How world-class diabetes research will contribute to Swedish growth

A VINNOVA Innovation agenda

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Karolinska Institutet

Lund University

Umeå University

Uppsala University

AstraZeneca

FoU-centrum Skåne

Karolinska Trial Alliance

KI Innovations

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1. Summary

The two Strategic Research Areas (SFOs) within the diabetes field, EXODIAB (Lund University and Uppsala University) and SRP-Diabetes (the Karolinska Institutet and Umeå University), have together with AstraZeneca and the clinical units of the Karolinska Institutet and Region Skåne, established an initiative aiming to identify key strategies that can accelerate the rate of innovation in diabetes and thus create new opportunities for life science in Sweden. By actively taking into consideration the views of other important stakeholders we believe that we have developed a genuinely national agenda, which will not only accelerate the pace of innovation in diabetes, but also increase the competitiveness of Sweden within the life science sector. This will be achieved by creating the missing links in the value chain from basic research to patient benefit.

Diabetes is a chronic disease associated with potentially fatal vascular complications with increasing cost to society. Today diabetes can be neither prevented nor cured as available therapies have failed to interrupt disease progression, resulting in a large proportion of treated diabetic patients unable to maintain proper blood glucose control. Consequently, novel therapies to treat the disease and prevent complications are urgently needed.

We believe that the possibilities for increasing diabetes innovation from basic research are particularly favorable in Sweden. With EXODIAB and SRP-Diabetes, Sweden has two of the world's largest centers of excellence committed to improving prevention and treatment of people with diabetes. Sweden also has some of the best biobanks and patient registries in the world, not the least so in diabetes, creating the foundation for truly translational diabetes research. Importantly, a global pharmaceutical company has focused its diabetes research activities in Sweden.

Early in the agenda process an analysis concerning challenges and opportunities in translational diabetes research was performed. Based on the analysis, workshops with stakeholders, and the experience of the partners, an agenda was developed which will lead to more collaborations and more commercial projects, ultimately leading to better prevention, diagnosis and treatment of diabetes patients.

The key elements of the agenda include influencing the culture and innovation "readiness" within academia, increasing interaction between partners in the eco-system, involving national healthcare providers in the innovation process, and bridging the competence and funding gap between basic research and test/verification.

The next steps include involvement of other stakeholders, interaction with other agendas and the development of a concrete program including both short and long term initiatives.

2. Introduction

A global life science industry in transformation

Governments have responded to increasing healthcare costs and aging populations by applying a number of cost cutting measures, for example delaying reimbursement and new drug access to patients. Regulatory authorities have sharpened their requirements and now require that new anti-diabetic drugs will not result in an unacceptable increase in cardiovascular risk. The timelines and costs for development of new anti-diabetic therapies have therefore increased substantially in the last ten years, which has resulted in a fewer number of biotech companies being involved in the diabetes area.

Development strategies used in the past appear no longer to be effective in generating new and improved drugs for chronic diseases such as diabetes, cancer, Parkinson and Alzheimer. In addition, many big pharma companies currently face expiring patents for their block buster drugs. Together this has turned into a major crisis for the pharma industry. In order to reduce development costs many large companies have re-structured their organizations, which has led to a substantial reduction in the work force.

Experts believe that the pharmaceutical industry is undergoing a phase of transformation and new business models are expected to emerge. These will most likely affect large pharmaceutical companies and new, smaller companies are expected to emerge. However, these smaller companies will still be dependent on the presence of the larger pharmaceutical companies for development and marketing. In an attempt to explore new and more efficient ways of collaboration several big pharma companies have begun opening their research organizations to external partners: open innovation models are being evaluated and various partnering models are developed.

Swedish universities are also engaging in this arena as part of their legislated task to interact with society (in addition to education and research, hence the name "the third task"). The purpose of the third task is to ensure that research results from academia will benefit society. The third task should include interactions with other universities, industry, the healthcare system and the general public. Early stage discoveries occurring in academia will continue to constitute an important source of innovation for life science companies.

The Diabetes epidemic

Today many governments, both in developed and developing countries have a list of prioritized health challenges to address; the diabetes epidemic is one of these challenges. The International Diabetes Federation estimates that the number of diabetes patients worldwide is 366 million today and the number is expected to grow by an additional 180 million over the next 20 years. In Sweden, it is projected to be in excess of 600.000 diabetics in the year 2030 and as much as 8-12% of the total healthcare budget is used for diabetes-related care today. Importantly approx.

50% of treated patients do not achieve satisfactory glucose control and diabetes is projected to become one of the world's main disablers and killers within the next twenty-five years, due to its association with cardiovascular complications. Given the complexity of the disease and the diversity of people affected, a new wave of diabetes innovation is urgently needed in order to stem this global epidemic and to introduce cost-effective treatment strategies.

Why innovation in the diabetes area should be supported in Sweden

Sweden invests more in research and development than any other OECD country and has the third highest number of registered patents per capita in the world, although many inventions are developed elsewhere. Swedish biomedical research also ranks high in international comparisons based on citation and publication indexes, in relation to population and R&D expenditure.

Sweden also has some of the best biobanks and patient registries in the world, not the least so in diabetes. This in combination with the existence of the personal identification number (PIN) for each individual makes Sweden one of few societies in the world where it is possible to perform genuinely population-based genetic studies of complex diseases, such as diabetes. By linking registries it is possible to follow each individual in terms of which diseases have occurred, kinship and when biological samples were collected and stored in biobanks during the entire life of the subject.

The two Strategic Research Programs (SFOs) EXODIAB (Excellence in Diabetes Research in Sweden) and SRP-Diabetes (Strategic Research Program - Diabetes) together have more than 600 scientists and form centers of excellence in diabetes research even in an international context thanks to the quality, width and depth of the conducted research, and the access to human validation models. To date however, only a modest amount of the research performed at the SFOs has been translated to commercially interesting projects. EXODIAB and SRP diabetes have therefore joined forces and now work together on this agenda to increase the pace of innovation in the diabetes area.

For the last two years EXODIAB has worked actively to identify and develop the innovation potential of its research (a project supported by the EU regional development fund). This project has concluded that there are several causes to the slow pace of innovation, including the lack of competence in drug discovery and development available to the academic researchers, lack of risk capital in Sweden, and lack of interaction between relevant parts of the eco-system (academia, industry, healthcare providers and innovation systems).

AstraZeneca, a global pharmaceutical company, recently announced that it will continue to pursue its research activities in the diabetes area in Sweden; therefore everything needed for genuinely cross-disciplinary life science projects in Sweden is concentrated in a small geographic area. In combination with a Swedish tradition of cooperation, the close proximity of the different stakeholders makes it easy to interact within the eco-system of diabetes innovation.

However, over the last couple of decades several Swedish life science companies have been acquired by large international companies. This has resulted in a movement of research activities to other countries, resulting not only in a number of lost jobs, but also so called "competence drain", as fewer life science experts remain in Sweden. A recent survey performed by Life Science Sweden indicates that the number of jobs has decreased by 17% between 2008 and 2012. Today Sweden has a modest biotech sector; with the shrinking base of large pharmaceutical companies there is an obvious risk that the competence drain will continue and that the Swedish biotech sector will become even smaller in the future.

There is therefore a need to act quickly if the current trend is to be reversed. The questions that need to be answered are: do we have a sound science base to build on to create new innovative projects that can feed a growing biotech sector and thus revitalize a life science industry in Sweden, and do we have the risk capital necessary to finance this development?

3. The agenda process

The issues described above (lack of drug discovery competence available to the academic researchers, absence of capital in Sweden, and lack of interaction between relevant parts of the eco-system) are at the very core of our action plan to create innovative new solutions based on Sweden's strong research in diabetes. We chose to focus the agenda on diabetes (in its widest possible sense, including obesity and metabolic as well as cardiovascular diseases) based on the fact that (1) diabetes is one of the major health and health economic issues today and continues, despite major treatment advances, to warrant new, novel therapies to further help patients gain better control of their disease; (2) there are two major strategic research centers (EXODIAB and SRP Diabetes) in Sweden performing world-class diabetes research; and (3) a strong pharmaceutical company (AstraZeneca), active in the diabetes area is present in Sweden. We believe that this focus likely allows for less complicated strategy implementation, thus increasing the chances of success leading to long lasting improvements. Importantly, several of the challenges and opportunities in the diabetes area are true for other life science areas. If successful, our agenda could serve as a model for other strong research areas to initiate similar processes, thus accelerating the revitalization of the entire life science industry in Sweden.

The issues that will be addressed in the agenda include how to develop innovative, commercially viable projects based on both academic research and patient needs, and how to feed these projects to the industry, where the projects can be developed into new therapies for prevention, diagnosis and treatment of diabetes patients. The results from our suggested activities will strengthen links between academia, industry and the healthcare system, generate a number of new projects and companies creating new job opportunities, and a revitalized biotech sector in Sweden.

To address these issues, we chose a process combining a focused approach (on diabetes) with an open process (external analysis and dialogue with a large part of the eco-system). In the first

meeting the partners (see below) agreed on the remit, limitations, goals, and a common vision of the agenda. We then performed an analysis of challenges and opportunities concerning processes that are involved in translating diabetes research to innovative products (analysis performed by Ramboll; see Appendix 3). The analysis consisted of a literature survey, as well as interviews with important Swedish stakeholders. The analysis formed the basis for a brain storming workshop with the partners. The agenda group then agreed on a few initiatives that were further developed by smaller working groups. A second workshop took place at AstraZeneca in February 2013, where a large number of stakeholders from different parts of the eco-system were invited to give feedback on our proposed initiatives as well as to propose new ideas (around 40 participants representing industry, biotech, innovation systems, investors, academia, healthcare providers, authorities and patient organizations). The agenda process is described in greater detail in appendix 1. See also appendix 2 for a list of participants in the workshops.

It is important to mention that the workshops arranged within this agenda process were successful in several ways: firstly, participants felt that the initiatives proposed by the agenda group were highly relevant and important, and secondly, participants felt that it was beneficial to gather a large number of stakeholders from the different links of the eco-system to discuss these issues. In order to keep momentum, we agreed to continue to run a discussion forum similar to this.

4. Partners active in the agenda process

EXODIAB was created in 2010 as a joint strategic research initiative in the diabetes area at Lund University (LUDC -70%) and Uppsala University (30%). More than 300 scientists currently work in the EXODIAB consortium with the aim to develop tools for prevention and successful treatment of diabetes. A broad multidisciplinary approach which integrates genetics, bioinformatics, physiology, cell biology, clinical, epidemiological and nutritional research is required to achieve these goals. A central theme in EXODIAB is to generate not only local but also national platforms which can facilitate diabetes research in Sweden and the interaction between academia and industry. The EXODIAB consortium has access to some of the best biobanks in the world for diabetes research, incl. the Botnia study, Malmö Preventive Medicine, Malmö Diet and Cancer, the ULSAM study, ANDIS, TEDDY, DiPiS etc. In addition, the Human Tissue Lab (HTL) is a collaboration between EXODIAB and the Nordic Network for Clinical Islet Transplantation. The creation of the EXODIAB consortium has thus created the foundation for truly translational diabetes research. EXODIAB is funded by a Strategic Research grant from the Swedish government. An Innovation Officer from the industry was hired in 2010 to develop a platform for innovation, allowing for the translation of EXODIABs research into innovations that can be developed together with the industry to the benefit of diabetes patients.

SRP DIABETES – The Strategic Research Program in Diabetes at the Karolinska Institutet was initiated in 2010 through support by the Swedish government as part of the strategic research area

initiative and by funds from the Karolinska Institutet and Stockholm County Council. The program is a multidisciplinary consortium and incorporates expertise in physiology, cell biology, molecular biology, neurobiology, biochemistry, human genetics, epidemiology, genomic technologies, and bioinformatics as well as clinical expertise in endocrinology/diabetology, transplantation surgery and nephrology. The principal investigator profile supported by the program is comprised of both clinical and experimental researchers and thus has a strong emphasis on translational research. Based on thirteen different research groups from Karolinska Institutet and one from Umeå University, the program encompasses more than 200 scientists. The program develops important infrastructures such as Phenotyping Centre for Diabetic Animal Models, a Centre for Clinical Metabolic Research in Diabetes, a Beta Cell Imaging Facility and support for Enabling Technologies (genomics and bioinformatics), it also supports translational research projects as well as education of the next generation of researchers. There is an entrepreneurial tradition within the program and innovation is further supported by hiring a dedicated Innovation Manager.

KI Innovations is specialized in turning life science research into successful business. In close collaboration with scientists, KI Innovations secure relevant immaterial rights through patent applications and subsequently develop the projects to a point where they can be commercialized by company formation or by out-licensing. KI Innovations serve researchers from all Nordic countries with primary focus on projects coming from the Karolinska Institutet. During the 15 years that the company has existed, approximately 40 companies have been founded and around 30 license agreements have been signed.

AstraZeneca is a global, innovation-driven pharmaceutical company and a world-leader in diabetes and cardiovascular medicines. AstraZeneca has concentrated its diabetes and cardiovascular research to its research site in Mölndal, Sweden and the company recently announced that Mölndal will become one of three strategic global R&D centers with approx. 2200 co-workers employed in research activities. AstraZeneca is confident that new research collaborations with academia, as well as with biotech companies, will increase its access to expertise and innovation projects, thereby speeding up the drug discovery process and help put new drugs on a fairly stagnant market.

Karolinska Trial Alliance (KTA) is an independent clinical research support organization with its own phase I unit affiliated with the Karolinska University Hospital, Stockholm County Council (Stockholms Läns Landsting) and the Karolinska Institutet. The close connection with researchers at Karolinska University Hospital, and the easy access to hospital infrastructure have contributed to establishing KTA as a strong clinical research center. KTA engage in activities with small and medium-sized companies as well as global big pharma and has received approval of the Swedish Medical Products Agency (Läkemedelsverket) for “first-in-man” studies and has undergone successful inspections by the U.S. Food and Drug Administration (FDA).

FoU-centrum Skåne is a clinical research organization with its own clinical trials unit (12 beds) where it can set up its own trials, in addition to offering support in all phases of clinical trials to researchers in the entire southern healthcare region (södra sjukvårdsregionen). The location at Skåne University Hospital (SUS), secures easy access to advanced medical knowledge, techniques and equipment, enabling a wide range of pharmacokinetic and pharmacodynamic assessments, as well as other medical examinations. FoU-centrum Skåne has approx. 45 employees and can perform clinical research covering all phases required by the authorities for drug registration.

5. Challenges and opportunities for innovation in diabetes

This section is based on a study commissioned by the project group as part of the work within the agenda (See appendix 3). The analysis (based on both document studies and interviews with experts) identified challenges and opportunities regarding how to obtain more innovation from diabetes research in each of these phases. The challenges and opportunities identified were further divided into three different societal levels: structural, institutional and inter-personal. The **structural level** contains challenges and opportunities on a macro level, such as regulations and economic factors. The **institutional level** is made up of challenges and opportunities related to norms and values. The **inter-personal level**, finally, consists of challenges and opportunities in inter-personal relations between actors, for example triple helix. These levels are used in a "Contribution Analysis", a method used in evaluation to identify factors that can influence an intervention (Pawson 2006). It should be made clear that commercialization aspects are important in all three phases and that these three phases are a way to simplify the analysis.

5.1 The basic research phase

Challenges

In basic research, challenges and opportunities for innovation are found mainly on a structural and institutional level.

On a structural level, a potential challenge is that the Committee on Civil Liberties Justice and Home Affairs (LIBE) has put forward a proposal for a new General Data Protection Regulation in the European Union. This proposal aims at increasing the integrity of individuals but may concomitantly have severe consequences for the possibility of performing leading edge medical research in Sweden and Europe. For example the proposal limits the use of personal data and donated biomaterial for purposes specified when the data and material was collected. We believe that it should be allowed, after ethical vetting, to use collected data/material in medical research, for example to answer novel questions not predicted when data/material was collected. It follows that uncertainty about ethical rules and regulations associated with the use of biobanks and patient registries is a possible challenge for more innovation.

Another challenge identified in the study is that universities do not have the financial power to prioritize commercialization activities and help academic scientists to become inventors. In addition to lacking financial opportunities, the incentives for universities to help researchers become inventors are weak, at least when comparing Sweden with the US.

On an institutional level, basic scientists frequently underestimate the time, resources and competence needed for developing a research idea into an innovation with commercial value. Furthermore, one of the big challenges for innovation stemming from basic research is the incentive for the basic scientist to participate. The poor financial opportunities and incentives at the university may lead to inadequate financial/merit incentives for researchers to commercialize. Involvement in commercialization activities will almost always be associated with a cost for the individual researcher, as the academic merits will suffer. Due to the lengthy process to commercialization (from early stage development until research results reach a point where they can become commercially viable) and concomitant absence of incentives and financial bonuses, academic scientists frequently loose interest in dedicating the necessary hours to take research to a commercial stage. Given that successful knowledge transfer from universities to the commercial sector requires the active participation of basic scientists, incentives that promote mobility between academia and industry, are needed.

Moreover, commercialization of basic research may not be compatible with established research standards. Some scientists argue that due to the development of research policy over the past two decades, academic biomedical research has become increasingly reliant on funding from the commercial sector. This dependence may lead to undesirable consequences as expectations and norms differ in academic research and in the market. For example, the need for peer review prior to academic publication may not be compatible with market demands for quick information and access to results.

Opportunities

The challenges presented above can also be interpreted as opportunities. Turning the argument around Sweden presents an interesting case of a substantial critical mass and diversity of actors within the field of diabetes. The fact that Sweden is a small country means that all links required for truly cross-disciplinary life science projects are within easy reach of each other. It should therefore be easy to meet and interact with key decision makers and colleagues in the eco-system. Sweden still has a large number of companies within the life science area and an increase in the number of postgraduates within the life science sector can be seen. Sweden has a number of unique biobanks and patient registries available for research and the research is being conducted on a high level. When combining these factors in Sweden, the prerequisite for turning challenges into opportunities is present. These opportunities are summarized below:

- Simplify regulations around biobanks and patient registries
- Create better incentive for basic scientists to engage in commercialization activities

- Display good examples of researchers that have become entrepreneurs within diabetes
- Educate researchers in leadership issues and in commercialization
- Discuss commercialization before publication within research institutions
- Increase interaction between academy and industry
- Invest in basic research
- Work in multidisciplinary research teams
- Increase the interaction between research institutions in Sweden

5.2 The test/verification phase

Challenges

In the test/verification phase challenges and opportunities have been identified on a structural, institutional and inter-personal level.

On a structural level, there is a lack of bridging capital and lack of funding for cooperation projects between companies and researchers. A lack of test/verification facilities and weak links between academic basic research and clinical validation is a general challenge in life science; scientists and small research intensive companies lack the expertise and financial resources needed in this phase. Since this phase comes after traditional basic research but at a too early stage to be attractive for investors and pharmaceutical companies, many projects are developed abroad instead, or not at all. According to the so-called "pre-clinical paradox" investors with commercial interests take over development of pharmaceuticals at a stage, when it had better be developed in an academic, patient-centered environment. In this phase, there is a risk that academic researchers and investors do not understand each other's motivations and interests: when academic researchers loose influence and early-stage companies lack funding to do basic research, the end result is that treatment methods fail the test, even though the basic idea is often correct.

On an institutional level, one challenge identified is limited drug development competence among actors supporting innovation. This may be related to the regional organization of the innovation systems in Sweden, which may obstruct knowledge transfer between its different organizations and make it difficult for potential entrepreneurs requiring support to find the appropriate organization in the system.

On an inter-personal level, academic scientists and small research intensive companies often lack the competences and resources for developing projects further, and academic scientists and investors have different and sometimes contradicting motives and interests.

Opportunities

There are a number of factors within the test/verification phase, which can be regarded as possibilities. For instance, standardized agreements for efficient technology transfer between research and business are relatively easy to bring into existence. Also, in Sweden there tends to be

a culture of trust and an absence of a "litigation culture", which in contrast is highly present in the US where legal disputes are more common.

Our analysis identified numerous opportunities that may increase the innovation potential within the test/verification phase. These are summarized below:

- Create financing for projects in early phases of development
- Increase investment in clinical testing possibilities within the healthcare sector
- Involve the healthcare providers in the innovation process to convey patient needs
- Create bridges between research and innovation

5.3 The innovation/commercialization phase

Challenges

In the third and final phase, there are challenges and opportunities on all three levels: structural, institutional and inter-personal. The challenges identified in the basic research and test/verification phases are also relevant in the final phase, but challenges specific for commercialization have also been identified.

Challenges on the structural level result from different government ministries being responsible for different political issues related to innovation/commercialization: the Ministry of Education is responsible for research policy, the Ministry of Finance for taxes and the Ministry of Enterprise is responsible for efforts to support, for example cluster organizations and public venture capital investments. This division may inhibit coordinated efforts at the national level. In addition, efforts/reforms in the area will be subject to political compromises since different political parties in a coalition government are in charge of different ministries.

Academia, industry and political actors are not the only relevant actors when it comes to promoting innovation in life sciences. The healthcare sector also has an important role, both as generators and adopters of innovation. Research shows that when top management in healthcare organizations lacks research experience, the healthcare sector is less likely to adopt innovation. Our analysis indicated that the Swedish healthcare system is relatively conservative and does not prioritize research. Moreover, healthcare organizations are facing the laborious task of staying up-to-date in an environment in which medical information, technologies, and relationships with other healthcare systems are increasingly dynamic at the same time as the demographic structure of the population is changing and there is pressure on governments to reduce healthcare costs (Länsisalmi et al, 2006). In summary, there are challenges on the institutional level for innovators and entrepreneurs when it comes to getting access and reaching out to healthcare organizations.

On an inter-personal level, buyers of products originating from basic research ideas frequently are large companies, often creating challenges in the dialogue between scientists and the potential buyer.

Opportunities

There are a number of opportunities connected to the challenges presented above. For instance, in Sweden academic scientists own the intellectual property (IP) rights to their research results ("lärarundantaget"). This should potentially increase the motivation for the scientist to engage in commercialization activities. Also, there is a largely untapped possibility in strengthening the links between the universities, industry and healthcare through cluster initiatives and networks. When combining these factors in Sweden the prerequisite for turning challenges into opportunities is present. In our analysis a number of opportunities were identified that could increase the innovation potential within the phase of commercialization. These opportunities are summarized as follows.

- Increase the coordination within the national innovation system for life science: develop a national vision for innovation in life science
- Create better coordination between different government ministries regarding innovation: one commission for innovation
- Create better cooperation between different parts in the Triple helix, based on tradition of cooperation that already exists in Sweden
- Initiate a dialogue between industry and academia in order to increase the academic awareness of drivers for commercialization, i.e. identify which type of innovation that could most easily be commercialized within the diabetes area (this could be products and services making life easier as a diabetes patient or diagnostics).

With starting-point in the challenges and possibilities presented above, the focus of this agenda is on opportunities that are specific enough to increase innovation from diabetes research. There are additional factors that can be targeted in parallel, as discussed above. Actions have to be taken on a national level regarding framework conditions for the life science sector. In section 7 strategies that address some of the opportunities identified above, are presented. We believe that implementing these strategies will be important stepping stones towards achieving more innovation from diabetes research.

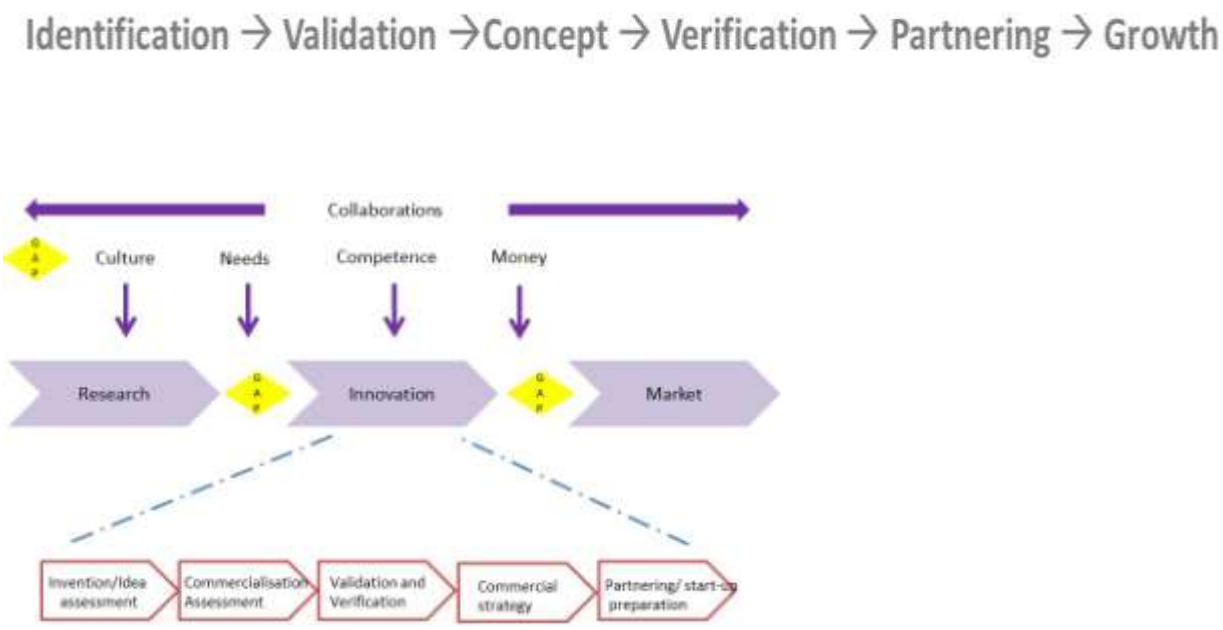
6. The vision

Our vision is to revitalize the life science industry in Sweden by creating optimal conditions for close collaboration between academia, industry and healthcare providers, building on our strong research tradition and biobanks, and by providing an increased flow of commercially viable

projects from our SFOs in diabetes. Part of our vision is also that this initiative once successful will inspire other SFOs by presenting a process and set of actions that can be applied to other medical areas, thus accelerating the process of revitalization of the Swedish life science sector further.

The identification and development of new processes will create new job opportunities in life science in Sweden and it will lead to new cross-sectorial collaborations between academia, industry and the healthcare system, which will attract global pharmaceutical companies. This in turn will help position Sweden as an "innovation motor" in life science based on strong basic research, thus attracting new funding and partnerships, which will create even more new job opportunities.

This vision builds on linking the elements in the process illustrated below and by addressing the gaps/bottlenecks that are found in several places in the value chain today:



7. Strategies for increasing the pace of innovation in diabetes research in Sweden

Based on our analysis of challenges and opportunities in different phases (Appendix 3), we have identified strategies for increasing the innovation capacity within the diabetes area. These overall strategies are presented below.

- **Impact culture and commercialization aspects within academia**

An important strategy will be to address the cultural aspects within academia in order to increase the understanding of basic scientists of what is required in the commercialization phase. This will increase the interest of academic scientists to get involved in the innovation process (there are already today initiatives, such as the Innovation Officer Programs at Lund University and the Karolinska Institutet that can be developed further). This also addresses the motivation factors for scientists, a discussion that needs to be taken on a national level, and be an integral part of a Life Science Strategy for Sweden.

- **Increase interaction in the ecosystem of diabetes**

Today a limited number of interactions between different stakeholders lead to a limited number of collaborations, an absence of cross-sectorial knowledge sharing and a limited number of ideas generated. Increased interaction between academia, industry, the healthcare system and innovation supporting systems, as well as between different research institutions is needed. Our initiatives will create a platform for interaction between all stakeholders in the eco-system and at the same time map and identify competences available. Our aim is to create sustainable platforms that increase the interaction as a means to create new project ideas.

By involving healthcare providers more actively in the innovation process, we will bring patient needs into the center of the innovation processes. Key stakeholders and major bottlenecks, as well as some initiatives that address the bottlenecks will be identified in order to achieve a more active involvement of the healthcare sector in diabetes innovation. Collaboration platforms linking clinics, biobanks, and patients, with scientists and industry, will be proposed.

- **Increase competence and bridging capital in the "Valley of Death" between basic research and test/verification.**

Several competences are needed to mature academic projects to a point where they are "investment ready" and can be presented to potential project takers. These competences include among others pre-clinical drug discovery, protein chemistry, assay development, project management, market understanding etc. We will suggest strategic initiatives that will address this issue.

Most experts agree that there is a poor risk capital market in Sweden, in particular for life science projects. Without early bridging capital to support the maturation process, academic projects will not reach an "investment ready point" and consequently cannot be handed over to external "project takers". We will propose strategic initiatives that can increase commercialization of research findings by addressing the lack of funding in this phase.

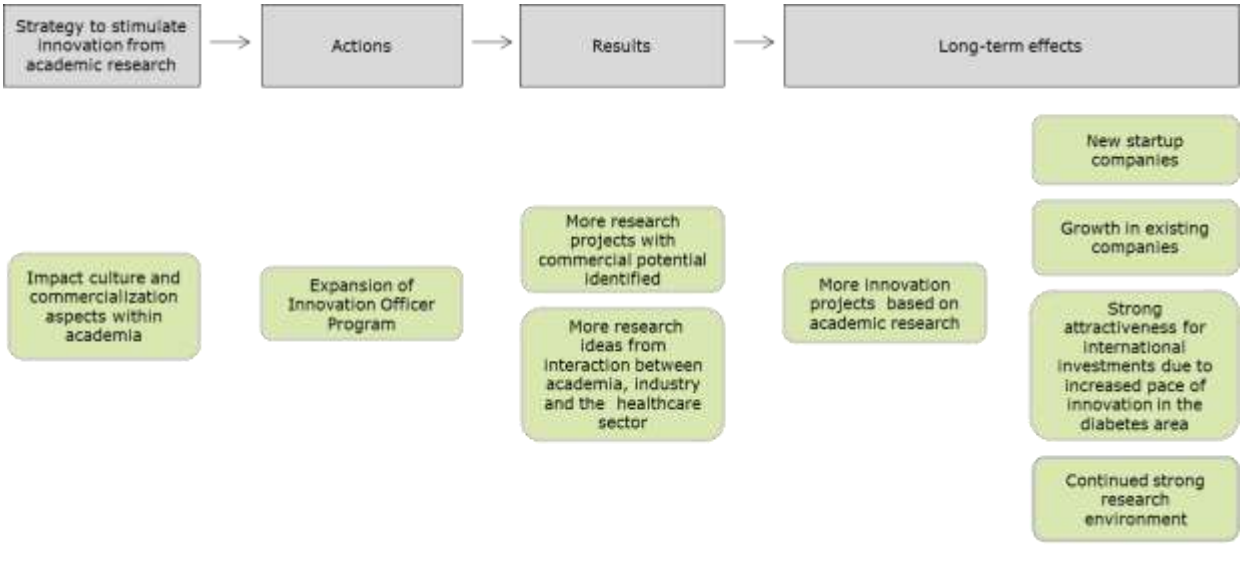
8. Objectives and long term effects

The figures below illustrate how our strategy will be implemented by the different actions and how these actions will lead to better results and long-term effects regarding innovation from diabetes research. The figure should consequently be seen as a means of clarifying the strategic idea of how our agenda will generate an increased pace of innovation from diabetes research.

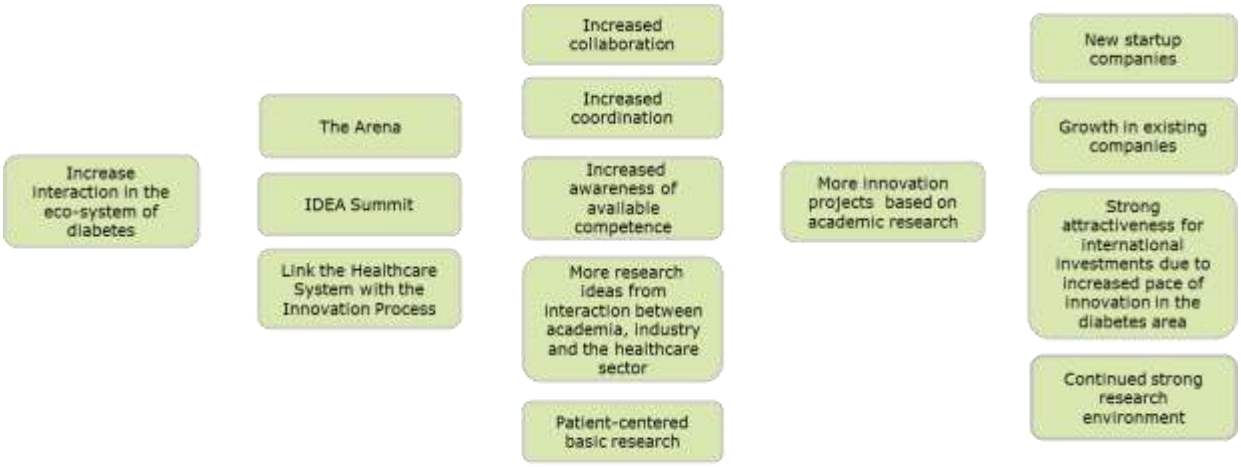
The short-term results obtained with the proposed initiatives will be more positive attitudes towards innovation among researchers, increased interaction and collaboration between academy, industry and the healthcare system, a more patient-centered basic research focus, increased coordination, increased awareness of available competence, new research based on the needs from healthcare and industry, facilitated identification and development of academic projects with commercial potential, and more competence and funding in the eco-system of diabetes innovation. Another important result will be earlier involvement of the pharmaceutical industry in external innovation projects, compared to today. This will give academic projects with commercial potential easier access to drug development competence.

Concerning more **long-term effects** the proposed actions will lead to a stronger structure for financing of innovation projects, and more innovation projects based on strong academic research, creating better conditions for growth effects in companies (new start-ups and growth in existing companies), and a continued strong research environment in Sweden. This will ultimately lead to an increase in Sweden's attractiveness for international investments.

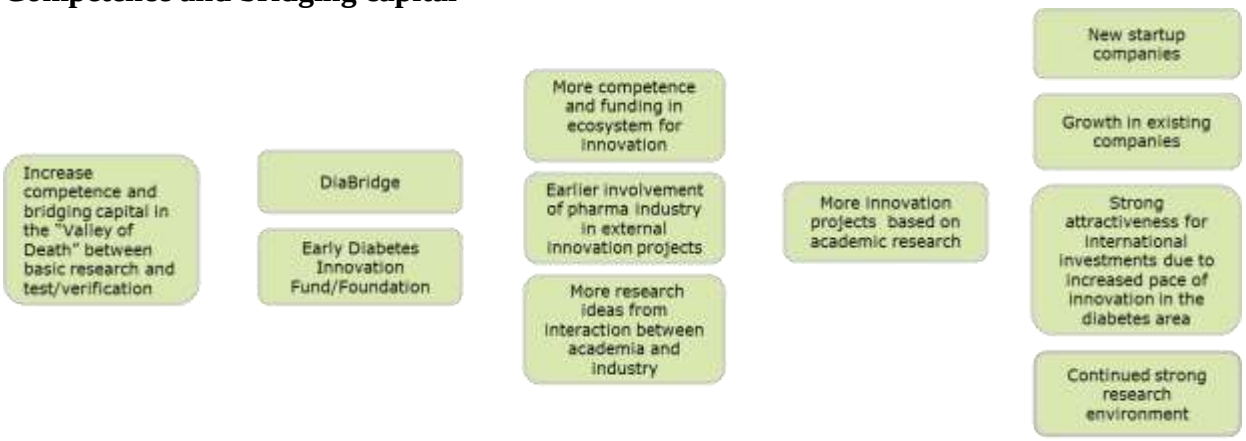
Culture and commercialization aspects within academia



Interaction in the ecosystem



Competence and bridging capital



9. Key Success Factors

A major success factor we believe is in creating a sense of urgency and keeping the focus of the agenda. This is one of the reasons we chose a clear delimitation of this agenda to address challenges in Diabetes innovation. It allows for a clearer identification of stakeholders, mobilization of interest and creation of motivation to join and participate. A successful implementation of this agenda creates a stronger motivation to pursue innovation activities within the Life science sector in general in Sweden.

By addressing cultural and interaction issues early in the process, we keep the momentum created in the workshops arranged during the development of this agenda, leading to lowering of the barriers to starting companies through mentorship, and creating an interaction platform to share experiences and develop new projects (both innovation and research focus).

We believe that working with short-term ("low-hanging fruits"), as well as longer-term structural changes will be an important way forward. In the action plan some of the activities proposed are low-hanging fruits that can be initiated relatively rapidly in order to keep the focus and momentum of the agenda. Another important success factor is found in the legitimacy, strong management and networking capabilities of the leadership as well as management structure of the national agenda.

Some challenges and possibilities identified in the analysis are general for the entire life science sector in Sweden. For example, the Innovation Officer Program can be used in a broader life science context and can be replicated in other academic research organizations. The same applies to an early innovation fund/foundation for life science. These can be implemented for other areas in life science, thus creating a multiplication effect without dilution of the efforts.

Some initiatives in the agenda will require a national effort for successful implementation, for example in defining the role and involvement of healthcare providers in life science innovation in Sweden.

10. Key Initiatives

Based on our analyses and discussions, we propose an agenda consisting of several initiatives, which together will create an environment that provide the conditions for accelerated pace of innovation within the diabetes area. The initiatives are subdivided into activities that impact culture (objective 1), interaction (objective 2) or competence/funding Gap (objective 3) and will be presented starting with short term initiatives, followed by longer-term ones. It is important to point out that the agenda group will continue to develop the action plan into a SIO application during the autumn of 2013, which may contain additional initiatives not mentioned in this agenda. It follows that the SIO application will not be limited to the initiatives proposed in this agenda.

10.1 Impact culture and commercialization aspects within academia

- Expansion of the **Innovation Officer program**

The Innovation Officer Program (funded by EU regional development grant 2011-2013) was established at Lund University Diabetes Center in August 2010 as a pilot project to translate the scientific strength of LUDC into innovations that can benefit patients and society. It aims at creating processes and structures that facilitate the identification and maturation of innovative projects with commercial potential, as well as facilitating collaboration between academic research centers and industrial partners. Innovation Managers are responsible for developing research-based projects to a point where they can be delivered to existing innovation systems. Translation of basic research into clinical outcomes of benefit to patients is a key component of

the program. A unique feature of the Innovation Officer Program is that Innovation Managers are placed within the core of the strategic research facilities allowing immediate and easy interaction with the basic scientists. The Innovation Officer Program is part of the innovation system at Lund University and also supports commercialization processes along the conventional intellectual property-based path leading to start-up companies as part of the university based TTO.

The Innovation Officer Program was recently expanded to the Karolinska Institute, where dedicated innovation managers now are placed within SRP-Diabetes, with the aim to support innovation in the SFO.

We propose that the Innovation Officer program is further expanded and that the model is presented to other academic research centers in Sweden.

10.2 Interaction in the ecosystem

- Innovation in Diabetes: **European Action Summit**

The aim of this European 1-day meeting is to strengthen the ties between academia and industry by identifying concrete initiatives that can create an optimal environment for innovation in Diabetes, thereby accelerating translation of academic diabetes research to products providing benefit to patients and society. The meeting will establish a European platform for dialogue between academia, healthcare providers and industry, in which we together can pinpoint what is required to achieve major breakthroughs in diabetes research. The meeting therefore presents a great opportunity to fight diabetes by addressing the declining trend in global diabetes innovation.

IDEA Summit is organized by LUDC and the organizing committee consists of a number of representatives of European organizations involved in translational diabetes research, including Karolinska Institute, Oxford University, Cambridge Biomedical Campus, Eurasanté, Medicen, Medicon Valley Alliance, Munich Biotech Cluster, and Region Skåne. The meeting is dedicated to people involved in translational diabetes research and targets key decision makers from academia and pharma, as well as other stakeholders, such as biotech companies, biobanks, innovation systems, and venture capitalists. The meeting is sponsored by AstraZeneca, Novo Nordisk and Sanofi.

The meeting will take place in Lund on September 18, and more information can be obtained on its website: www.ideasummit2013.se

- **The Diabetes Arena** – A platform for open dialogue between academia, industry, and the healthcare system.

The aim of the Arena is to facilitate the first contact between academia, industry and the healthcare system in Sweden. A cross-disciplinary platform for early knowledge sharing, which aims for an increased understanding of each other's incentives, competences, and needs, will be created. It is expected that this will lead to new collaborations between partners as areas of common interest are identified, and that knowledge sharing will benefit all partners. We believe that a continuous exchange and dialogue will create trust and competence for all parties, as well as learnings in the form of new knowledge that is useful for both academia and industry.

Commitment from all academic diabetes research centers in Sweden will be key to a successful arena, which is viable in the long-run. We suggest that the arena shall meet systematically and that it should alternate between Swedish cities where academic diabetes research is performed.

As a complement to the arena we will create a Diabetes**-portal**, which will act as a "who is doing what in diabetes innovation"-forum. Scientists in need of specific competences will easily be able to identify potential collaboration partners in the Diabetes-portal.

- **Linking the national healthcare system** with the diabetes innovation process

Healthcare providers can play a key role in acceleration of innovation in diabetes by conveying the needs of patients to academic scientists as well as by providing test facilities and access to patients for clinical trials. Moreover, linking access to patients to strong biobanks and patient registries provides a unique opportunity to create durable collaborations with the pharmaceutical industry, allowing for faster screening and testing of potential novel therapeutic approaches. However, many healthcare providers are focused on optimization of operation, and participate only intermittently in the innovation process. There is therefore a need to identify bottlenecks in this process today and subsequently suggest solutions that can allow research and innovation partners to gain access to this essential part of the eco-system. The arena mentioned above aims to do exactly that, but additional **processes and funding may be required to facilitate this change.**

In order to increase the involvement of the healthcare system in innovation processes we propose that **a dialogue between the four largest healthcare regions in Sweden** (Stockholm, Göteborg, Skåne, Uppsala-Örebro) and the strategic research centers within the diabetes area is initiated. Representatives of Göteborg and Skåne healthcare regions have already expressed an interest in such an initiative. The aim of this dialogue is to identify bottlenecks and develop initiatives that will allow healthcare providers to take a more active role in life science innovation. Since this initiative ultimately is about improving healthcare, the regions should be interested in increasing its involvement in research and development. Examples of activities where healthcare regions can increase their involvement are: (1) creation of biobank platforms; (2) provision of and access to

large databases containing different types of patient-related information; and (3) contribution to funding for population-based studies.

10.3 Impacting Competence and bridging the funding Gap

- Early Diabetes Innovation **Fund/Foundation**

The global economic crisis in combination with high risks and escalating costs for drug development have led to a significant reduction in venture capital for life science projects. Both the number of investments in life science start-ups and the number of active investors are declining. This is particularly true in Sweden. Many new ideas are not being developed because the financial climate cannot support them: obtaining funding for early validation studies (preclinical and early clinical validation; proof of concept, PoC), has become a most significant bottleneck in drug development.

Early projects from academia are in the majority of cases not sufficiently mature to attract funds from big pharma or investors. At the same time, academic researchers frequently lack expertise and interest in developing the projects further. There is a Valley of Death for many basic discoveries that have significant promise because they are not far enough advanced to be of interest to an industrial partner.

We suggest that Sweden establishes a not-for-profit public-private partnership in the form of a fund/foundation. The fund/foundation will work in partnership with one or several pharmaceutical companies already from the start. The fund/foundation will provide initial funding for development to a certain point, for example Candidate Drug/IND. In subsequent phases, expenses could, and should, preferably be covered by industrial partners.

The fund/foundation will replace early venture capital (and seed money) and instead of paying a premium price for early projects, the industry will cover expenses for driving the project towards PoC, i.e. capital will go to the project and not to venture capitalists. By sharing development risks more equally between owners, inventor and industry, we believe that big pharma will increase their involvement in external innovation projects at a considerably earlier development stage compared to today. Consequently, this structure does not only address the funding gap, it also introduces industry competence earlier on.

Individual projects can be run in the form of a company or foundation allowing different industrial partners/investors to enter specific projects that fit their particular R&D portfolio.

We propose that the ownership structure involve academia, philanthropic capital, industry and the healthcare system. This will assure that market and healthcare perspectives are considered at an early development stage.

- **Commercial Translation Units**

In order to bridge the gap mentioned above, a concrete initiative has been taken by LUDC to establish a commercial translation unit, which will manage collaborations with the pharmaceutical industry, providing access to its platforms and knowledge, offering services for target validation and biological pathway determination. The translation platform will also develop a portfolio of research projects with commercial potential, and develop these projects to proof of principle (PoP). Once PoP is established, innovations and associated IP will be out-licensed to life science partners, e.g. biotech or pharma companies.

This approach differs on several points form the start-up strategy adopted by most universities today; the main difference being that projects will be matured for a longer period, allowing generation of greater value. Business and development plans will be developed within the unit and suitable "customers" to the projects will be identified and involved at an early stage. Several benefits in terms of, for example optimized project management processes, easier contractual handling, easy access to pre-identified third party service providers (pre-clinical and clinical services) and more professional establishment of partnerships will be obtained. A team of professionals (scientific project managers) will be employed by the commercial unit with the task to assist academic scientists in developing the initial inventions to a point where they are more substantially validated. The commercial entity will become a center of diabetes excellence, which in turn will make contracts and deal negotiations more focused and efficient.

This kind of commercial units could be one element in bridging the gap between academia and industrial partners, thus accelerating the rate and quality of innovations from academic research.

11 Concluding remarks

The global life science industry currently faces significant challenges. We believe that the prerequisites for turning challenges into opportunities are present in Sweden and that the initiatives proposed in this agenda have the potential to give rise to an increased pace of innovation from diabetes research, creating better conditions for growth in companies, and a continued strong research environment. Our aim is that these initiatives will lead to revitalization of the Swedish life science sector and ultimately to an increased ability of Sweden to attract international investments.

This agenda is the result of discussions between the partners. Since the starting point was academic research and big pharma, the agenda has a natural "bias" towards new therapeutic treatments. This does not mean that projects allowing for prevention, early diagnosis or monitoring of diabetes patients will be excluded. It is our ambition that by creating the Diabetes Arena, new collaborations between new stakeholders will be formed, leading to an increase in all types of innovations, relevant to present and future diabetes patients.

Discussions will now be intensified with other life science agendas in order to find synergies and develop a structure that will ultimately lead to strengthening of the entire life science sector in Sweden. Based on this agenda, we will in the coming months develop a program with initiatives, that are concrete, actionable and can be implemented relatively rapidly, leading to real changes both in the near future and in the more longer-term.

Appendix 1: The working process leading to the agenda

The process with creating our innovation agenda was initiated on September 11, 2012, when a kick off was arranged at the Clinical Research Center in Malmö (see list of participants, appendix 2). The purpose of this meeting was to agree on goals and vision, and establish the working process. We decided that it was important to perform an independent analysis around processes involved in translation of diabetes research (see appendix 3). The analysis was based on document studies (scientific literature and other reports focusing on commercialization of medical research) and on interviews with 15 experts representing the different links in the value chain (academics, big pharma, biotech, biobanks, investors, cluster organizations, authorities, and innovation systems). An external partner, Ramböll Management Consulting, was contracted to perform these analyses in October-November 2012.

The results of the analysis were discussed in a 1-day workshop at Karolinska Institute on December 11, 2012 (see list of participants, appendix 2). The analysis clearly pinpointed a number of bottlenecks that contribute to slow translation of diabetes research specifically, and of medical research, in general. Based on the analysis and the experience of the agenda group, we decided to focus our efforts on developing a few key initiatives, which will address significant bottlenecks at different levels in society and in different phases of the value chain. Small work groups were formed and given the task to develop these initiatives. At this point it was important to find an appropriate level between vision and concrete detailed suggestions, and the proposals had to be sufficiently clear to be easily comprehensible by external stakeholders. The following work groups were agreed upon:

1. An Arena for Open Dialogue between Academy, Industry, Healthcare and Innovation Systems.

Responsible persons: Jan Oscarsson (MD, Director Diabetes & Obesity, AstraZeneca), Hans Tornqvist (Professor, Senior Research Physician, AstraZeneca), Erik Renström (Professor, Lund University & Co-ordinator EXODIAB), Holger Luthman (Professor, Lund University), Nils Wierup (Principle Investigator, Lund University)

2. An Early Diabetes Innovation Fund/Foundation

Responsible persons: Magnus Björsne (Business Development Director, VC Liaison, AstraZeneca), Helena Edlund (Professor, Umeå University), Ulf Malmqvist (Operations Manager, FoU-centrum Skåne), Patrik Blomquist (Project Manager, KI Innovations), Thomas Gunnarsson (Innovation Manager, Lund University)

3. A Link Between the National Healthcare System and the Diabetes Innovation Process

Responsible persons: Peter Arner (MD, Professor, Karolinska Institute), Claes-Göran Östensson (MD, Professor, Karolinska Institute)

The proposals were developed by the work groups over a period of two months and were subsequently presented to a group of approximately 40 stakeholders representing the different links in the value chain, from academic scientists to patients, in a whole-day workshop at AstraZeneca in Mölndal on February 7, 2013 (see list of participants, appendix 2). The purpose of this meeting was to (1) anchor our proposals in a wide group of stakeholders and (2) if possible obtain new ideas, which we had not thought about.

The workshop was initiated with an introduction to the agenda process (background, aim, vision), and a presentation of the work process and the analysis performed. The three action groups subsequently presented their proposals. Group exercises concerning reflection around current and new proposals and the different perspectives of academia, industry, healthcare sector followed. The agenda group feels that the presented proposals were very well received by and firmly anchored in the stakeholder group.

On four different occasions we have presented our working progress to other agendas in the life science area. The purpose of theses interactions has been to identify common areas of interest. Although some areas where collaboration could make sense have been identified, it has been decided that individual life science agendas should be submitted to Vinnova at this stage. It is possible that activities from several life science agendas will be merged into a new agenda when the application for a SIO program is prepared.