580k from the EU to validate our digital solution within the cardiovascular field and to further develop it together with the University of Oslo and Bayer in their ASTORIA study.

But Pilloxa is more than an adherence tool, we also provide a platform that keeps users engaged, well-informed and healthy. This is showcased by the feedback we receive from patients who have used our pillbox and are sad to return it at the end of projects or studies. Our ultimate aim is to enable patients to live healthier lives and we are always happy to support them. We are excited to drive the development in this field and are looking forward to making a difference for the millions of patients who medicate daily.”

*Per Nilsson*

## Promoting a personalised approach for carers

Minnity founder and CEO Katarzyna Hess-Wiktor has a personal story of growing up with a relative with dementia, a PhD in psychology and over ten years' experience of working internationally with training in elderly and dementia care. This has allowed her to create a solution for personalised care based on both research and experience.

The Minnity app is a working tool and a learning solution for professional caregivers. A relationship-based and personalised approach in care services has benefits for both caretakers and caregivers. Together with the provision of appropriate caring skills, it will help people in the later stages of life to remain independent for longer.

Information accessible via the app allows an individual's needs and preferences to be better understood and means they can become more comfortable with the carer. Even with inevitable staff changes, it provides a feeling of continuity and helps to ensure that care is of consistent quality. Interaction with relatives through the app promotes more effective communication with the care team, which increases the quality and efficiency of time spent with each carer. Through microlearning features in the app, the carer is able to develop person-centred care skills, leading to greater job satisfaction.

Minnity were finalists of the Stockholm Innovation Scholarship 2019. They were also nominated for 'Startup of the Year' and 'Best Health Tech Startup' in the Swedish finals of the Nordic Startup Awards.

“

The focus is on social care rather than health care and medical solutions. We are very much on the soft side of things, providing personalised, individualised care. The first step is to focus on professional carers so that they understand whom they are taking care of.

Approaching the market commercially is a challenge as it is very price sensitive. However, an increasing number of stakeholders realise that high quality care translates to savings and better use of resources. We have tested the app in both homecare and in nursing homes, thanks to Stockholm Digital Care, and are currently pilot testing the solution in Sweden and France with over 200 home and day care professionals who assist over 600 older people.



PHOTO: JUSTEM JOHNSON / JOHNER

In the upcoming months we will provide sufficient evidence to show that Minnity is helping companies to save money and at the same time delivering better care.

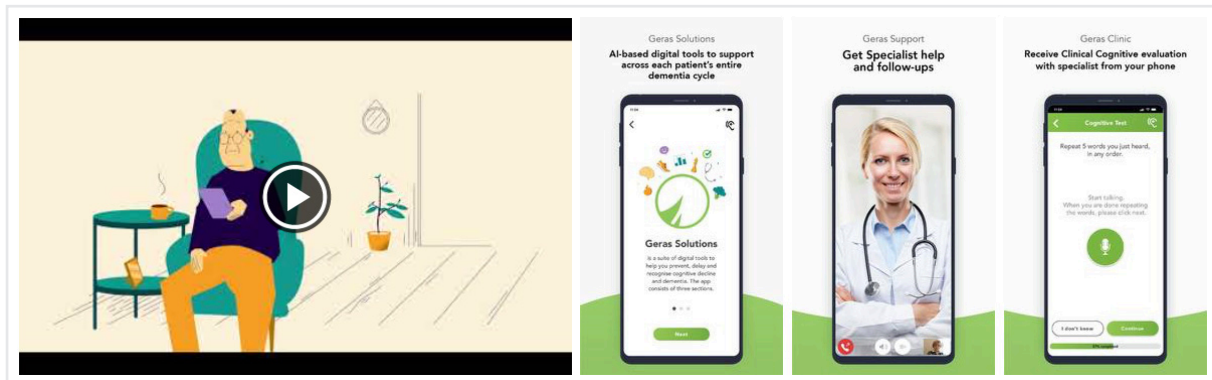
Many people are afraid of elderly care being taken over by robots and digital solutions, and the human touch being taken away. In reality, there is a fantastic opportunity to let people spend more time with their patients, while the technology takes care of the more mundane aspects of the work. This means that we can focus on what is most human and individualised in caring. This is going to happen because all around the world there is a lack of manpower – robots can be used to take over aspects of work that people don't like doing.

Swedish companies generally have a reputation for reliability and Invest Stockholm have helped in marketing and branding. Being part of their life science network opens the way for investment opportunities. We have also had the opportunity to host their #move-tostockholm Twitter account, which helped to increase our international presence.

The amount of positive feedback that we get from caregivers and the recognition that we have recently received in national awards are very motivating for our team. In the future there are likely to be many opportunities for integration and collaboration, for example with solutions that enable early screening or medication or care management. We have already established partnerships with companies providing elderly care training in France and Finland and are planning for further international expansion in Europe and beyond.”

*Katarzyna Hess-Wiktor*

## Geras Solutions – revolutionising the diagnostics of cognitive disease, such as Alzheimer's



Obtaining a correct diagnosis for a cognitive disease or dementia often involves long waiting times, which reduces the potential benefits of early interventions. Geras Solutions' mobile platform uses AI to simplify and streamline cognitive assessments, while processing and organising collected data to provide a clinically reliable overview. By digitalising traditional tools of dementia care, the app can help overcome obstacles that currently face this vulnerable group of patients and relatives.

CEO Rickard Forsman believes that Stockholm offers start-ups an ecosystem that simplifies access to guidance and resources that can be difficult to find elsewhere. Such access provides a pathway and door opener for young companies, primarily focused within the health-care or life science field, to implement innovative ideas and meet an increasingly growing need.

“

We strongly believe face-to-face engagement between patients, doctors or caregivers will always be necessary for healthcare. Still, with the ongoing COVID-pandemic and an ageing society in general, it is essential to ensure that adequate care is available by using technology to enhance our capabilities. Data analytics and AI offer a far superior decision support for better decision making.

Users have their cognitive abilities screened with digital diagnostic tools, consisting of self-administered tests and forms that objectively measure cognition via thousands of digital data points. The data is then interpreted by Geras' computational scoring tools and presented to professionals to obtain a comprehensive understanding of the patient's cognitive abilities.

The Geras platform is based on cognitive assessment methods developed and clinically validated by Karolinska University Hospital Memory Clinic in Stockholm. The cognitive tests are also complemented with other validated frameworks, already used in clinical practice since years on pen-and-paper. Geras Solutions has taken this into the modern age, having obtained the exclusive rights to digitalise the data.

Geras Solutions is also providing an open-for-all risk reduction tool that can empower individuals to delay cognitive decline through lifestyle changes, and encourages patients to track and manage their health over time based on the FINGER-study guidelines.

Stockholm has a great start-up community, with plenty of experts nearby at Karolinska Institutet, KTH or Stockholm University who are often open to collaborations and positive towards driving innovation. Besides that, there are excellent incentives, organisations and programmes that support start-ups such as Stockholm Science City, EIT Health and Vinnova. Invest Stockholm has recently connected us to pharma organisations that have a strong foothold and focus within the dementia field.

We always knew that Sweden would be an excellent place for us to test, develop and start our journey. But cognitive disease and dementia is a global problem which will impact more individuals as our society ages. We are just getting established in Sweden and are also about to explore other markets.”

*Rickard Forsman*



**Interested in knowing more or exploring  
this region further, get in touch!**

### **Invest Stockholm**

Invest Stockholm is the official investment promotion agency of Stockholm, owned by the city of Stockholm. The Stockholm region covers 53 municipalities and attracts more than 50% of the total foreign direct investments into Sweden. Our team will provide tailor-made information and advice for companies wanting to establish a new business in the region, as well as for companies wanting to expand an existing business. For investors we assist you to identify relevant investment opportunities within the region.

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