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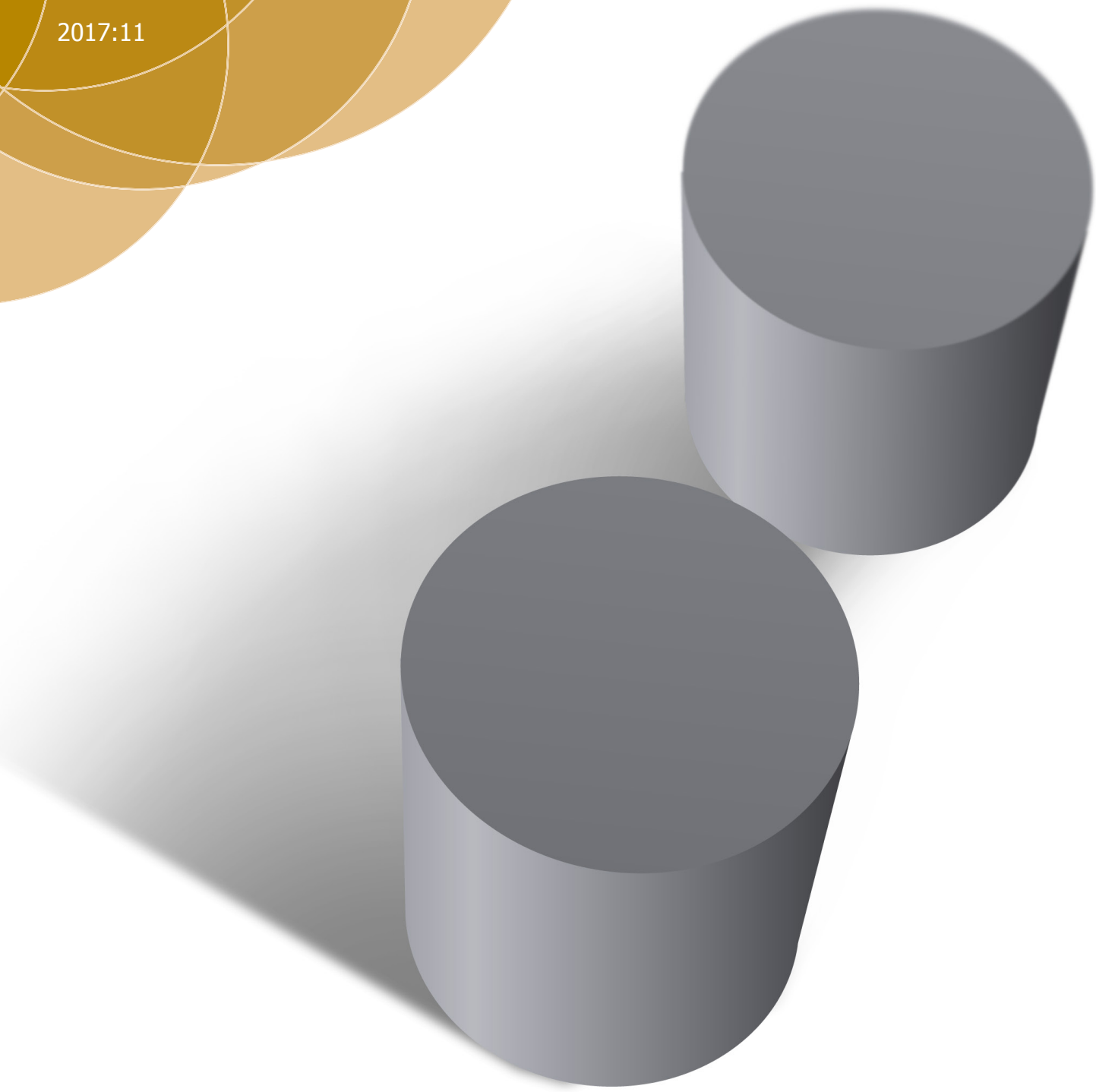

# Towards a **Swedish megafund** for life science innovation

**This report shows** how a Swedish megafund for life science innovation could, by applying financial engineering techniques, provide adequate early-stage funding to start-ups. The report also reveals how other countries are considering setting up this type of financing tool and lists several aspects that require further investigation before implementation.

tillväxtanalys

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# Foreword

For many innovative start-up companies, access to early-stage venture capital is crucial to their development and growth. Hans Rydstad's investigation in 2015 presented a number of proposals aimed at strengthening the supply of early-stage venture capital in Sweden. Several of these suggestions have been implemented. However, both the investigation and some of the consulting responses concluded that the proposed solutions were unlikely to satisfy the capital requirements of the life science sector.

This report assesses whether a Swedish megafund could fill this funding gap in the life science sector. Interviews with various stakeholders suggest that the timing and conditions for setting up a megafund in Sweden are quite favourable. The report also shows how several other countries are considering setting up this type of fund.

The report has been written by Andres Laguna Fernandez, who is an assistant professor at the Karolinska Institute, and Carl Wadell, who is an analyst at the Swedish Agency for Growth Policy Analysis. The study was conducted as part of an internship programme funded by the Karolinska Institute Career Service.

Stockholm, May 2017

Enrico Deiaco
Director
Growth Analysis

# Förord

För många innovativa uppstartsföretag är tillgången till riskkapital i de tidiga skedena viktigt för deras utveckling och tillväxt. Hans Rydstads utredning från 2015 presenterade ett antal förslag med syfte att stärka utbudet av riskvilligt kapital för svenska företag i de tidiga faserna. Flera av dessa förslag har implementerats. Både utredningen och ett antal remissvar pekade dock på att life science är en sektor där de föreslagna lösningarna inte matchar kapitalbehovet.

Denna rapport undersöker huruvida en svensk megafond skulle kunna fylla detta finansieringsgap inom life science. Intervjuer med olika intressenter vittnar om att timingen och förutsättningarna är relativt goda för att sätta upp en svensk megafond. Rapporten beskriver även hur flera andra länder överväger att sätta upp den här typen av finansieringsinstrument.

Rapporten har skrivits av Andres Laguna Fernandez som är assisterande professor vid Karolinska institutet och Carl Wadell som är analytiker på Tillväxtanalys. Studien är genomförd inom ramen för ett praktikprogram finansierat av Karolinska institutets karriärservice.

Stockholm, maj 2017

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# Summary

An ageing population is directly associated with the rise of chronic diseases and the subsequent increase in healthcare costs. Unless something changes, the percentage of GDP dedicated to healthcare in Sweden, as well as in many other countries, will dramatically escalate, making the situation unsustainable. Innovation is key to face this development and create a better and more cost-efficient health and elderly care. Although Sweden has a strong tradition and expertise in all segments of the life science industry early-stage venture capital investments have decreased over the last decade, hampering the development of new companies.

This exploratory study investigates whether a novel investment structure termed "megafund" could fill the financing gap in the Swedish life science sector. The megafund would apply financial engineering techniques, such as portfolio theory, securitisation, and dynamic leverage to fund a large number of high-risk/high-reward projects. Theoretically, the size and structure of the megafund would simultaneously reduce risks and provide significant returns. Moreover, by issuing both equity and debt, the megafund would pave the way for investments from institutional investors who traditionally do not invest in the early stages.

In order to investigate the appropriateness and feasibility of a Swedish megafund for life science innovation, 23 interviews were conducted with leaders from the Swedish life science industry, academia, venture capital industry, pension funds and healthcare system.

The results show that a Swedish megafund for life science innovation may be an effective tool to bridge the existing funding gap in the early stages. Furthermore, the megafund could promote disruptive ideas by integrating knowledge from the different life science segments (*i.e.* pharma, biotech, medtech and ICT) and thereby realise a larger part of the country's innovation potential. The report enumerates a number of countries currently implementing, or considering the implementation of, "megafund-like" solutions and lists several aspects that require further investigation before implementing a megafund. Among other things future analyses may take a closer look at the investment focus, size, duration and governance of the megafund, as well as to what models to apply for risk and profitability forecasts.

Overall, the establishment of a Swedish megafund for life science innovation is considered a timely and viable opportunity to foster innovation, attract global talent, and boost the competitiveness and growth of the Swedish life science sector.

# Sammanfattning

En växande och åldrande befolkning är direkt kopplat till en ökning av kroniska sjukdomar vilket bidrar till ökade kostnader för hälso- och sjukvård. Utan åtgärder kommer hälso- och sjukvårdens del av BNP i Sverige och många andra länder öka dramatiskt, vilket kommer att vara ohållbart. Innovation är centralt för att motverka denna utveckling och skapa en bättre och mer kostnadseffektiv hälso- och sjukvård samt äldrevård. Sverige har en stark tradition och kompetens inom alla segment av life science-industrin men under de senaste decennierna har tillflödet av riskkapital i de tidiga skedena minskat, vilket hämmat utvecklingen av nya life science-företag.

Denna explorativa studie undersöker huruvida en megafond skulle kunna fylla finansieringsgapet i svensk life science och därmed gynna innovation och tillväxt. Megafonden skulle använda finansieringstekniker såsom portföljteori, värdepapperisering och dynamisk hävstång för att finansiera ett stort antal projekt med stor risk och stor potential. Enligt teorin skulle megafondens storlek och struktur reducera risken samtidigt som den ger en betydande avkastning. Genom att megafonden kapitaliseras genom investeringar i både ägarandelar och obligationer öppnar den upp för investerare som traditionellt sett inte har investerat i tidiga skeden.

För att kartlägga lämpligheten och genomförbarheten av en svensk megafond för life science-innovation genomfördes 23 intervjuer med ledande personer från den svenska life science industrin, akademin, riskkapitalbolag, pensionsfonder samt hälso- och sjukvården.

Rapporten visar att en svensk megafond för life science-innovation har potential att brygga finansieringsgapet i de tidiga faserna. Megafonden tros även kunna främja disruptiva idéer genom att integrera kunskap från de olika life science-sektorerna och på så vis realisera en större del av landets innovationspotential. Rapporten visar hur ett antal länder nu implementerar, eller överväger att implementera, ”megafondsliknande” investerings-instrument och lyfter fram flera aspekter som behöver undersökas närmare innan en megafond kan implementeras. Bland annat bör framtida studier analysera fondens investeringsfokus, storlek, varaktighet och styrning samt vilka modeller som bör användas för att göra risk- och lönsamhetsprognoser.

Sammantaget anses etableringen av en svensk megafond för life science-innovation vara en läglig och genomförbar möjlighet att främja innovation, attrahera globala talanger och bidra till life science-sektorns konkurrenskraft och tillväxt.

# 1 Introduction

Sweden has historically been a country of innovation in the life sciences. Swedish innovations such as the pacemaker, stereotactic radiosurgery, omeprazole and beta-blockers have made an impact on the health and quality of life of millions of people. Thus, Sweden possesses considerable expertise in all segments of the life science industry, *i.e.* pharmaceuticals, biotechnology, medical technology and health-oriented information and communication technology (ICT). Indeed, the life science industry is one of Sweden's most important sectors with a high level of exports, as well as gross value added; in addition, life science innovation is key to the development of better and more cost-efficient health and elderly care.

Even so, the number of employees in the Swedish life science industry has decreased over the last decade mainly due to the downsizing of Astrazeneca.[1] At the same time there are several business segments such as ICT, in vitro diagnostics and medical biotechnology in which the number of employees has increased over the same time span. Moreover, between 2006 and 2016 the number of Swedish pharma companies with projects in clinical development increased from 24 to 67.[2] Evolving technologies such as gene editing, next-generation sequencing and immunotherapy, together with more sophisticated electronic medical records, wearable healthcare devices, as well as the use of real-world evidence and data analytics, indicate that there is a significant potential for innovation in the sector.

Sweden is well-positioned to take part in this technological development. In general, Sweden is one of the countries in the world that invests most in R&D per capita. Sweden also has a comparatively large proportion of researchers in relation to the total population (just over 1 percent).[3] According to the Swedish Research Council, Sweden is also a global leader in terms of co-publications with international scholars (especially with US and UK based researchers).

The Swedish government provides various means to transform science and innovative ideas into innovation and economic growth. Some examples are innovation offices, holding companies, incubators, and science parks, as well as a number of innovation-promoting programmes from the Swedish innovation agency, Vinnova. Sweden has also made significant investments in biomedical infrastructure over the last decade. Some examples are the Science for Life Laboratory (SciLifeLab), national quality registries, as well as a national biobank infrastructure.

Despite these promising conditions and initiatives, private early-stage venture capital investments in Swedish life science companies have decreased over the last decade and the majority of assets have been deployed at later stages.[4] In general, public venture capital has increased over the last decade, but this capital has also, to a large extent, been deployed at

[1] Tillväxten i svensk life science-industri 2012-14 – fortsatt nedgång eller nytändning?, Tillväxtanalys, PM 2016:04
[2] The Swedish Drug Discovery and Development Pipeline 2016, SwedenBio, December 2016
[3] The Swedish Research Barometer 2016 – An overview of the Swedish research system in international comparison, Swedish Research Council, October 2016
[4] Riskkapitalstatistik 2015 Venture Capital, Tillväxtanalys, Statistik 2016:06

later stages.[5] Several inquiries stated that it would be beneficial if a larger proportion of public venture capital was directed towards the early stages.[6] [7]

However, recently some adjustments have been implemented. As a result of Hans Rydstad's investigation in 2015, the Swedish government has created a fund-in-fund structure called Saminvest AB, which aims to provide a better means of early-stage investments. However, given the substantial capital requirements in the life science sector, it has been pointed out by both the investigation and consulting feedback that these initiatives will not be sufficient.[8] In life science, the journey from basic scientific discovery to fully approved product can span 10 to 20 years and require investments exceeding 2 billion USD.

So, what are the options for Sweden to promote adequate conditions for early-stage venture capital investments in life science companies?

This exploratory study aims to investigate whether a novel investment structure termed "megafund" could fill the financing gap in the life science sector, thereby promoting innovation and growth. In brief, the megafund would use novel financial engineering techniques, such as portfolio theory, securitisation, and dynamic leverage, to fund a large number of high-risk/high-reward projects. Theoretically, the size and structure of the megafund would simultaneously reduce risks and provide significant returns. Moreover, by issuing both equity and debt, the megafund would pave the way for investments from institutional investors who traditionally do not invest in the early stages.

The report is structured as follows: Firstly, the challenges and opportunities that are calling for an acceleration of life science innovation are elaborated on. Secondly, the megafund concept is presented in detail, including some international experiences. Thirdly, the results of the interviews with key stakeholders in Sweden, regarding the feasibility of implementing a megafund in Sweden, are presented and discussed. Lastly, some conclusions are presented and recommendations for future work are proposed. Information about the applied methods for data collection and analysis, and further issues of interest can be found in the appendices.

[5] Riksrevisionsverket. (2014). RiR 2014:1 Statens insatser för riskkapitalförsörjning - i senaste laget.
[6] En fondstruktur för innovation och tillväxt, SOU 2015:64
[7] Svensson R, (2011), "Statligt venture capital i stort behov av omstrukturering", I Ekonomisk Debatt, Årg. 39, Nr. 6, s 14-27
[8] SwedenBio:s remissvar till utredningen "En fondstruktur för innovation och tillväxt (SOU 2015:64)", September 2015

# 2 The outlook for healthcare

This section provides an outlook for healthcare by presenting some of the major challenges, as well as the need for innovation as an effective strategy to confront them.

## 2.1 A growing and ageing population

Swedish life expectancy projections for 2060 show an increase of 5 years in the case of women and 7 years in the case of men, reaching the age of 89 and 87 years, respectively.[9] Although improved individual health will decrease the cost of health and elderly care per person, the total cost will increase due to the rapid growth of the population segment comprising the elderly. In concrete terms, by 2050 the cost of elderly care in Sweden is expected to have grown by 70 percent and the cost of healthcare by 30 percent. Given that the healthcare system will continue to increase its ambition and introduce new treatments, the cost of healthcare is expected to rise by about 80 percent.[10] Virtually all countries in the developed world are facing a similar challenge.

## 2.2 Unmet clinical needs and the burden of chronic diseases

Chronic diseases, defined as health problems which affect patients over an extended period of time, as opposed to short-term illness and injury, represent the major share of the burden of disease in Europe and are responsible for 86 percent of all deaths. 700 billion Euros per year (70–80 percent of the overall healthcare budgets) are spent on chronic diseases in the European Union.[11]

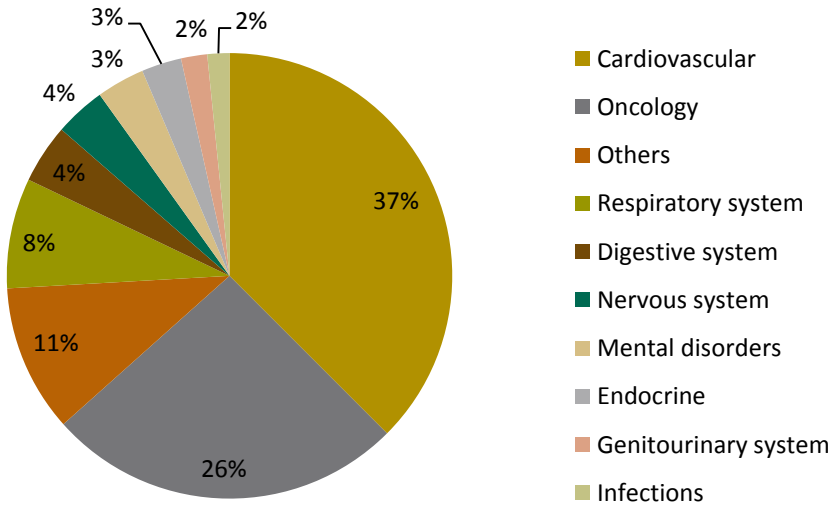
Cardiovascular diseases remain the most significant cause of death, and atherosclerosis is responsible for the vast majority of them. Atherosclerosis is an arterial disorder characterised by lipid accumulation and inflammation, the final consequences of which are myocardial infarction and stroke. In 2013 in the EU-28, there were 1.9 million deaths resulting from diseases of the circulatory system (Figure 1).[12]

After cardiovascular diseases, cancer is the most significant cause of death and morbidity in Europe. In certain countries, 1 in 2 men and 1 in 3 women will develop cancer during the course of their life. In fact, more than 3.7 million new cases, classified into more than 200 types of cancer, are diagnosed each year in Europe.[13]

Diseases affecting the respiratory, digestive, nervous, endocrine and genitourinary systems account for 20 percent of the overall mortality. Despite its importance in other geographies, infectious diseases are responsible for only 1.6 percent of the total number of deaths; however, the appearance of species of bacteria resistant to antibiotics may represent a future challenge (Figure 1).

[9] Statistics from the SCB website (www.scb.se), Mars 2017
[10] Den ljusa framtid är vård – delresultat från LEV-projektet, Socialdepartementet, 2010
[11] 2014 EU Summit on chronic diseases conference conclusions
[12] European Federation of Pharmaceutical Industries and Associations' calculations (May 2016) obtained from Eurostat data relating to 2013.
[13] www.euro.who.int/en/health-topics/noncommunicable-diseases/cancer/data-and-statistics

Figure 1 Causes of death by major disease areas in Europe (EU28)




*Source: European Federation of Pharmaceutical Industries and Associations' calculations (May 2016) obtained from Eurostat data relating to 2013.*

## 2.3 The need for innovation

The increase in healthcare costs described in the previous section would imply that the percentage of Swedish GDP dedicated to this purpose would increase from 13 to 16 percent. In order to maintain the current share of GDP, an annual efficiency increase of 0.6 percent would be required.[14] Innovation will be crucial to accomplishing sufficient efficiency improvements. For example, compared with the costs of hospitalisation, surgery and lost productivity, drugs have been, and still are, a highly cost-effective option in limiting healthcare costs. Another example is cost-effective digital solutions.

[14] Den ljusa framtid är vård – delresultat från LEV-projektet, Socialdepartementet, 2010

# 3 A changing landscape for life science innovation

Over the last decade Astrazeneca has closed and downsized its facilities in Lund (2010) and Södertälje (2012), which has resulted in a loss of more than 2,000 jobs. Moreover, in 2011 St. Jude Medical closed its site in Järfälla outside Stockholm, dismissing about 650 employees. As a result, a larger proportion of the employees in the Swedish life science sector are now employed in small and medium sized companies (SMEs). [15]

During the same time period (between 2006 and 2016) the number of Swedish pharma companies with projects in clinical development increased from 24 to 67, indicating a growing innovation potential.[16] Moreover, the innovation and growth models of the life science sector have been changing rather drastically over the last decade.

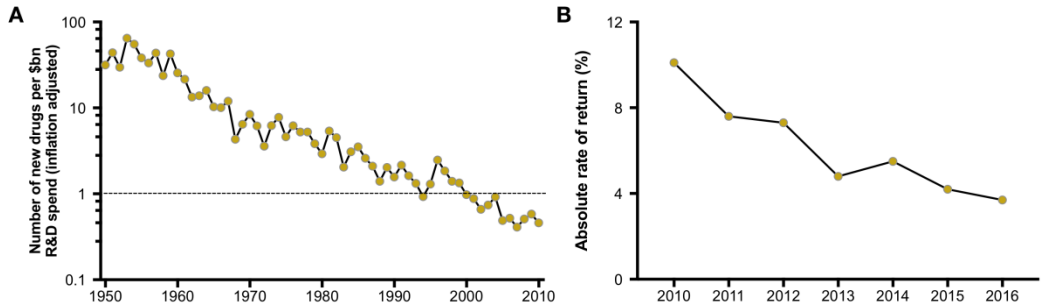
Given this new environment, what are the opportunities to strengthen the Swedish life science sector? This section addresses this issue by elaborating on a few of the most significant developments and on the financial challenges for innovative start-up companies.

## 3.1 Changing innovation models

The main driver for growth in the pharmaceutical industry is innovation. A major challenge that the industry has been facing for many years is a deterioration in R&D productivity. The efficiency of the industry measured as the number of new drugs approved by the regulatory authorities per billion USD, inflation-adjusted, spending in R&D, has steadily declined for decades (Figure 2A).[17] In concrete terms, there has been an 80-fold decline from 1950 to 2010.

In addition, recent studies have shown a historical trend towards the reduction of the projected return on investment associated with pharmaceutical industry R&D (Figure 2B).[18] Other significant challenges for the industry are continued patent expiration, regulatory obstacles, as well as access, pricing and reimbursement.

Figure 2 Trends in the current R&D model. A) Number of new drugs approved per billion USD (inflation-adjusted) invested in R&D over 60 years. B) Average return on investment for R&D expenditure of the 12 leading biopharma companies.




[15] Tillväxten i svensk life science-industri 2012-14 – fortsatt nedgång eller nytändning?, Tillväxtanalys, PM 2016:04
[16] The Swedish Drug Discovery and Development Pipeline 2016, SwedenBio, December 2016
[17] 2012 Diagnosing the decline in pharmaceutical R&D efficiency
[18] 2016 Deloitte - Balancing the R&D equation

Currently, all the large pharmaceutical companies are adapting their innovation models to the new circumstances. Several large players such as Abbott, Bayer, Eli Lilly, GSK, J&J, Merck and Sanofi are diversifying their businesses through the incorporation of, for example, diagnostics, generics, medical devices, innovative drugs, consumer health and animal health, under a single umbrella organisation. On the other hand, there are also pure biopharma companies such as AbbVie, Astrazeneca, Bristol-Myers Squibb, Novartis, Pfizer and Roche, which primarily focus on innovative drugs.[19]

A common trend in all these companies is that they are, in one way or another, focusing on developing personalised medicines. The genetic variation exhibited by every human being implies that each person displays certain traits that make us unique. Traditionally, the efficiency of new drugs has been tested in large populations and medicine is practiced with the median concept in mind. As a result, millions of patients take medications that are not effective or cause potentially avoidable side effects. Personalised medicine implies that drugs, to a much larger extent, specifically target health problems on an individual scale.

To accomplish this, new innovation and growth models are being implemented. These new models include, for example, partnerships with academia and SMEs.[20] This change is also taking place in Sweden. For example, in 2015, Johnson & Johnson and the Karolinska Institute jointly created a hub to promote innovation. Another example is Alligator Bioscience AB, a Swedish biotech company developing antibodies for cancer immunotherapy, which entered into collaboration with Janssen Biotech in 2015.

## 3.2 The digitalisation of healthcare and life sciences

As previously stated, the healthcare system 10 years from now will be very different from the existing one. It has been argued that eHealth and mHealth tools, as well as the improved dissemination and evaluation of information (big data), will enable a transition towards a more person-centric model. This paradigm shift implies the design of new systematic patient care processes, the implementation of new management systems, the construction of new facilities and training of the personnel running them, the participation of non-traditional players who can offer a value-based solution and finally, the involvement of citizens in their own health management.[21]

This development will be crucial to creating more cost-efficient healthcare systems. As an example, McKinsey estimated that the Swedish healthcare system could save SEK 180 billion by 2025, merely through implementing existing digital solutions. The saving could probably be larger given that the future will, most likely, bring new technologies that we cannot envisage today.[22]

This convergence of ICT and healthcare will also influence big pharma's innovation model. For example, several big pharma companies are currently marketing new medicines together with companion diagnostics and integrated ICT solutions. Moreover, real evidence based on individuals will enable the correct patient to get an accurate dose of the proper drug at the right time. The implementation of real-world evidence and other recent aspects of the drug development process will also help identify the drugs that will fail due

[19] Gautam, A. and Pan, X., 2016. The changing model of big pharma: impact of key trends. Drug discovery today, 21(3), pp.379–384.
[20] 2017 Rethinking pharma productivity – McKinsey
[21] Topol, E. J. (2012). The creative destruction of medicine: How the digital revolution will create better healthcare, Basic Books, 2013, New York
[22] Värdet av digital teknik i den svenska vården, McKinsey & Company, June 2016

to a poor performance in terms of efficacy or safety, or will generate new therapies that do not rely on drugs at all. In any case, the need for health innovation is a major priority and technology giants, such as Apple and Google, have seen the opportunity to apply their innovation capabilities in order to position themselves in the health space.

## 3.3 Lack of early-stage venture capital

The life science sector has a strong tradition of attracting venture capital. In Sweden, life science and ICT have been the sectors that attracted most assets in recent years.[23] The same is true for the United States[24] and Europe as a whole.[25]

At the same time, private early-stage venture capital investments in Swedish life science companies decreased over the last decade and the majority of assets have been deployed at later stages. In general, public venture capital has increased over the last decade, but this capital has also, to a large extent, been deployed at later stages.[26] As previously mentioned, several inquiries have argued that a larger proportion of public venture capital should be directed towards the early stages, where the shortage of capital for start-ups is most severe.[27] [28] However, given the substantial capital requirements that start-ups in the life science sector are demanding, it has been stated that such redirection of funds would not be sufficient to cover the life science sector's investment necessities.[29]

It is worth noting that this situation is not a unique for Sweden but a common European problem. Compared to biotechnology companies based in the US, European ventures receive less funding, and less funding per company. European biotechnology ventures have also been less successful than US ones, at least in terms of IPO valuations.[30] The success of US venture capital investments in biotechnology can be traced back to the early 1980s when American entrepreneurs exploited technological breakthroughs more rapidly than their European counterparts. Other factors behind this success were a strong level of funding for biomedical science, a supply of highly skilled scientists, as well as legislative measures such as the Bayh-Dole Act of 1980. Hence, in recent decades the US has had a first-mover advantage over Europe.

[23] Riskkapitalstatistik 2015 Venture Capital, Tillväxtanalys, Statistik 2016:06
[24] http://nvca.org/pressreleases/2016-nvca-yearbook-captures-busy-year-for-venture-capital-activity/
[25] 2015 European Private Equity Activity - Statistics on Fundraising, Investments and Divestments. Invest Europe, 2016.
[26] Riksrevisionsverket. (2014). RiR 2014:1 Statens insatser för riskkapitalförsörjning - i senaste laget.
[27] En fondstruktur för innovation och tillväxt, SOU 2015:64
[28] Svensson R, (2011), "Statligt venture capital i stort behov av omstrukturering", I Ekonomisk Devatt, Årg. 39, Nr. 6, s 14-27
[29] SwedenBio:s remissvar till utredningen "En fondstruktur för innovation och tillväxt (SOU 2015:64)", September 2015
[30] Bains, W., 2006. What you give is what you get: Investment in European biotechnology. Journal of Commercial biotechnology, 12(4), pp.274–283.

# 4 The megafund concept

This chapter introduces the concept of a megafund as a mechanism to promote early-stage life science investments in order to exploit the innovation and growth potential of the Swedish life science sector.

## 4.1 What is a megafund?

The megafund is an investment structure that uses financial engineering methods, or more specifically portfolio theory, securitisation and dynamic leverage, to fund a large number of early-stage and preclinical drug development projects. Theoretically, its size would allow a reduction of the risk associated with drug development and provide significant returns for its investors. The concept was first introduced in the Laboratory for Financial Engineering at the Massachusetts Institute of Technology (MIT) in 2012.[31]

The megafund provides a bridge for the existing funding gap in the early stages of start-ups and has the potential to generate a beneficial effect in society in the form of new solutions for health and wellbeing that might affect the quality of life of citizens, as well as job creation and economic growth. The return on investment of a megafund might not be attractive to the venture capital industry; however, it is likely that it appeals to institutional investors such as pension funds, insurance companies and other large financial institutions.

## 4.2 Financial engineering techniques

The use of the mathematical framework known as "modern portfolio theory" permits lowering the risks of an investment while maintaining or increasing the expected returns. Essentially, the combination of a large number of diversified high-risk and potentially high-return projects, and their simultaneous development in the context of a single financial entity, considerably decreases the risks and facilitates the task of raising capital.

Securitisation is a common financing method in which capital is raised by issuing debt of different risk-reward profiles (seniorities) as well as equity, which permits access to larger sources of capital from a diverse population of investors. The result of the application of securitisation to early-stage assets would thus be *research-backed obligations,* which are issued to investors.

A remarkable aspect of the megafund is that it aims to have access to debt financing, a much larger market compared to the equity market, and one that has traditionally not been able to invest in early-stage drug development. To exemplify this aspect with some figures, in 2014 the venture capital industry in Sweden had SEK 2.6 billion in investable assets,[32] whereas the Swedish debt market in the same period had a value of more than SEK 3,000 billion.[33] Importantly, the costs of financing the megafund with debt instead of equity would be lower and the different tranches of the capital structure would allow investors to choose between different risk-reward alternatives.

[31] Fernandez, J.M. et al. 2012. Commercializing biomedical research through securitization techniques. Nature biotechnology, 30(10), pp.964–975.
[32] Riskkapitalstatistik 2015 Venture Capital, Tillväxtanalys, Statistik 2016:06
[33] The Swedish Financial Market 2015, Sveriges Riksbank, Stockholm 2015

The use of dynamic leverage would allow the gradual introduction of debt once the portfolio started generating cash, which is thought to further increase the yield in the different tranches.[34]

It should be noted that similar financial techniques were used to build complex financial products that historically have been associated with the 2008 financial crisis. The MIT economists who conceived the megafund argue that the techniques worked as effective tools in raising capital and that the crisis was caused by a negligent use of these tools.

## 4.3 Theoretical modelling of megafunds

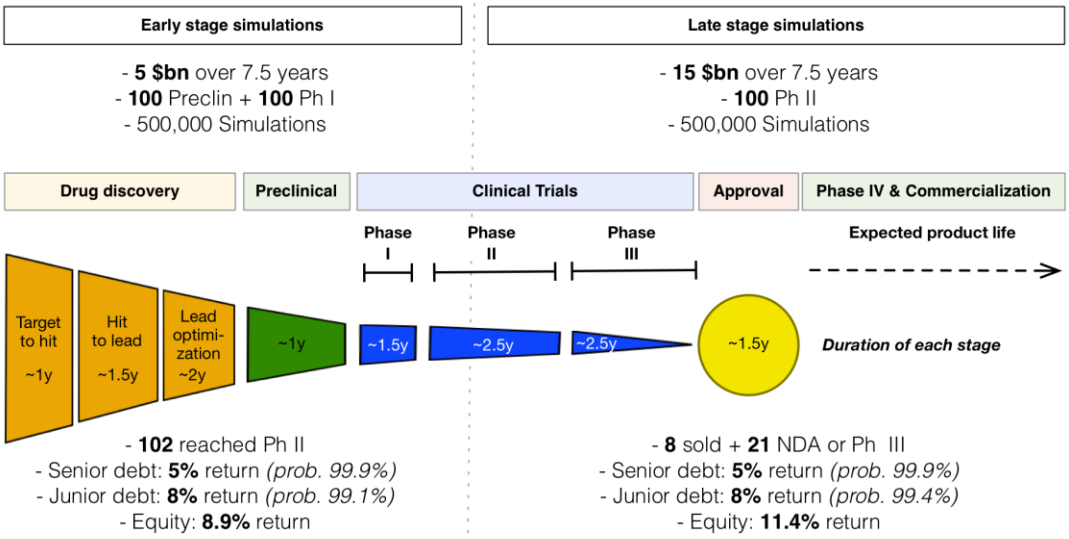
In their first paper, the economists from the MIT provided a comprehensive, simulation-based analysis of the application of a megafund in oncology drug development. Oncology was chosen because this therapeutic area is visible to society, offers opportunities for portfolio diversification (see section 2.2 for additional information), and because the existence of comprehensive databases makes it possible to realistically estimate the probability of a drug candidate successfully transitioning from one stage of development to the next, as well as additional relevant parameters[35]

The study included two simulations consisting of 500,000 independent sample paths each. The first simulated a USD 5 billion megafund investing in 100 preclinical and 100 phase I compounds (early-stage) over 7.5 years, in which the capital structure was divided into three tranches (senior debt, junior or mezzanine debt and equity), and the goal was to sell the projects after having entered phase II trials. The second simulated a USD 15 billion megafund investing in 100 phase II projects (late-stage) over 7.5 years, in which the capital structure was similar to the one in the previous simulation and the goal was to develop the compounds as far as possible or sell when appropriate.

The returns on investment for the different tranches provided by the simulations were as follows: Both simulations yielded a 5 percent annual return for the senior debt and an 8 percent annual return for the junior debt with associated default probabilities below 1 percent. The equity tranche in the early-stage simulation generated an average annual return of 8.9 percent; on the other hand, the late-stage simulation yielded an average annual return of 11.4 percent (Figure 3).

[34] Montazerhodjat, V. et al., 2016. Financing drug discovery via dynamic leverage. Drug discovery today, 21(3), pp.410–414.
[35] Fernandez, J.M. et al. 2012. Commercializing biomedical research through securitization techniques. Nature biotechnology, 30(10), pp.964–975.

Figure 3 Example of a megafund in oncology drug development. Application of a megafund in early-stage *vs.* late-stage oncology drug development. Abbreviations: $bn (billion USD), preclin (preclinical stage), Ph (phase), prob (probability), NDA (new drug application).




The megafund theoretical concept has also been applied to drug development in the area of rare diseases. It has been estimated that a megafund of USD 575 million investing in 10–20 early-stage projects could yield a 5 and 8 percent annual return for the senior and junior debt, respectively, and a double-digit rate of return for the equity tranche.[36] The particular nature of rare diseases (with higher success rates, shorter times to approval and specific regulations) enabled the megafund to deliver excellent results with less capital and a smaller portfolio than in the oncology example.

The potential shown in rare diseases has been tested using a real-world example. Using the portfolio of the American National Health Institute's National Center for Advancing Translational Sciences (NCATS), consisting of 28 rare disease projects spanning a diverse range of therapeutic areas, the application of a megafund yielded similar results for the different tranches (5 and 8 percent annual return for the senior and junior debt, respectively, and a double-digit rate of return for the equity transche). Additional simulations indicated that funding guarantees from third parties, such as philanthropists and patients' organisations, could generate even higher figures.[37]

Moreover, a recent study shows how the risk exposure of life settlement companies could be more effectively managed by investing in megafunds issuing research-backed obligations connected to specific diseases.[38]

[36] Fagnan, D.E. et al., 2014. Financing drug discovery for orphan diseases. Drug discovery today, 19(5), pp.533–538.
[37] Fagnan, D.E. et al., 2015. Financing translation: Analysis of the NCATS rare-diseases portfolio. Science translational medicine, 7(276), pp.276ps3–276ps3.
[38] MacMinn, R.D. and Zhu, N., 2017. Hedging Longevity Risk in Life Settlements Using Biomedical Research-Backed Obligations. Journal of Risk and Insurance.

## 4.4 International experiences of megafunds

### *The Rare Diseases Megafund in the United States*

Following the original concept of the megafund in drug development proposed by the MIT economists, the H.R. 3731 Rare Diseases Fund Act[39] was introduced in the United States House of Representatives in September 2015, although it has yet to be approved. The bill aims to create a USD 400 million pilot megafund to fund early-stage rare disease therapeutics. The megafund would be privately owned and operated and the capital structured would be tentatively formed by 50 percent equity and 50 percent debt.

### *London megafund*

In 2015, the mayor of the City of London (at that time, Boris Johnson), together with investors and drug companies, announced that the creation of a GBP 10 billion megafund to invest in early-stage drug development was being considered; however, no additional information has been published since this time.[40] The current geopolitical situation in the United Kingdom may have put this initiative on hold.

### *The Australian Medical Research Future Fund*

One of the most ambitious elements of Australia's National Innovation and Science Agenda is the Medical Research Future Fund (MRFF).[41] This fund is being developed as a public-private partnership and aims to invest ASD 20 billion in the coming years to bridge the gap between the medical research community and the health system in order to implement new practices, services and products in the latter. The authors of the report describing the MRFF emphasise the opportunity that the fund represents in providing economic prosperity through the commercialisation of Australian research as a driver of GDP.

### *Other relevant initiatives*

There are further examples of funds created to address the difficulties that start-ups face during the early stages of their development. In Sweden, the Karolinska Institute initiated Karolinska Development in 2003, a system to secure financing for the innovations produced by its researchers. In France, the tax-free scheme *Fonds Commun de Placement dans l'Innovation* raised over 6 billion euros from hundreds of thousands of investors (crowdfunding-like scheme). At least 60 percent of the fund was destined for biomedical innovation.

The main difference between these initiatives and the megafund is that the latter uses securitisation of its assets to issue debt in the form of research-backed obligations.
A particular case is Royalty Pharma. This company uses portfolio theory and securitisation but invests in royalty streams of approved drugs and avoids the high-risk early-stage companies.

[39] https://www.congress.gov/bill/114th-congress/house-bill/3731/text
[40] www.reuters.com/article/us-biotech-london-idUSKBN0P516320150625
[41] MRFF A Research Australia Perspective Report 2016

# 5 The feasibility of a Swedish megafund

The following section presents and elaborates on the interviews' findings and how the answers relate to previous work.

## 5.1 Would a megafund fit in the Swedish ecosystem?

The interviewees agreed that there is a lack of early-stage venture capital for Swedish life science companies and found the megafund concept an interesting solution that would fit well in the Swedish ecosystem for life science innovation.

A representative of Vinnova stated that a megafund in Sweden, if successful, has the potential to propel the life science sector and accelerate the transformation of the healthcare system. In addition, the expert suggested genomic medicine as a potential investment area for the megafund.

Representatives from academia argued that the megafund would promote collaboration with the industry, provide opportunities for junior members to develop their scientific findings into commercial assets and offer alternative career options at a time in which only a few members will have the opportunity to occupy a senior position in the future. They also indicated that in order to avoid competition, the nature of the capital that would nurture the megafund should be different than the sources that usually fund academia.

An initial concern of the authors was that the megafund would create a degree of overlapping and destructive competition, in particular in relation to venture capital firms. However, these preconceived ideas were discarded by the interviewees. For example, venture capitalists were optimistic about the notion of a megafund and argued that they would primarily see it as a potential investment partner. The only time they would view the megafund as a competitor would be when they raised capital from institutional investors.

Although the interviewees had an overall positive view on the realisation of the megafund, they also made some critical remarks regarding its feasibility; these will be described in the next sections.

## 5.2 Defining the investment focus

In the original articles by the MIT economists, the megafund solely focuses on investments in drug development projects. A remark made by several interviewees was that the Swedish pipeline would probably not provide enough high-potential drug candidates to serve the megafund. When asked about an alternative investment focus, two major ideas emerged.

The first suggestion was that the megafund could pave the way for making some of its investments in companies located abroad. Investing in foreign companies could have a positive influence on the decisions taken by investors in other countries, create valuable international collaborations and provide a benchmark for Swedish innovation potential. On the other hand, this approach might limit potential job creation in Sweden.

The second and more supported alternative proposed widening the scope of the megafund and also included medical technology, biotechnology and health-oriented ICT. Several interviewees emphasised that a megafund like this could benefit from investing in solutions that integrate the knowledge and expertise from these different domains. It was

highlighted that Sweden has a strong tradition of innovation in all these sectors and also a culture of collaboration across disciplines.

## 5.3 Make the megafund attractive to investors

The megafund capital structure makes it possible to offer different investment alternatives to a broad spectrum of investors. The investors aiming for more risk and potentially a greater return might be interested in equity and the more conservative investors might be attracted by debt. During the consultation process, the following entities were cited as possible sources of capital that might be interested in participating in a Swedish megafund:

*State or public capital*: European Union funds, Swedish public pension funds, international pension funds, Industrifonden, Saminvest and Vinnova.

*Private capital*: Private pension funds, sovereign funds (*i.e.* Norwegian oil fund), insurance companies, venture capital firms, investment banks, business angels, pharmaceutical and biotechnology companies.

*Philanthropists*: Wallenberg foundation, Cancerfonden, Novo Nordisk trust, Welcome Trust, Chan Zuckerberg Initiative and Gates Foundation.

*Crowdfunding*: A Crowdfunding classic scheme or alternatives mediated by companies.

The primary concern expressed by the investors when considering an investment was the return on investment as well as its incumbent risk levels. The yield and level of risk that was calculated in the theoretical model of the megafund (annual return on investment of 5–8 percent for the different debt tranches with default probability below 1 percent, or a higher return on equity) was considered as being quite attractive. The investors also thought dynamic leverage would make the megafund more attractive since it would improve the overall return on the different tranches by allowing the assets to mature and start generating cash flows before debt is introduced.

The investors also highlighted the importance of the operational aspects of the megafund. First and foremost, the management team should have a strong background in finance with an excellent track record in life science venture capital investments, and their economic incentives should be connected with the degree of efficiency of the megafund. In addition, they emphasised that the megafund should have a sound governance structure with a long-term perspective in order to be attractive (additional information regarding the importance of choosing the right projects to be included in the portfolio and operations of the megafund can be found in appendices B and C).

One way to accomplish this would be to design the megafund as a public-private partnership, in which the government takes some risk-protection measures (for example, a certain degree of risk asymmetry that is beneficial to investors), with a small and dynamic management team with cross-disciplinary expertise.

The interviews revealed that institutional investors would most likely play a central role in the megafund. These investors have a long-term investment view and a strategic asset allocation which, in a prolonged era of low interest rates and high stock market values, might consider the megafund an appealing opportunity. Moreover, these investors generally aim at spreading the risks across a broad group of assets since it protects them from correlated risks and, as a result, can lead to steady long-term returns. Another positive note is that an increasing number of institutional investors are looking for investment opportunities with a demonstrable social benefit.

## 5.4 Is the timing right for a Swedish megafund?

The interviewees cited several arguments supporting the fact that the right moment for a Swedish megafund is now. First of all, competition in life sciences is becoming tougher and many other countries are making significant investments in order to become more competitive. At the same time, the interviews confirm that the innovation potential in the life sciences is higher than ever before.

Finally, the geopolitical environment in the United Kingdom and the United States is changing with Brexit and the new US Administration. In these countries there is growing uncertainty regarding the future of science and scientists. A megafund in combination with the teachers' exemption (the rule which lets Swedish university employees own the rights to their inventions) and adequate policies (e.g. entrepreneurs' visas) might contribute to attracting international experts, as well as to secure national talent and allow their good ideas to grow in Sweden.

## 5.5 Complementary initiatives would be required in order to succeed

Although the focus of this report and the interviews has been the feasibility of the megafund, a number of complimentary initiatives were postulated as crucial in order to successfully implement the megafund. In general, the interviewees argued that creating a competitive climate for science, innovation and business in Sweden, with an attractive risk-reward ratio for individuals and companies, is fundamental. These general conditions included, for example: investments in basic science, attractive career paths for scientists, educational programmes about entrepreneurship and innovation for academics, incentives to implement innovation in the Swedish healthcare system and a competitive tax system for entrepreneurs and experts.

# 6 Concluding discussion

The interviews reveal that access to early-stage venture capital is a challenge for many Swedish life science companies and that a megafund could be a plausible solution for addressing this funding gap. Nevertheless, the analysis highlights a number of critical issues that have to be considered in the initiation and design of a megafund.

Regarding the investment focus of the megafund, several interviewees argued that the fund should strive to address disruptive solutions integrating knowledge from the different life science segments (i.e. pharma, biotech, medtech and ICT) in order to realise the full innovation potential of the sector. Much less attention was being paid to whether the fund should target specific diagnosis or disease groups. Given that healthcare costs and innovation opportunities vary between different disease areas, there is a need to further investigate this aspect before setting up a fund.

The report reveals how other countries such as the UK, US and Australia are considering setting up megafunds for life science innovation. In times of disruptive scientific discoveries, history, and research, tells us that a "first mover advantage" may be of great importance to gaining a competitive edge.[42] As brought forward in some of the interviews, if Sweden wants to be a global leader in life sciences and it is believed that a megafund would support this vision, it has to be implemented quite soon. Moreover, given the current geopolitical situation, a megafund could also be a way of attracting talent.

There is a risk that the underlying assets would be valued too optimistically, as they were in the financial crisis in 2008. Ensuring the transparency of megafund operations would prevent the issues which led to the mortgage crisis. Another aspect for further investigation is whether Crowdfunding could play a major role in the megafund. Several interviewees pointed in this direction and the French initiative *"Fonds Commun de Placement dans l'Innovation"* exemplifies the possibilities of such an approach.

Before a megafund could be implemented there would be a number of elements to define. For example, the fund's investment focus, size, duration, and number and type of portfolio projects need to be considered as well as how to assess risk, forecast profitability, and structure the capital. Other considerations relate to operational and technical procedures, economic, financial, regulatory and legal aspects, as well as governance. Running different simulations and exploring complementary initiatives would probably help define an adequate megafund model for Sweden.

Hence, the following conclusions can be drawn from the study:

[42] Bains, W., 2006. What you give is what you get: Investment in European biotechnology. Journal of Commercial biotechnology, 12(4), pp.274–283.

- A Swedish megafund for life science innovation could bridge the existing funding gap in the early stages of life science innovation and entrepreneurship.
- Other countries are currently setting up megafunds or similar solutions to promote life science innovation.
- The megafund could be an opportunity to develop disruptive ideas by integrating knowledge from the different life science segments.
- There are several aspects that need further investigation before implementing a megafund for life science innovation.
- In order for Sweden to succeed with a megafund for life science innovation, it would have to be combined with other initiatives for promoting innovation.

# Appendix A Data collection, analysis and limitations

### *Authors*

The study was conducted by Andres Laguna Fernandez Ph.D., Assistant Professor in Translational Cardiology at the Karolinska Institute, from January 9 to March 31, 2017. The relationship between the Swedish Agency for Growth Policy Analysis and the author was made possible through a part-time (70 percent) internship supported by the Karolinska Institute Career Service. The scientific background and personal interest of the author in innovation were the source of several ideas included in the report.

Carl Wadell Ph.D., Analyst at the Swedish Agency for Growth Policy Analysis, conceived the idea of exploring the megafund concept in Sweden, coordinated the internship with the Karolinska Institute Career Service, wrote specific parts and supervised the development of the project.

### *Literature review*

At present, there is limited information describing the use of megafunds to support the development of innovative life science projects on a large scale. Around a dozen peer-reviewed publications address the topic. The available documents can be classified into theoretical research papers and opinion articles. The most relevant aspects described in these publications have been included in this report.

Multiple opinion leaders from diverse backgrounds, consulting companies and government agencies have presented their ideas and theories about the future of the medical practice and life science industry. Some of those ideas have been compiled in this study.

### *Interviews with key stakeholders*

A total of 26 opinion leaders working in the Swedish pharmaceutical, biotechnology, medical technology and ICT industries, academia, venture capital, pension funds, private investors and healthcare were identified, contacted via email or LinkedIn, and invited to participate in a face-to-face interview. Of these, 23 accepted the invitation, the remainder did not respond. The authors acknowledge the valuable contribution made by all the participants in the consultation.

The interview started with a presentation by the author in which the following concepts were introduced: Current R&D model, a megafund as a possible tool to improve the drug development process and to generate profits, current trends and future outlook of the healthcare system and the idea of a customised megafund for Sweden. After the presentation, the interviewees were asked to express their opinions about the ideas presented, identify the challenges and offer suggestions regarding how to further develop the project. Their opinions are reflected in the results and discussion sections of the report.

### *Limitations*

*Author bias:* Until the time the author started his internship at the Swedish Agency for Growth Policy Analysis, his main professional activity had been performed in academia. In order to overcome his limited perspective concerning the issues being addressed in the report, the author planned and executed an extensive set of interviews with key stakeholders.

*Interviews:* Further interviews with additional experts from the above-mentioned sectors and other innovative areas of the Swedish economy (for example, FinTech and the interactive entertainment industry) might have revealed additional relevant aspects.

*Opportunity for further research:* The author and supervisor of the report agree that because of the relevance of the conclusions presented here, there is an opportunity to further analyse the feasibility of a tailored Swedish megafund as an innovative mechanism for creating prosperity and life science innovation.

## *Abbreviations*

ASD: Australian Dollar

eHealth: Use of information and communication technologies for health-related tasks.

ICT: Information and communication technologies.

GBP: Great Britain Pound

MRFF: Medical Research Future Fund (Australian)

mHealth: Mobile health (practice of medicine and public health supported by mobile devices).

R&D: Research and Development

SEK: Swedish Krona

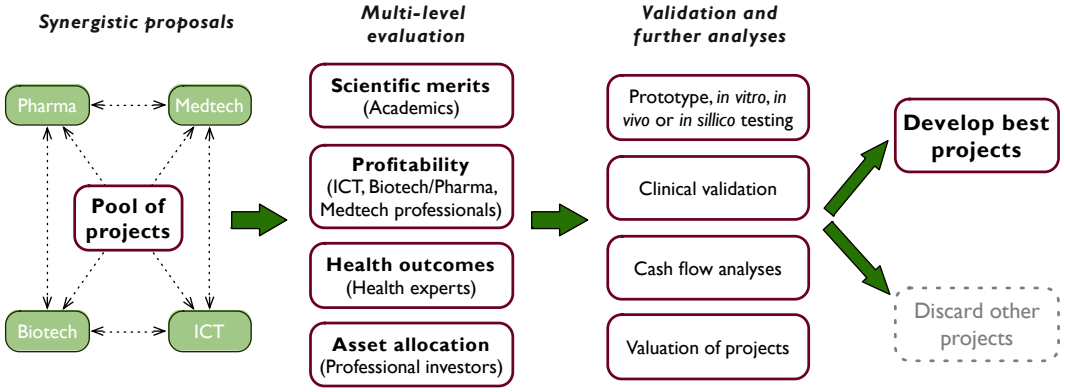
SMEs: Small and medium-sized enterprises

USD: United States Dollar

# Appendix B Building the megafund's portfolio

A possible selection scheme for the candidate projects to be included in the megafund's portfolio would involve an independent multi-level evaluation process in which the unique expertise and knowledge of: (1) academics, (2) professionals from the ICT, pharmaceutical, biotech and medtech segments, (3) health experts and (4) professional investors, would be used to rank the projects based on their scientific merits, estimated profitability, potential health and wellbeing outcomes, and overall asset allocation. A validation stage aimed at increasing the chances of developing the strongest projects and identifying and discarding the projects that might not possess sufficient quality as soon as possible was also encouraged (Figure 4).

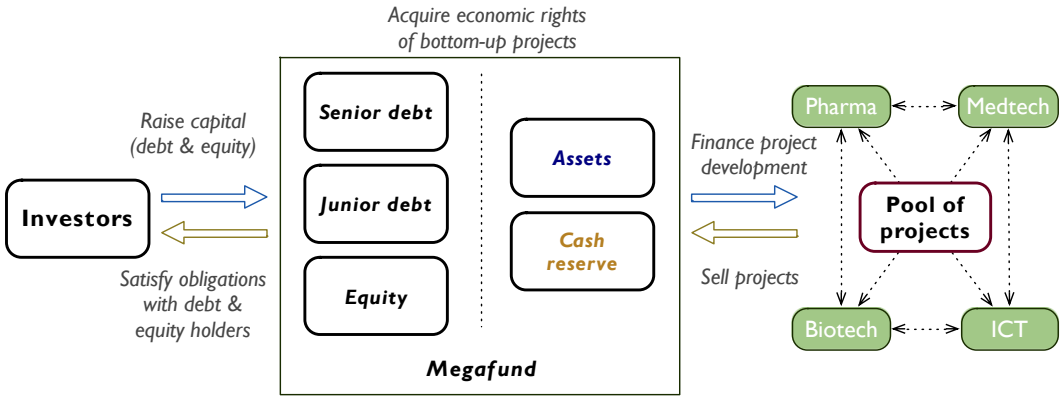
Figure 4 Proposed selection scheme to for the projects to be included in the portfolio



# Appendix C Description of the Swedish megafund structure

The following subsection summarises the structural aspects of a megafund as described in the literature and takes into consideration the opinion of the interviewed experts. The original description of the megafund implies a capital structure divided into different tranches: debt with different risk/reward profiles and equity. With the capital, the megafund would finance the development of a large number of well-diversified projects and cover all the associated costs. The funds generated from the portfolio sale would be used to satisfy obligations of the debt and equity holders (Figure 5). The economy of scale associated with the megafund considerably decreases costs and maximises the return and the application of dynamic leverage would further optimise the yield in the different tranches.

Figure 5 Proposed structure and operating model for the Swedish megafund




Research Institutes of Sweden (Rise) was identified as an example of an organisation that might have the requisite expertise to manage the megafund. Moreover, as suggested by the MIT economists, the megafund should probably have its portfolio assessed and valued by a third party on a regular basis to ensure transparency.

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