A Work Project, presented as part of the requirements for the Award of a Master's degree in **Management** from the Nova School of Business and Economics.

PREVENTICO - TACKLING CHRONIC KIDNEY DISEASE USING WEARABLE BIOSENSORS: MARKET AND COMMERCIALIZATION

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Group Contribution

Abstract

The Building Companies Based on Science Field Lab (FL) challenged students to explore a scientific breakthrough and build a business plan with the ultimate goal of creating a new venture. Throughout the FL, the group of students explored a real problem and its effects on society. From then, they identified a new and unique solution to tackle the initial problem, by pursuing market research, sizing, and a deep analysis of all stakeholders involved. In later stages, students also developed a financial analysis where fundraising needs were identified, as well as potential strategic partnerships, critical skills, valuation, and possible exit scenarios. This final document encompasses all the elements necessary to pitch to potential partners and investors.

Keywords: Venture Capital, Entrepreneurship, Innovation, Science, Leadership, Market Research, R&D, Start-up, Entrepreneurial Finance, MedTech, Kidney Disease, Wearables, Biosensors, Commercial, Business Strategy, Operations.

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EXECUTIVE SUMMARY

850 million people are affected by chronic kidney disease (McCullough 2019), and its treatment in the late stages imposes massive financial burdens on the patient and the country's economy. But the progression of chronic kidney disease can be slowed or completely stopped if diagnosed and treated early. (National Kidney Foundation 2015)

Our soon-to-be-founded company, Preventico, will introduce the first commercially viable wearable device, the SIKMA, to the U.S. market. The device will allow medical professionals to actively monitor and manage patients at risk of getting a chronic kidney disease. On our way to market, we will:

- Raise an initial seed funding round to establish our company in the U.S. and hire an internal software development team to start work on the accompanying software.
- Engage an experienced agency providing electronic manufacturing services to handle the development of the hardware product until it is ready to market.
- Secure existing knowledge by retaining the current scientific advisory board and pursuing an active intellectual property strategy for existing and future inventions.

The successful setup of our company and teams will allow us to be the first company to enter the market with a commercial, clinically validated product that allows for the monitoring of chronic kidney disease. Initial responses show that this would create value for all levels of users: patients, doctors, and health insurance providers. A successful market entry will allow the company to continue research and development efforts in biomarkers to treat more chronic diseases. It will demonstrate the company's value to enable us, the founders, and the initial investors to exit the company through an acquisition.

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INTRODUCTION

Today, 10% of the worldwide population is affected by chronic kidney disease, with 2 million people receiving treatment through dialysis or a transplant. A number that might only cover 10% of people that need treatment to live. (National Kidney Foundation 2015) Chronic kidney patients must closely monitor their disease daily to mitigate the consequences and live longer lives. But precise monitoring requires frequent in-person visits to the doctor's office, and in the current climate only happens once a month. Chronic kidney disease is costly for the patient mentally and physically, but it also grows increasingly expensive to treat as the disease progresses. The earlier prevention can be done, the better for the patient and the cheaper the treatment will be.

Our new health tech company Preventico is setting out to solve these problems because we see a future where preventing diseases is the new standard instead of treating them. We believe that you can get preventive treatment right on time by actively monitoring your health status and communicating it with your medical team. That is why we are developing the first commercially available smart device for the U.S. market that combines hardware, advanced algorithms, medical knowledge, and user-friendly software to bring healthcare providers and patients the ability to treat chronic kidney disease earlier and communicate more effectively.

Chronic kidney disease is just the start. In the future, we are aiming to expand our product offering with an extensive library of chronic diseases that can be monitored through newly discovered biomarkers by simply wearing a smartwatch.

THE PROBLEM: CHRONIC KIDNEY DISEASE

Chronic Kidney Disease (CKD) is generally referred to as a “silent killer” since it shows no symptoms early, leading to an inaccurate assessment until it is in advanced stages, affecting individuals in many ways. It can either go undiagnosed for several years before presenting any symptoms or progress rapidly in a few months. CKD is defined as the presence of kidney damage or decreased kidney function for three or more months, having significant repercussions on the patient's general state of health. It affects approximately 10% of the population worldwide, and millions die each year due to a lack of access to treatment. (Damien, et al. 2016)

CAUSES

CKD is typically caused by diabetes mellitus and arterial hypertension, both non-communicable diseases that impact morbidity and mortality and have a high prevalence globally. Better management of these two leading causes of CKD would slow the progression of kidney disease and reduce healthcare expenditures. (Damien, et al. 2016). Additionally, aging has a solid link to kidney disease, being a risk-related factor of multi-morbidity, meaning the person is affected by more than one chronic illness at the same time, which culminates in more extensive use of healthcare services and a significant increase in treatment costs. (Junior, et al. 2018)

DIAGNOSIS

To diagnose CKD, performing a Glomerular Filtration Rate (GFR) blood test is essential to check how well the kidneys are filtering and highlight how much kidney function is left. It

estimates how much blood passes through the glomeruli per minute (tiny blood vessel networks in the kidneys that filter waste from the blood). (Dugdale 2021)

The GFR may be estimated from the blood level of creatinine, a waste product that derives from the digestion of dietary protein and muscle activity. This substance is removed from the blood to the kidneys in normal conditions, but the creatinine level increases when kidney function starts to deteriorate. Estimating GFR is crucial for identifying kidney disease, as it generally shows no symptoms until right before kidney failure (National Kidney Foundation 2022). Additionally, urine tests can also detect the presence of blood or albuminuria (an excess amount of a protein called albumin). The constant presence of protein and urea in the urine are the predominant markers of kidney damage, acting as an early and sensitive marker for several types of kidney diseases (National Kidney Foundation 2022).

CKD has several levels of severity, and it is possible to classify the disease into five stages (Table I): stage one constitutes the mildest state with few apparent symptoms, and stage five represents severe illness with low life expectancy if not treated (Damien, et al. 2016). In the early stages (stages 1-3), care focuses on treating complications, slowing the disease, or preventing it from worsening. In the later stages, commonly referred to as end-stage renal disease (ERDS) (stage 4-5), the focus changes to planning for kidney failure and adequate treatment. (Maciejewski, Onstad and Tamayo 2020)

STAGES OF CKD	AMOUNT OF REMAINING KIDNEY FUNCTION	POSSIBLE SYMPTOMS	TREATMENT OPTIONS
STAGE 1	- Mild kidney damage - >90%	- High blood pressure - Leg swelling - Urinary infections - Abnormal urine test (protein in urine)	- See doctor regularly for monitoring - Change into healthy lifestyle (e.g., eating habits, enough sleep) - Report any unusual or unexplained symptoms
STAGE 2	- Mild loss of kidney function - 60% to 89%		
STAGE 3	- Mild to severe loss of kidney function - 30% to 59%	- Changes in urination patterns - Hand and feet swelling - Weakness or fatigue - Dry and itchy skin - Back pain - Muscle cramps	- Referral to a nephrologist - Address any nutrition concerns with renal dietitian and for patient education
STAGE 4	- Severe loss of kidney failure - 15% to 29%	- Anemia - Loss of appetite - Bone disease -Abnormal levels of phosphorus, calcium, vitamin D	- Plan and create access site for dialysis - Receive assessment for possible transplant
STAGE 5	- Kidney failure or close to failure - <15%	- Uremia - Fatigue - Shortness of breath - Nausea - Vomiting - Abnormal thyroid levels - Limbs swelling - Lower back pain	- Start renal replacement therapy (dialysis or transplant)

Table I: The different stages of CKD (Fresenius Kidney Care 2022)

TREATMENT & PREVENTION

In more advanced stages of CKD, where there is a severe decline in the Glomerular Filtration Rate (GFR), individuals initiate one of the options of renal replacement therapy (RRT), such as dialysis or kidney transplant, and these patients are further classified as having End-Stage Renal Disease (ESRD). Of these two treatments, the transplant tends to be the preferred one. However, there are very few organ donors. On the other hand, chronic dialysis causes collateral damage, which, through the years, may increase the pathology related to renal failure itself, being the case of cardiovascular disease (Wieringa, et al. 2017). Dialysis is a procedure used to replace kidney function to remove waste products and excess fluid from the body when they stop working correctly. There are two types of dialysis:

- In **hemodialysis**, blood is pumped out of the body to a machine that works as an artificial kidney, filtering it, and then it is returned to the body through tubes that connect the patient to the device. The blood flows from the body to the dialysis machine through a fistula that

needs to be surgically implanted in the patient's vein. The dialysis machine purifies the blood and corrects any chemical imbalances before returning it to the body. This type of dialysis is done 3-4 times a week and typically must be done in a dialysis center. (National Kidney Foundation 2022)

- In **peritoneal dialysis**, the peritoneal membrane located inside the abdomen acts as a natural filter. Solutions that remove the toxins are put into the abdomen through a catheter that is both inside and outside the body. The solution remains in the abdomen for a specific time and is drained out. This type of dialysis is done daily and can be done at home. (National Kidney Foundation 2022)

These therapies require a high degree of expenditure from the healthcare system, given that its users are susceptible to extended hospitalizations, continuous treatment, and high-cost medications. Both dialysis and kidney transplants consume excessive amounts of healthcare budgets, given that less than 1% of the population consumes about 5% of the budgets (Junior, et al. 2018). Not all kidney disease patients evolve to kidney failure, so the best ally is early detection and adequate treatment, making it possible to stop or slow its progress. Early treatment includes diet, medication, lifestyle adjustment, and monitoring risk factors like diabetes and hypertension (National Kidney Foundation 2022).

WHY IS THIS A PROBLEM?

Kidney disease has a tremendous effect on global health, being a cause of worldwide mortality and an important risk factor for cardiovascular disease. Even though it is largely preventable and treatable, CKD requires greater attention in global health policy decision-making ((GBD Chronic Kidney Disease Collaboration 2020).

CKD has become a severe public health concern due to its increasing incidence and prevalence globally (Junior, et al. 2018). As the kidney damage aggravates, the increased death risk rises, mainly attributable to death by cardiovascular disease (Wieringa, et al. 2017). The diagnosis implies blood samples and kidney tissue analysis, obtained via biopsies involving frequent trips to hospitals and high-skill workers. It's estimated that 90% of these individuals are unaware they have early-stage CKD, as they experience few or no symptoms, and so, the disease silently progresses until there's no other choice than to start dialysis or do a kidney transplant.

The treatment costs for CKD increased after the 1960s, as renal replacement techniques started to be available, making possible the application of lifesaving but costly long-term treatment in the case of patients with End-Stage Kidney Disease (ESKD) (GBD Chronic Kidney Disease Collaboration 2020). In 2017, almost 700 million cases of CKD were recorded worldwide, accounting for a global prevalence of 9.1%. Additionally, since 1990, the prevalence of CKD has increased by 29.3%. The number of people receiving renal replacement surpasses 2.5 million, a value that is expected to double to 5.4 million by 2030 (GBD Chronic Kidney Disease Collaboration 2020). From 1990 to 2017, the global increase in mortality from CKD was 41.5%, which resulted in CKD and cardiovascular disease deaths accounting for 4.6% of global deaths, making CKD the 12th leading cause of death globally in the referred year, an increase from 17th in 1990 (GBD Chronic Kidney Disease Collaboration 2020).

BURDEN TO HEALTHCARE

Globally, CKD represents a great cost burden to healthcare systems. However, the high prevalence and existing evidence that intervention is essential in reducing complication events demonstrate a need for initiatives that slow the progression to later stages of renal disease and reduce cardiovascular disease-related episodes in CKD patients (Hill, et al. 2016). CKD is one of the costliest diseases in healthcare, with a considerable heavy economic burden already in

the early stages. It can be equal to or greater than the costs imputed to cancer or cerebrovascular accident in adults. As the disease progresses and, consequently, the need to start dialysis, the direct costs of health maintenance increase substantially (Junior, et al. 2018). In addition, managing CKD patients before and after the beginning of dialysis treatment and managing comorbidities in individuals with CKD have a considerable potential to reduce the costs of patients in the line of care (Damien, et al. 2016). Globally, it represents a heavy burden, and the costs associated with it have serious implications for public health policy worldwide:

- **SPAIN:** hemodialysis is five times more expensive than the treatment of the more advanced stages of CKD and three times more expensive than a kidney transplant.
- **SWEDEN:** patients on hemodialysis and kidney transplant present 45- and 11-times higher cost relative to the healthcare costs of the general population, respectively.
- **AUSTRALIA:** CKD patients represent an 85% higher healthcare cost and require 50% more government subsidies than the general population.
- **INDIA:** kidney transplant-associated costs are tremendous and responsible for a second financial crisis (Junior, et al. 2018).
- **USA:** over the past decade, the number of Medicare beneficiaries with CKD increased by 89% (United States Renal Data System 2020).

WHAT IS THE SOLUTION FOR THIS?

It has been proven that therapeutic interventions in the early stages of CKD effectively slow its progression. Additionally, implementing preventive care measures such as continuous follow-up of patients and their families, screening new cases in the population, and increasing the chances of an early diagnosis is crucial for controlling disease progression and thus reducing the need for dialysis, transplant, and complications. (Junior, et al. 2018). As such, it is crucial to implement new ways to closely monitor kidney disease daily in a non-invasive way. Early

diagnosis could deliver cost savings of up to $1.1 billion over five years per 100,000 patients with CKD (Renalytix 2021).

This solution can be achieved by leveraging wearable biosensors. This emerging technology has become progressively important in personalized healthcare as it can continuously collect data from the human body and alert about health problems. Currently, there is a major gap in collecting chemical molecules continuously, in a non-invasive way, which constitutes a great opportunity in this field.

OUR PRODUCT

In recent years, wearable biosensors have become a new product category. Their ability to provide continuous real-time data about a person’s physiology and the increased accuracy and effectiveness have made these devices reliable and commercially viable. Developments made in recent years have focused on electrochemical and optical biosensors, and major advancements have been made in the non-invasive monitoring of biomarkers such as bacteria, hormones, and metabolites. (Kim, et al. 2019)

Developing a new commercial product is influenced by normative, cognitive, and regulatory institutions. Normative institutions encompass the principle of evidence-based medicine and practical guidelines. Cognitive institutions deal with product and industry standards and users' expectations of the product category. Lastly, the medical industry is heavily influenced by regulatory requirements for medical devices, patent laws, public procurement laws, and reimbursement systems. (Hidefjall and Titkova 2015)

Preventico will introduce our first product in the wearable biosensors category: the SIKMA. SIKMA focuses on monitoring patients suffering from or at risk of getting chronic kidney disease (CKD). The product is more than a wearable device, as it includes hardware, advanced machine learning algorithms, and user-friendly software.

Looking at the hardware, SIKMA is a novel, discrete wearable device that can be worn all day long. The device is a skin-born solution, a group of devices that have gotten increased attention as the other layer of skin, the epidermis, covers our body. The device features an optical mini near-infrared sensor and two small electrodes that allow the device to measure the wearer's hydration status and sample interstitial fluid (ISF) through reverse iontophoresis, from which the infrared sensor can measure the concentration of urea and potassium with.

ISF is the fluid surrounding the cells that provide nutrients that disseminate directly from the capillary endothelium, which means that correlations can be made between blood and ISF concentrations of different chemical substances such as potassium and urea. To bring ISF to the skin's surface in a non-invasive manner, SIKMA will use reverse iontophoresis that transports molecules through the skin using small amounts of electricity without harming the surface or being in contact with blood. (Kim, et al. 2019) (Xu, Yunsheng and Chen 2021). The device measures urea as this is currently the gold standard for detecting CKD, traditionally measured through blood samples. The kidney will normally remove urea if it is functioning, and higher than average concentrations are, therefore, a clear sign of CKD and can be used for diagnosing. (Mayo Clinic 2021) Potassium is a mineral present in food, which helps keep the heartbeat regular and muscles working right. Healthy kidneys will ensure that your body contains the right amount, but with CKD, the levels can reach dangerous levels that can result in an irregular heartbeat or a heart attack. Therefore, it is vital to know when suffering from a CKD to take proper measures, e.g., adjusting your diet. (National Kidney Foundation 2022)

After the sensor has measured the values, the SIKMA transfers the data to the user’s phone for further processing via the Bluetooth protocol. After the data has been transferred, SIKMA’s companion app will upload it to Preventico’s cloud for processing. Our proprietary machine-learning algorithms use the data to determine the user’s health condition to try and predict how a user currently suffering from a CKD’s condition might evolve. The algorithms are trained based on data from previously diagnosed patients at various stages and aim to provide insights into the prognosis of a CKD patient.

The resulting values from the algorithms are then returned to the app for the user, and a copy is shared with the user’s linked medical team. In the app, the user will see the measured value of urea, potassium, and hydration on a scale of low, regular, and high. The user will also be able

to see historical values from previous measurements to understand how they have developed over time. The app will also allow the user to securely communicate with the medical team about their numbers through chat messages. On the other end, the medical team will have access to a dashboard, where they can log in and access the data of all the patients who have chosen to share their data with them. This enables them to see how the patient is performing and gives greater insight to help create a better diagnosis and prognosis for the patient and optimize the treatment the patient is receiving. The patient's health status data will also automatically trigger follow-ups, so the medical team can efficiently handle their patients based on severity.

All in all, SIKMA aims to create value for both patients and medical professionals by allowing for more precise data and disease tracking so that the patient can feel secure every day and the medical professional can provide more accurate treatment.

MEDICAL PRODUCT APPROVAL

Medical devices sold in the United States are regulated by the Food and Drug Administration (FDA), where companies need to register the product and gain approval. The FDA regulates the sale of medical devices and monitors the safety of every regulated medical device to ensure safety and effectiveness for its use case. (FDA 2018)

For SIKMA to obtain FDA approval, it will have to go through the following five steps:

1. **Device Discovery and Concept** – first, we'll have to know which class SIKMA belongs to, from Class I to Class III. This classification is based on risk, meaning the risk the product presents to the user (lowest to highest). Class II and Class III are subject to pre-market reviews, unlike Class I medical devices. Usually, wearable devices to monitor health parameters are classified into Class II, which have special controls, in addition to

general controls, including labeling requirements, guidance, tracking, plan, performance standards, and post-market observation. (FDA 2018)

2. **Preclinical Research** – Prototype: the second step is to develop a prototype to be used for testing in laboratory environments, reducing its risk enough before it is used in humans, and answering basic questions about safety. (FDA 2018)
3. **Pathway to Approval** – the product is tested on humans to ensure that it is safe and effective. The regulatory controls for devices include, for example:
    a. **510(k) process:** requires proof that the device is substantially equivalent to a legally marketed device, that is if it has the same expected use and technological characteristics as a legally marketed device. If the FDA determines that the device is not substantially equivalent, we might be asked to submit a premarket approval application.
    b. **Premarket Approval Application (PMA) –** scientific and regulatory review necessary to determine a device's safeness and effectiveness, requiring scientific evidence that the possible benefits surpass the potential risks and that it will substantially benefit an extensive portion of the target population.
4. **FDA Review** – FDA review teams examine all submitted data, and if they have enough information on the device's safety and effectiveness, they can apply to market the device to the public. (FDA 2018)
5. **FDA Post-Market Safety Monitoring** – FDA controls the device's safety once it is available for public use through manufacturer inspection, developing programs to allow for problem reporting, and keeping active surveillance. (FDA 2018)

For Class II devices, which the SIKMA is expected to fall into due to its similarity to existing products such as the Apple Watch 4 (Su 2018), the average length of time for FDA approval is

normally six months. However, it may take three to seven years from concept to approval, including the device lifecycle, R&D, and testing.

CHALLENGES IN PRODUCT DEVELOPMENT

In our development of the SIKMA, we will face a set of challenges that has to be overcome to make the product commercially viable:

1. **Data security.** As Preventico and the SIKMA is reliant on storing and processing medical records for the product to function, we fall under the rules of the Health Insurance Portability and Accountability Act (HIPAA) that protects individually identifiable health information, such as your current health status (U.S. Department of Health & Human Services 2013) (U.S. Department of Health & Human Services 2022). We solve this issue by actively thinking data security into our software while developing it and conducting cybersecurity audits regularly in our company.
2. **Hardware.** We are facing three main challenges at the hardware level: connectivity, battery life, and portability. The first two challenges are universal across all wearable devices and will be mitigated with BLE (Bluetooth low energy) for communication and spacing between information sent to the wearer's device. This will also positively impact battery life together with the choice of using the phone for further data processing.
3. **Medical approval.** Lastly, the challenge is getting the device approved by the FDA as a medical device. This is a crucial step to ensure its reliability and that we can introduce the product to the market as a clinical device, significantly increasing our credibility. This process can take between 3-7 years, and as our product category is new to the market, we find that 7 years from initial conception to an approved product is most realistic.

ROADMAP FOR PRODUCT DEVELOPMENT

To pursue the development of a first device like the one described above, the following roadmap for the hardware device and its accompanying software will be followed by the company within the first two years of operating to create our first fully working prototype:

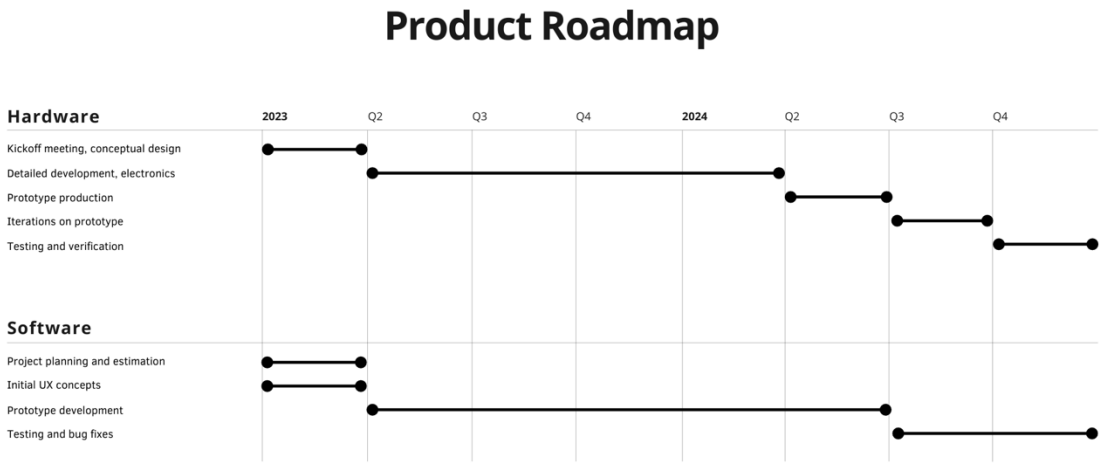

Figure I: Roadmap for the development of the SIKMA

OUR COMPANY

Preventico is a health-tech startup developing the SIKMA by combining the power of advanced machine learning, modern wearable technology, and user-friendly software to assist the world's medical professionals in providing chronically ill patients with the best possible disease management program adapted to their unique situation and health condition.

Preventico will be founded in 2022 by Karema Haschemi, Madalena Lara, and Sigurd Koldste in Boston, MA, USA, to initially help chronic kidney disease patients to get treated earlier and more efficiently manage their disease, in collaboration with their team of medical professionals. The group met during their studies at Nova School of Business and Economics and decided to take on the challenge of creating a new solution that could successfully move how chronic diseases are treated late to facilitating a more preventative approach, where they can be uncovered early before they seriously impact people's lives. We see our mission as being:

Keeping your health up to date every single day, empowering you and your medical team to act before it is too late.

Preventico has a strong vision for the future, where we aim to move the medical world from treating to preventing disease, empowering medical professionals along the way to act in their best interest:

Imagine a future where looking at your wrist, you do not only know what time it is, but you know how your overall health is.

In the pursuit of this vision, we are sticking to a core set of five fundamental values that encompass all our work:

- ***Integrity.*** We treat our users and customers with integrity in all interactions and design our products to do the same.
- ***Transparency.*** Our entire company aims to be fully transparent, so you can safely entrust us with your personal life.
- ***Collaboration.*** We collaborate with everybody interested in detecting the fingerprints of more diseases, so we as a team can help more people worldwide.
- ***Curiosity.*** We were born out of curiosity, and we stay curious about everything, so we might learn how to help you better.
- ***Diversity.*** If we are indeed to help everybody, we need to embrace diversity as part of our organization and when developing our company.

WEARABLE BIOSENSORS MARKET

TRENDS

Health monitors come in all shapes and sizes, ranging from wearables like wristbands to smartwatches integrated with mobile phones. Due to technological advances, the capabilities of these devices and applications are increasing, enabling them to be more accurate and thus expanding into healthcare solutions. Due to the growing health awareness and focus on maintaining an active lifestyle, consumers are increasingly choosing wearable wireless devices for sports, fitness, and wellness. Smart devices for remote monitoring, wearables, apps, and other digital healthcare innovations are making it easier for people to stay engaged with their health and allowing providers to stay connected with their patients and other healthcare professionals, which helps keep costs under control. Factors such as the increasing spending power, large-scale modernization, and highly advanced and cost-effective wireless healthcare technology are driving the market growth. (Research and Markets 2022)

With the arrival of smartphones and other mobile devices, wearable sensors have received massive attention due to their capacity to provide essential insights into an individual's performance and health. The first steps taken in this direction focused on physical sensors that could monitor parameters related to mobility and vital signs, being the case of steps, calories burned, or heart rate (Kim, et al. 2019). In fact, the wearable technology industry is rapidly growing, with researchers changing their focus from physical activity to undertaking bigger challenges in healthcare applications. In 2019 this market was estimated to be worth $32.63 billion worldwide and is expected to expand annually at a growth rate of 15.9% until 2027 (Brophy, et al. 2021). A large portion of this future market share consists of wearable

biosensors, primarily non-invasive glucose monitoring. As such, the future of healthcare will depend on leveraging advanced technologies that keep patients healthier and costs lower.

To tackle several healthcare challenges such as high costs, researchers have accomplished huge advances in what concerns the development of wearable biosensors, which can be defined as "wearable sensing devices that incorporate a biological recognition element into the sensor operation" (Kim, et al. 2019, 2). A traditional biosensor has two basic functional units: a bioreceptor responsible for recognizing the chemical substance and a physicochemical transducer that will translate the biorecognition outcome into a useful indicator (Kim, et al. 2019). Due to their characteristics like high specificity, speed, portability, low cost, and low power requirements, biosensors present significant potential for wearable applications. Substances such as sweat, tears, saliva, or interstitial fluid (ISF) have been used in innovative biosensors platforms for non-invasive chemical analysis since they can be sampled in a non-invasive manner, providing easy access and no contact with blood is needed. (Kim, et al. 2019).

The broad approval of this kind of technology takes an extensive understanding of the biochemical composition of body fluids (e.g., sweat, tears) and their relation to blood chemistry. The wearable sensors can provide information about the biochemical processes in these biofluids through ongoing monitoring of important biomarkers that can reflect the wearer's health and, as a result, enhance the management of chronic diseases (the leading cause of death worldwide, representing 60% of total deaths), eliminating painful and risky blood sampling procedures (Kim, et al. 2019).

Since this technology provides the opportunity to measure physiological parameters continuously, it has the potential to improve the quality of healthcare delivery systems by addressing existing needs of disease prevention, offering more efficient ways to manage chronic conditions through patient empowerment (Hidefjall and Titkova 2015). As such, wearable

biosensors devices can reduce the number of diagnostic tests medical professionals must perform manually on patients and make faster and more accurate diagnoses, allowing the reduction of healthcare costs and thus improving healthcare efficiency (Kristoffersson and Linden 2020).

Once the wearable sensor technology is integrated through web-based solutions with the IT infrastructure of the healthcare providers, it can notify healthcare specialists if urgent intervention is necessary according to the biomarkers[1] measured, being particularly valuable within care settings where patient health can deteriorate quickly (Hidefjall and Titkova 2015), as it is the case of kidney disease. As such, this data can be used for disease detection, allowing for earlier diagnosis and potentially reducing the severity or even the occurrence of illness (Brophy, et al. 2021)

EPIDERMAL WEARABLE BIOSENSORS

Of the several types of wearable sensors, skin-worn devices have been receiving the most attention, as the epidermis covers a large part of the human body. They depend on samples of sweat or interstitial fluid (ISF) at the skin surface, as well as the transport of these biofluids over the biosensor surface. In the case of sweat, it represents the most easily accessed biofluid for chemical sensing applications since sweat glands are widely distributed across the body. However, research is still lacking to validate the clinical value of sweat as a diagnostic biofluid.

[1] "*a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention"* (Puntmann 2009, 1)

As an alternative, interstitial fluid has been targeted by epidermal biosensing for measurement of analyte concentration (Kim, et al. 2019). Skin cells are surrounded by ISF, which provides nutrients that disseminate directly from the capillary endothelium, allowing to make correlations between the blood and ISF concentrations of several chemical substances, including electrolytes (e.g., sodium, phosphate, magnesium, potassium, or calcium), metabolites (e.g., glucose), and proteins. To extract the ISF analytes to the skin surface in a non-invasive manner, a method called reverse iontophoresis can be used, which allows the transportation of molecules through the skin without harming its surface or being in contact with blood. (Kim, et al. 2019)

WEARABLE BIOSENSORS AND KIDNEY DISEASE

The wearable monitoring devices offer several opportunities to mitigate CKD progression speed and increase the quality of life by managing the disease and its associated complications and comorbidities (Wieringa, et al. 2017). These opportunities include monitoring blood pressure, electrocardiogram, oxygen saturation, and biomarker tracking offering potentially valuable guidance for customized treatment of comorbidities such as cardiovascular diseases, congestive heart failure, and chronic obstructive pulmonary disease. The monitoring of fluid overload status, particularly on what concerns information about its distribution across the different compartments of the body, together with the tracking of body composition, which includes muscle, fat, and water, may also complement the nephrologists' means to provide better disease management in a more individualized way to CKD patients (Wieringa, et al. 2017). In addition to treating the disease, wearable devices that measure the level of physical activity, motivate patients to practice physical exercise, and advise them on their diet are potentially valuable. (Wieringa, et al. 2017).

OUR MARKET

Globally, the kidney disease market size is worth $133,444.71 million, and it is estimated to grow at a CAGR of 6.5% until 2027. On the other hand, the size of the global medical devices market is expected to reach $657,98 billion by 2028, with a CAGR of 5.4%. The market for medical devices is geographically divided into five regions: North America, Europe, Asia-Pacific, South America, and the Middle East and Africa (MEA). In 2020, the North American region detained the largest share in the global market, and this tendency is predicted to continue. Factors such as the increased use of innovative medical device technologies, the growing digitalization of medical devices, and an increased emphasis on improving treatment results are the drivers for market expansion. Moreover, the upsurge in the medical device market is also a consequence of the prevalence of chronic diseases in the American population, accounting for one of the most common and expensive health problems in the United States, fueling the demand for several medical devices (Fortune Business Insights 2022). As such, we believe that the U.S is the segment with the greatest market potential to launch the SIKMA, as it is also the largest market for the kidney disease market.

THE U.S. KIDNEY DISEASE MARKET

In the U.S., CKD is the 9th leading cause of death, and more than 15% of the adult population is estimated to have CKD, accounting for approximately 37 million people, which means that more than 1 in 7 adults are affected by it, most being undiagnosed (Centers For Disease Control and Prevention 2022). Moreover, 90% of the individuals affected are unaware of having kidney disease, and 2 out of 5 adults with the severe form of CKD do not know they have it. Every 24 hours, 360 people initiate dialysis treatment for kidney failure. (Centers For Disease Control and Prevention 2022)

In the U.S., diabetes and blood pressure are the two leading causes of kidney failure, accounting for 3 out of 4 new cases, and the prevalence of CKD is higher, in part due to the higher incidence of risk factors such as diabetes and obesity (Centers For Disease Control and Prevention 2022). In what concerns the annual medical costs, in the U.S., these are higher for more advanced stages of CKD, so it is crucial to identify it in the earliest stages and keep close monitoring. Without a larger investment in prevention, the total number of patients with kidney failure (end-stage) will likely surpass 1 million by 2030 (National Kidney Foundation 2022).

According to the National Kidney Foundation (2022), in 2018, 785,883 Americans suffered from kidney failure and needed dialysis or a kidney transplant to survive. 554,038 of these patients were on dialysis to replace kidney function, and 229,887 lived with a kidney transplant. In 2020, from the 100,000 Americans waiting for a kidney transplant, only 22,817 received one.

WHY THE U.S.?

We chose the U.S. market to launch the SIKMA, as it is the nation with the highest health care spending in the world, and currently, the need to control costs is a pressing matter. As such, the SIKMA will help tackle this problem by allowing to bet on prevention but also by offering a technology that improves patient care, reducing avoidable hospital services at the same time.

In what concerns the kidney disease market, in 2019, the treatment segment accounted for more than 56.80% of the market share, with the diagnosis segment expected to grow at a fast pace from 2020 to 2027 (Bloomberg 2021).

The North American region holds the largest market share of the kidney disease market, and the U.S. represents the biggest one. The market is expected to grow because of factors such as

the increase in the fast-growing end-stage renal diseases, the presence of key market players, and large-scale R&D led by several institutes.

Additionally, the prevalence of diabetes and hypertension is expected to increase, which, together with other chronic diseases, is expected to grow the prevalence of CKD. This will ultimately provide a lucrative opportunity for the growth of the market (Bloomberg 2021). Another primary driver for this market is the growing older population since aging is a significant risk factor responsible for a large part of the rising cases of kidney disease. The Centers for Disease Control and Prevention revealed that around 96% of the individuals with CKD are unaware of their health issue, serving as an indicator of the underlying market prospective in the kidney disease market, thereby enhancing the expectations of market growth during the forecast period (2020-2027) (Bloomberg 2021).

In the U.S., CKD treatment is estimated at 48$ billion per year, consuming 6.7% of the Medicare budget dedicated to less than 1% of the covered population (Damien, et al. 2016). In 2019, treating Medicare beneficiaries with CKD cost $87.2 billion and an additional $37.3 billion for patients with end-stage renal disease (Centers For Disease Control and Prevention 2022).

According to the United States Renal Data System (2020), in the past 20 years, expenditures for Medicare beneficiaries with CKD have increased at a higher rate than expenditures for the general Medicare population or beneficiaries with diabetes mellitus or heart failure. Moreover, the rapid increase in costs for the CKD population reflects, to a certain extent, more rapid growth in the population suffering from kidney disease, and, in this particular case, the total beneficiaries with CKD increased by 89% during the last decade (United States Renal Data System 2020).

OPPORTUNITIES IN THE U.S. MARKET

In the U.S., the healthcare system has been reluctant to promote good health to its patients since essential care regarding chronic diseases is mainly delivered after a critical illness attacks an individual and not previously. However, a paradigm shift has slowly been occurring that aims at moving away from a fee-based healthcare system, as it is nowadays, to a value-based and outcome-based model.

Currently, one of the main priorities for The Centers for Medicare and Medicaid Services (CMS) is to get the health care budget spending under control in what concerns kidney disease, as from the $1.2T 2021 budget, around 20% was consumed for a patient either with CKD or ESRD. To do so, CMS carried out a reform in 2021 and changed the payment model for kidney disease intending to incentivize better outcomes and lower costs. With this shift from CKD and ESRD payment models, already hundreds of billions in healthcare spending have transferred to value-based and outcome-based structures. (Daso 2019)

As such, implementing the SIKMA in the U.S. represents a unique opportunity, serving as an important asset in what concerns decreasing Medicare costs substantially. Further, this solution can be expanded to other chronic diseases by shifting the focus to a model that pays for proactive and preventive care and thus improves the patient's life quality while eradicating adverse outcomes and significant costs.

COMPETITORS

There are several features that allow Preventico to deliver a superior solution to tackle kidney disease more efficiently than its competitors. Our product, SIKMA, integrates a patient application that allows the user to see the values continuously, alerting both patient and health professional about potential harming values, all done in a non-invasive manner. We also provide an all-in-one solution by gathering the data, treating it with machine learning algorithms, and presenting it to the healthcare team and patient without needing to access data from external sources, unlike the other companies that are reliant on data from 3rd party devices, since they do not have their own device.

Table II shows the direct competitors we have identified in the U.S. market. They can be classified into two groups: 1) focused on assisting healthcare professionals, and 2) on assisting patients through their CKD journey:

- *Monogram Health* and *Strive Health* are more oriented towards the patient experience with CKD, helping clinicians to k with patients during the development and implementation of their disease management plan. With machine learning technology, these companies identify gaps in the cycle of care, predict avoidable acute events and keep track of crucial biomarkers remotely. *Monogram Health* furthermore provides additional services such as hotlines patients can call to ask for advice from a team of specialists.
- *Renalytix* and *pulseData* are more oriented towards medical professionals, being data-based companies that aim to help with the earlier detection and diagnosis of CKD based on proxies and biomarkers collected from a range of different sample types.

Group Contribution

- All four companies mentioned above work to predict the patient journey, following individuals through the whole cycle of care, with the purpose of optimizing their disease management plan.
- Of the listed competitors, *One Drop* is an outlier since it does not tackle CKD directly. However, it monitors parameters of other underlying diseases that can lead to kidney disease. *One Drop* focuses on promoting a healthy lifestyle for the patient by having a balanced diet and doing physical exercise, with an approach more focused on health data tracking and coaching.

Company	Location	Commercially available?	For CKD patients?	Patient app?	Non-invasive?	Score
One Drop	New York, NY	✓	✓	✓	(✓)	3.5
Monogram Health	Nashville, TN	✓	✓	✓	?	3
Strive Health	Denver, CO	✓	✓	?	✗	2
Healthy.io	Boston, MA	✓	✓	(✓)	✓	3.5
Renalytix AI	New York, NY	✓	✓	✗	✗	2
pulseData	New York, NY	✓	✓	✗	✗	2
Preventico	**Boston, MA**	✓	✓	✓	✓	4

Table II: Comparison of competitors for the SIKMA by Preventico

SUBSTITUTES & ALTERNATIVES

The main substitute products for the SIKMA can be found within several wearables designed for comorbidities and complications that CKD patients commonly suffer from. These include cardiovascular disease, diabetes, and general fitness (Wieringa, et al. 2017). For monitoring these related illnesses, the most common products are: 1) weighing scales to determine the fluid

weight, 2) blood pressure monitors to assess the risk of heart failure, 3) glucometers as diabetes is a common related disease, 4) pulse oximeters to measure oxygen levels and heart rates, and lastly 4) wearable ECG monitors a growing feature among smartwatches such as the Apple Watch. (DrKumo Inc. 2021)

The substitutes are wide-ranging, and some share closer characteristics with being alternatives, as they become more distant for directly monitoring and optimizing the treatment and conditions of living with CKD. In our analysis of the direct competitors, these devices can be found as used as part of the data input used on their platforms. The common issue is that they are proxies around CKD but do nothing to monitor the condition itself directly.

Our market survey also highlighted a growing number of companies offering a similar solution to that of the SIKMA but targeted at diabetes at different stages of commercial availability. This range of products will be kept under consideration, as they are for now not directly competing with the SIKMA but will grow to become a part of the substitute and alternative products.

MARKET POSITION

We consider there to be two different types of segments for our product: users and buyers. Within users, we have two unique segments that are using the product in different ways:

1. CKD patients wear the device daily and use it to get information about their health status and communicate this to their medical team.
2. Medical professionals prescribe the device to their patients, so they can more easily track their patients remotely and optimize their treatment.

A secondary set of segments are then the actual buyers of the product. Here we are considering the following three segments that would purchase the product for different reasons:

Group Contribution

1. Insurance providers, both private and public, will reimburse the purchase of the product as part of the treatment of one of their customers.
2. Government hospitals and health services buy the product through public procurement procedures in larger volumes to apply in their operations.
3. Individual CKD patients, regardless of their current treatment, buys the device for themselves to better follow their disease.

TARGET SEGMENTS

For our first product, the SIKMA, we have decided to focus among the buying segments on individual CKD patients. The segment of individual diagnosed CKD patients consists of 37 million people in the U.S. market (National Kidney Foundation 2022, National Kidney Foundation 2022). It is characterized as having the fastest and least formal buying process among the proposed segments. The consumers are adults and are struggling to manage their CKD. They are moderately sensitive to price considering the potential impact on their everyday life, where CKD is starting to take its tool mainly on their psyche, where they seek to get more autonomy.

To address this segment, our promotional activities need to cater additionally to the medical professionals, which enables our customers to buy the SIKMA with a prescription. A prescription or reference from a medical professional is crucial, as this allows our customers, the CKD patients, to seek reimbursement from their insurance provider. Around 68% of all Americans are covered by private health insurance-, while the remaining 32% are covered by the government programs Medicare and Medicaid (Mordor Intelligence 2022). The private market consists of 907 companies (Stasha 2022), where the leading 25 companies are responsible for 60% of the total market value (Mordor Intelligence 2022). In summary, the

segment contains the CKD patient as the purchase decision-maker and partial buyer, the medical professional as the enabler of the purchase, and lastly, the insurance provider as the indirect payer through reimbursement.

We have decided not to directly target government entities within the health sector, as they are characterized by more prolonged and formal processes for making purchasing decisions through tenders and are affected by public procurement laws, where it might be challenging to find a fit for our device initially. Therefore, we aim to utilize the selected segments to create awareness in the market and start building a reputation around our product and the science behind it.

POSITIONING

Looking at the current market, we see ample freedom to position our product. From the existing market and feedback from potential users, we see the main factors as being Completeness and Invasiveness, which we define as the following:

Completeness: We define it as the product or service's ability to cover the entire process from collecting data to prognosis and presenting it to the patient and the medical team. Partial products only offer elements of this process.

Invasiveness: The need for the invasive collection of samples to obtain data. Blood samples are the most invasive (worst), and reverse iontophoresis is the least invasive (best).

Group Contribution

Preventico aims to enter the area of being non-invasive and an all-in-one product that facilitates everything from collecting data to presenting it and a prognosis to patients and their medical team (see Figure II).

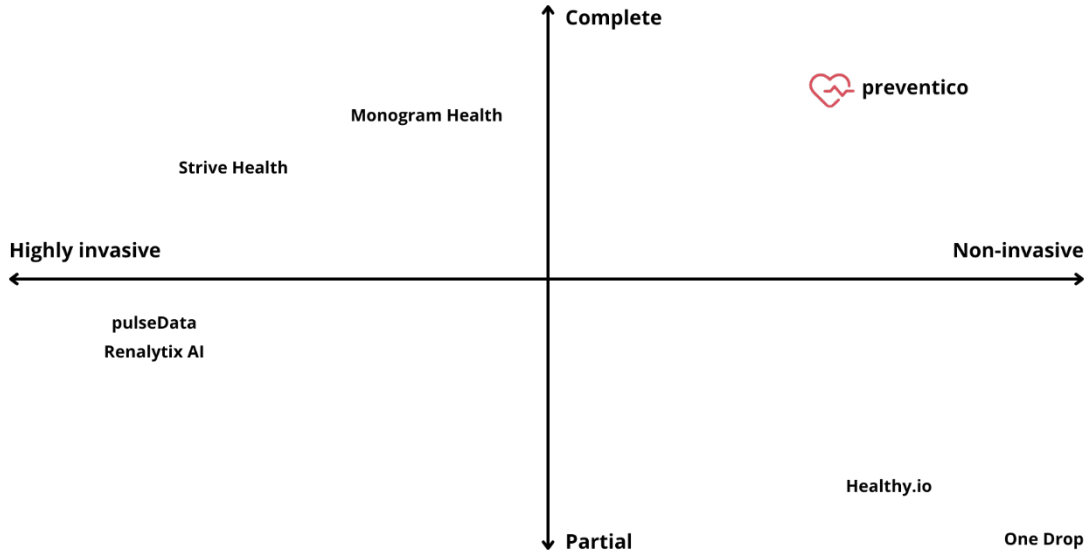

Figure II: Positioning of the SIKMA by Preventico in the competitive landscape

MARKETING PLAN

VALUE PROPOSITION

SIKMA will have three value propositions for the different stakeholders:

CKD patient: we want to provide CKD patients with the best quality of life possible, allowing them freedom of choice in their everyday lives. We collected several testimonials from CKD patients during our active search in the kidney disease market. From the CKD patients' interviews, we were able to understand that one of their main constraints was the lack of

independence they felt in their day-to-day lives, as they did not have constant monitoring of elements that are crucial for their well-being, such as phosphorus, potassium or sodium levels, three examples of minerals that can build up to unsafe levels in the bloodstream when kidneys are not functioning correctly, leading to heart attacks, for example. These patients mentioned that for them to have more quality of life, it would be essential to track these levels continuously, which would allow them to live less restricted, knowing what type of food they can eat or how much fluids they can drink every moment, promoting autonomy and independence. SIKMA will enhance disease management and allow to slow/stop the deterioration of kidney function. As a patient mentioned: “anything that can alleviate the issues and make each day a better day would be absolutely fantastic.”

Healthcare professional: SIKMA will offer optimal treatment, less need for checkups, fewer unnecessary consultations, saving time on checkups, and making it easier for patients to stick to a treatment plan. Additionally, SIKMA will allow for intelligent scheduling of patients according to the severity of patients’ health status. Less frequent check-ups enable doctors to have more consultations with other patients, and collecting data in an automated way (that would happen in a typical doctor’s visit) has the potential to give a patient more face time with the doctor. Moreover, as doctors will have the opportunity to do remote monitoring of patients’ healthcare status, they can also opt for telemedicine instead of in-person consultations. In addition, with access to more consistent and accurate patient health data, healthcare professionals can intervene as soon as there is a problem to help prevent costly complications, ER visits, and hospital admissions.

Furthermore, nowadays, the healthcare sector is shifting towards value-based reimbursement models rather than volume-based care, meaning that healthcare providers are paid based on the quality of the care provided and not on the number of tests and procedures they order (fee-for-

service care). Currently, in the U.S., value-based programs are rewarding providers for the quality of the care provided to Medicare beneficiaries. As such, the SIKMA will serve as an asset for healthcare professionals allowing them to reduce costs and eliminate redundant care and hospital visits through continuous monitoring of their patients' healthcare status. With this paradigm shift from volume to value, the SIKMA will also contribute to decreasing healthcare professionals' burnout since the fee-for-service model is characterized by a high volume of documentation, leading to doctors spending time and energy doing administrative work.

Insurance provider: the SIKMA will generate cost savings and cheaper treatment, as medical costs attributable to CKD are substantial among Medicare beneficiaries. Since these costs increase as the disease severity worsens, our product will allow for an early intervention to help slow the progression of CKD and prevent patients from progressing into later stages of the disease, where they would need hemodialysis or kidney transplant, resulting in high costs savings. Such savings will also be generated through less frequent blood tests since patients will have continuous monitoring allowing for a close follow-up without needing an appointment. Additionally, insurers will be able to reduce the rising cost per patient, as using SIKMA will reduce the need for hospital visits and readmissions due to poorly managed personal health.

PROMOTIONAL ACTIVITIES

We will advertise the SIKMA through several promotional activities, which will include:

- Medical trade shows, expos, and congresses, allowing other experts in the wearable biosensors industry and medical doctors to put a face to the product and showing to our peers how the SIKMA works:

Group Contribution

- The **Chronic Kidney Disease Drug Development Summit, Boston** (only industry-driven event dedicated to accelerating the edge of preventative and regenerative therapies to target kidney disease, being the single end-to-end convention presenting scientific advancements as actionable insights);
- **DeviceTalks Boston** (unites MedTech's most innovative professionals and helps companies overcome troublesome bottlenecks in several critical stages, such as prototyping & product development, manufacturing & sourcing, and engineering tools and technology);
- **BIOMEDevice, Boston** (brings together recognized leaders, top global researchers, medical professionals, and innovators in healthcare, biotechnology, and MedTech sectors to showcase emerging technologies and trends that will push forward the medical device industry).

- Thought leadership: invite recognized leaders in both nephrology and wearable biosensors fields to provide state-of-the-art contributions about the SIKMA.
- Advertise it through The National Kidney Foundation and other patient support groups through product endorsement patient-to-patient.
- Interviews on relevant healthcare podcasts with established audiences.
- Advertisement through social media accounts.
- Articles written by our scientific team that highlights the SIKMA's benefits for CKD patients.
- Company events to generate awareness among the scientific community about our product's benefits and potential adoption by medical doctors.

TIMELINE & KEY MILESTONES

Bringing SIKMA to market involves several challenges that significantly extend the commercialization process. Such challenges would arise, among others, if there is a mismatch with the regulatory authorities or if the raised capital is burnt quickly. These types of risks would lead to a drastic loss in the valuation of Preventico (htt). Over the next few years, the key milestones will be the various funding phases that will increase Preventico's enterprise value. Investors only choose to invest in Preventico when we are about to reach a particular milestone and need the necessary capital to do so (Arnold 2021).

After defining our clinical needs and conducting extensive market research and assessment of the potential size of the market, we will apply for the America's Seed Fund The Small Business Innovation Research Program (SBIR) and the Nephure Kidney's NEPTUNE Ancillary Studies Grant Program in 2023. In total, we would get $375,000 if our application is successful. In the early years, we focus heavily on the completion of a prototype, together with our Research & Development team. Once our proof of concept is in place, we work with the law firm Cooley LPC, which provides expertise in patenting medical devices, with the goal of developing an IP strategy and submitting our patent application.

Our proof of concept helps us to secure the first investors (Digitalis Ventures, Sky Ventures Group, and the National Kidney Innovation Fund) for our 10 million seed round in 2024. We will allocate this money to expand our team with several employees who are necessary for the development of the software. These would be the following roles: two Embedded Software Programmers, two Junior Developers, one Senior Project Manager, one DevOps, one Data Scientist, and one Optic Specialist. While selecting suitable candidates for our team, we begin our preclinical studies to predict treatment outcomes in patients and detect potential toxicities.

(R.S.Ness 2022). We will seek regulatory approval in the US, Europe, China, and Japan before we start our clinical trials to ensure that SIKMA is registered in these countries as well. Conducting clinical trials is associated with high costs, which is the reason why we seek to raise xx in Series A funding from the following investors: Fresenius Medical Care Ventures (CVC), Boston Scientific, Sonder Capital, and Shangbay Capital. Besides the funding amount, we ensure that our clinical expert, who manages the clinical trials, keeps the costs within reasonable limits. During our clinical studies, we file submissions with the FDA, seeking clearance for our wearable device SIKMA. We are seeking FDA approval at this stage primarily because we are targeting the domestic market first, and over the years, we will obtain the CE marking. Briefly, after we announced the results of our clinical study showing that the accuracy of our method for non-invasive measurement of biomarkers in CKD patients is confirmed, we will receive a 510 (k) clearance from the U.S. FDA in 2029.

In 2030, right after we got the FDA approval, we have planned to raise $25 million in Series C funding round from the following investors: kck Medtech, Perceptive Advisors, Softbank. With the raised capital we would like to expand our team by hiring a majority of sales representatives and allocate the remaining funds for the production of SIKMA and the planned marketing activities such as expos and conferences within the health industry. We will hand over the production and design of SIKMA to the Danish manufacturer Cre8tek Denmark Aps. We will obtain regulatory approval to register SIKMA in the US, Europe, China, and Japan. At the beginning of 2030, we will start with the first sales in the USA. Securing reimbursements is going to be the most difficult challenge for Preventico, since Coding and reimbursement channels for medical devices that are not based on a traditional technology do not fall under the existing coverage guidelines. As this applies to Preventico, we will need to prove the acceptability of our product and apply for a new reimbursement code in 2030. We expect to obtain our Common Procedural Terminology (CPT) reimbursement code by the end of 2030.

Group Contribution

In early 2032, we expect to reach our break-even point and stop relying on investors for future cash injections, and will expand to Europe, China, and Japan. Our reason for expanding to China and Japan is based on the latest results from The Insight Partners report. They concluded that Asia-Pacific is one of the fastest-growing regions. In Japan and China, in particular, we are seeing growing interest from investors in kidney disease (Bloomberg 2021).

For a successful exit, we plan to get acquired for $190 million by Google in 2033. While preparing for our exit process, we need to focus on providing data to Google's investors to ensure that we are among the top medical device startups.

As founders of Preventico, we are aware that at every stage of our venture, we need to have qualified advisors and experts at our side who are familiar with the legal requirements. This is the only way to guarantee that we can save money, and time, and ultimately reduce the risk of patient suffering when SIKMA is available on the market.

CONCLUSION

CKD affects 37 million Americans every single day, and Preventico will make their lives easier by introducing the SIKMA, a new wearable device that measures key values for a CKD patient and thereby gives them greater autonomy and quality of life. The SIKMA also creates value for the patient's medical team, as it allows them to follow the patient remotely and manage their disease treatment plan based on an updated health status.

The SIKMA combines groundbreaking research in the field of biomarkers and the ability to measure them using ISF. Today the product is at the proof-of-concept stage, but in the coming two years, Preventico will undertake the process of developing a working prototype and accompanying software, with the manufacturing process being outsourced to a key partner, while software development will remain in-house to keep control of the user experience. The final product will offer a novel all-in-one solution with its ability to measure, present and prognosis a CKD patient, which generates value for both patients, doctors, and insurance providers. We will pursue an aggressive IP strategy to ensure that the value of the developed product is secured within the company with filings both in the U.S. and the rest of the world leveraging the PCT.

The U.S. is one of the nations with the largest healthcare expenditure overall, with significant costs incurred for the treatment of CKD patients, with large parts of these incurred by the federal Medicare program. The U.S. is undergoing a trend where the focus is moved from quantity to quality in the remuneration of medical professionals. The SIKMA ties into that trend, as it has the potential to create a higher quality of care for patients and lower the number of admissions to the ER, critical care, and general medical consultations.

Group Contribution

With the market for products such as the SIKMA, only a small number of direct competitors are present, although substitutes and alternatives do exist. Compared to these, the SIKMA will enter a unique position by providing the most non-invasive way of gathering data while still facilitating the entire progress from data collection to final prognosis.

In our marketing efforts, we have identified the key person to convince as being medical professionals, as these have the power to facilitate the reimbursement of the costs of our product from insurance providers, the indirect payers, and present our product to the suitable patients, our users. To reach these audiences, Preventico will be present on digital channels and at recognized expos and conferences within the health industry. We will also be leveraging our R&D to be present throughout academic and scientific journals. The end goal is to have the product spread by word of mouth among CKD patients.

Preventico is on an ambitious track to create a single device for your wrist that can keep you up to date with your health status at a glance. The founding team consisting of Madalena Lara, Karema Haschemi, Sigurd Koldste, and Paulo Zoio will leverage their existing experience and knowledge to fill out the executive roles of CCO, CFO, CEO, and CSO. In addition to the founders, we will rapidly expand the team to strengthen our expertise in software development by recruiting for numerous roles within the early stages of the company, so we can bring the SIKMA to market.

Since the development from concept to the market launch of SIKMA is associated with high costs, raising capital from the right investors is necessary at every stage. We expect our selected investors to contribute with their expertise in the development of a medical non-invasive monitoring device and to work with us to develop clinical pathways that will raise physicians' awareness of the need for timely intervention and prevent the possibility of costly hospitalizations. We have planned to fund Preventico for the next 10 years mainly through the

American Seed Fund, government grants, corporate venture capital, and venture capital, and expect that we will raise a total of $69.4 million in funding. However, we need to be prepared for upcoming risks in the process of securing funding, like the opaque regulation process or the challenge of securing reimbursement. All these obstacles are causing delays and high expenditures in the process of commercialization of SIKMA. By keeping close track of our capitalization table, where the ownership structure is documented, we ensure that we have a good overview of which shareholders hold how many shares in Preventico. All four founders have decided on an evenly split equity as we strongly believe that all four of us will strongly contribute to taking Preventico to the next level. For a successful exit, we have planned to sell Preventico to Google for $190 million via a strategic acquisition in 2033.

Bringing the SIKMA to market involves several challenges that significantly extend the commercialization process. Such challenges would arise, among others, if there is a mismatch with the regulatory authorities or if the raised capital is burnt quickly. Among the key milestones are the patent filings, receiving a 510 (k) clearance from the FDA in 2029, and obtaining our Common Procedural Terminology (CPT) reimbursement code by the end of 2030.

Looking into the future of healthcare, we want to provide the possibility for anyone to know everything about their health with just a quick glance at the wrist.

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APPENDIX

Appendix I - CKD patients interviews insights

During our problem discovery we interviewed 4 individuals that suffer from Chronic Kidney Disease, who are currently on hemodialysis, to gain deeper insights about how the disease affects their daily lives. The insights described below are anonymized.

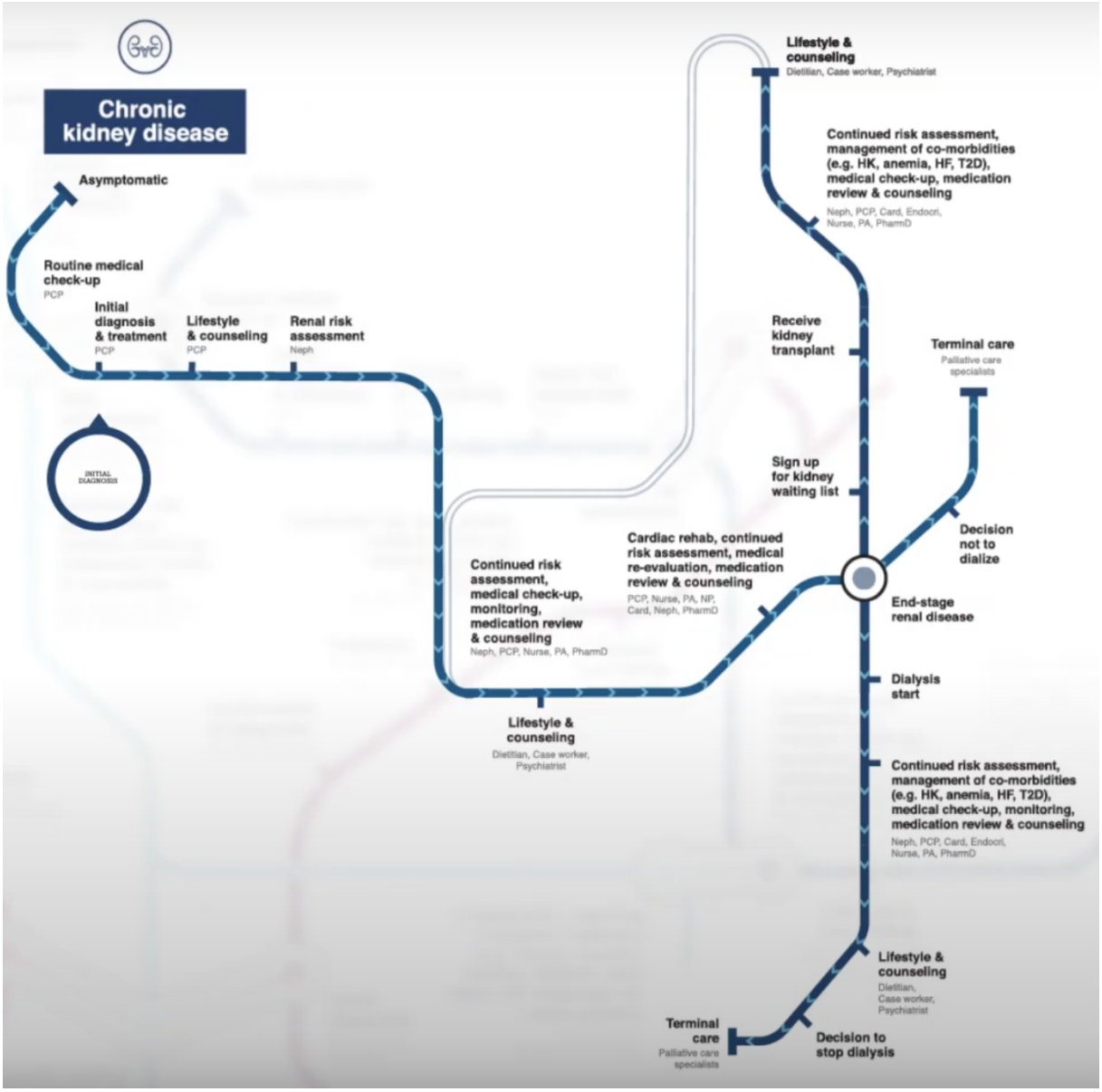
- "I just found my kidneys were not filtering correctly when I had to do those routine blood tests because I competed at a high level in sports." (Male CKD patient, 64 years old)
- "One of the signs is the blood pressure. The blood pressure and weight are related. If we have more fluids than what is our dry weight, the blood pressure will increase. But if we take out more fluids than the necessary the blood pressure will decrease. This would be an important indicator to measure during hemodialysis, so the nurses and doctors could know exactly the quantity of fluids the machine should extract." (Male CKD patient, 58 years old).
- "There is also the measuring of potassium, phosphorous, calcium, urea. These are the parameters. I would say maybe something to measure potassium, sodium… But potassium is really important because if there are high levels one could just faint without knowing why. If we had something that could measure potassium, we could really know what kind of food we can eat at the moment that has a higher or lower content of potassium according to the exact levels at that time. If there was something that could measure potassium, patients could be less restricted as they would know what they could eat" (Female CKD patient, 36 years old)

- “The dry weight for example, during hemodialysis. For the nurses and doctors to set the right dry weight, it is only possible for them to know they are taking too many fluids when we start feeling bad, the blood pressure drops, the person starts vomiting. On the other hand, if they leave a lot of fluids in the body our blood pressure shoots. It is a very hard equilibrium to find. I would really appreciate if it existed a way to know my dry weight without starting to feel sick (nausea, vomiting, cramps).” (Female, 36 years old)
- “Aside from this, measuring potassium would also be very important. Our diet is very restricted because of potassium and if we could measure it everyday we wouldn’t be so restricted. Me, being a CKD patient for so long, I already know how to recognize the potassium symptoms, such as lack of strength, muscle pain. With these symptoms I know I have to cut protein. But it is really difficult, it is a hard balance to reach. It would be important to know my daily levels of potassium so I could have more freedom to know that at that moment I can eat a certain thing or not. There is also the phosphorus issue. But we can fix it by taking medication to help remove it from the body. So, I would say the main concerns are the potassium levels and the dry weight.” (Female, 52 years old)

Appendix II - Additional potential investors for the current and upcoming rounds

Investor	Location	Investment focus	Potential Series
Catalio Capital Managmeent	Baltimore, Maryland, U.S.	biomedical technology companies (devices & diagnostics) globally	Seed
NEA (New Enterprise Associates)	Menlo Park, California, U.S.	2 sectors: tech (software, security, fintech, ecommerce, media) & healthcare (life sciences and digital health) globally; across all stages	Seed
Versant Ventures	Menlo Park, California, U.S.	biotechnology; globally; across all stages	Seed
OrbiMed Advisors	New York, U.S.	biopharmaceuticals, medical devices, diagnostics & healthcare services	Seed
Lightstone Ventures	Menlo Park, California, U.S.	biopharmaceuticals & medical technology; globally; across all stages	Series A
SV Life Sciences	Boston, Massachusetts, U.S.	biotechnology, dementia & medtech; across all stages	Series A
USVP (U.S. Venture Partners)	Menlo Park, California, U.S.	information technology, medical devices & biopharma; across all stages; globally	Series A
Ascension Ventures	London, England	services, medical devices and diagnostics; all investment stages; globally	Series A
Amed Ventures	San Francisco, CA, U.S.	medical device and medical technology globally	Series B
E-merge Capital Partners	San Diego, California, U.S.	early-stage medical device (class 2) companies and technologies	Series B
BioVenture	Suzhou, Jiangsu, China	biopharma, medtech, IVD, health services; across all stages; globally	Series B
Treo Ventures	Santa lara, California, U.S.	medical device & digital health innovation; US & Europe; across all stages	Series B
DeNovo Ventures	Saratoga, CA, U.S.	medical device, biotechnology & healthdiagnostics; late stage	Series C
Aperture Venture Partners	New York, U.S.	medical device, pharmaceutical, healthcare IT/services, diagnostic	Series C
Crescent Enterprises Venture Capital	Sharjah, Sharjah, United Arab Emirates	emerging tech; globally; across all stages	Series C
Action Potential Venture Capital	Cambridge, Massachuetts, U.S	bioelectronic medicine and technology across all stages	Series C
LifeSci Venture Partner	New York, U.S.	molecular medicine, medtech, healthcare delivery; mid-late stage	Series C

Appendix III: CKD treatment roadmap



(AstraZeneca 2020)

Appendix IV - Memo: Correspondence with Cre8tek

Continuous correspondence via email with Niels Harry Olesen, Business Developer and Customer Care (Partner) at Cre8tek Denmark ApS. Between 20 April to 2 May 2022.

Key takeaways:

- The typical product journey of bringing a product from concept to final delivery from China involves 12 steps: 1) Kick-off meeting, 2) Conceptual design, 3) Detailed development, 4) Prototype production, 5) Testing and verification, 6) Manufacturing of tools, 7) Manufacturing of mechanical components, 8) Supply Chain Management, 9) Assembly Manufacturing, 10) Quality control, 11) Packaging and shipping, and 12) Arrival at the customer.
- The proposed product journey incurs costs of between DKK 100.000 and DKK 1.000.000 depending on the need for bespoke parts and the manufacturer's willingness to do customization.

Appendix V - Memo: Interview with Andy D.

Continuous correspondence via email with Andy D., Business Development Manager at Virtue Legal Services. 17 May 2022.

Key takeaways:

- Using the Patent Cooperation Treatment, it is easier to file for patents in multiple countries for up to 30 months after the first filing.
- Ahead of the filing of a patent, it is normal to 1) Do a patentability search, 2) investigate the freedom to operate, and 3) potentially investigate the state of the art within the field one is seeking a patent. All these studies will provide insights into the existing patent market, and can be used to look for opportunities.
- A patentability search aims to uncover whether the product can be patented in the first place. It costs around 500$ and is applicable worldwide. A “Freedom to Operate” study costs around 2000$ per country and seeks to mitigate the risk of infringement of an existing patent.
- The filing for a provisional patent in one country, e.g., the U.S., can cost upwards of 15.000$ if performed by one of the big law firms. A provisional patent lasts 12 months whereafter you must file for a non-provisional/utility patent incurring similar costs.

Appendix VI - Memo: Correspondence with Paulo Zoio

Continuous correspondence via email with Paulo Zoio, the initial inventor and case provider. 4 April to 17 May 2022.

Key takeaways:

- Sweat was used for the proof of concept but faced complaints from volunteers due to the need to induce the sweat response using drugs. Hence ISF was chosen as the alternative.
- Currently, the device is in an early prototype stage using OEM parts and with a significant need ahead of it to make it smaller. It is therefore necessary to create further concepts and design for the hardware itself.
- The device mainly consists of microelectronics, chips, and optical elements for the sensor.
- Previous studies on sweat for prediction gave an AUC of 0.750 for diagnostics, and these are sought to be repeated using ISF and for prognosis as well. The software does signify a crucial element of the product.

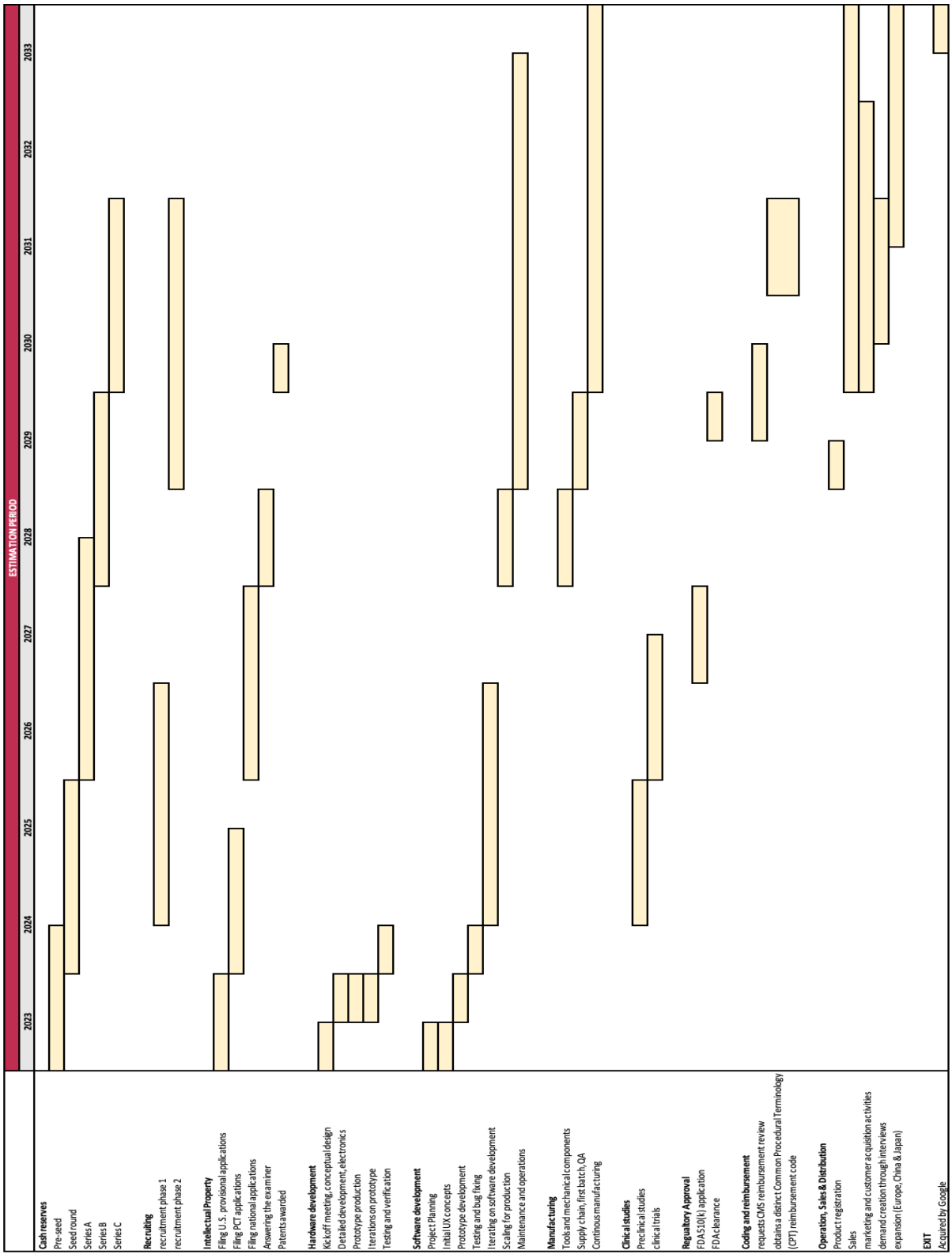
Appendix VII - Memo: Correspondence with Tony Orsi

Continuous correspondence via email with Tony Orsi, Partner, Bereskin & Parr LLP. 5 May to 18 May 2022.

Key takeaways:

- Patents are awarded based on 5 criteria: 1) Has to be in a patentable area, 2) Must include new features, 3) The features have to be inventive or non-obvious, 4) The invention must provide utility, and 5) It must be described with enough detail to be recreated.
- For our device, there might be opportunities to patent the sensor, circuitry, and the way our AI is used alongside how it is fed and preprocesses the data. In general, companies use a mixture of trademarks, design patents, utility patents, trade secrets, and copyright to protect their inventions and achieve different corporate goals.
- Normally one does a patent search to see what the existing state of the art is and determine whether the product is patentable in the first place. It also provides insights into the area one seeks to obtain one or more patents alongside potential competitors and collaborators.
- The cost of filing a patent in the U.S. will be between $7 - $15k CDN with $1k CDN in fees. A patent application in the EU is between $8 – $12k CDN. The cost of filing a PCT application is between $6 to $15k.
- After a patent is filed, it can take between 1 - 3 years for the first report from the examiner to arrive. The response to this report costs around $1.5 – $5k. The entire process to get a patent takes between 2 – 5 years.
- In general, the process goes 1) File for the provisional U.S. patent, 2) After 12 months elevate it to a PCT application, and 3) File for national patents after 18 months.

Appendix VIII: Timeline & key milestones



Appendix IX: Income statement forecast

In American USD $	ESTIMATION PERIOD										
	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033
Demand								8.510.000,00	28.720.000,00	68.845.000,00	88.645.000,00
Revenue								$16.169.000.000,00	$64.780.000.000,00	$175.481.500.000,00	$295.715.500.000,00
growth in %									301%	171%	69%
COGS								$936.100.000,00	$3.159.200.000,00	$7.572.950.000,00	$9.750.950.000,00
Gross Profit								$15.232.900.000,00	$61.620.800.000,00	$167.908.550.000,00	$285.964.550.000,00
Total Operating expenses	$1.371.510,00	$2.989.000,00	$3.385.000,00	$4.896.000,00	$3.385.000,00	$2.147.000,00	$3.189.000,00	$2.735.000,00	$3.005.000,00	$2.999.000,00	$3.579.000,00
% sales											
research & development	$467.000,00	$1.960.000,00	$2.629.000,00	$2.629.000,00	$2.629.000,00	$1.379.000,00	$1.379.000,00	$1.379.000,00	$1.379.000,00	$1.379.000,00	$1.379.000,00
general & administrative	$904.510,00	$1.029.000,00	$756.000,00	$2.267.000,00	$756.000,00	$768.000,00	$1.330.000,00	$834.000,00	$954.000,00	$948.000,00	$1.648.000,00
sales & marketing							$480.000,00	$522.000,00	$672.000,00	$672.000,00	$552.000,00
EBIT	-$1.371.510,00	-$2.989.000,00	-$3.385.000,00	-$4.896.000,00	-$3.385.000,00	-$2.147.000,00	-$3.189.000,00	$15.230.165.000,00	$61.617.795.000,00	$167.905.551.000,00	$285.960.971.000,00
EBIT margin								94,19%	95,12%	95,68%	96,70%
EBITDA	-$1.371.510,00	-$2.989.000,00	-$3.385.000,00	-$4.896.000,00	-$3.385.000,00	-$2.147.000,00	-$3.189.000,00	$15.230.165.000,00	$61.617.795.000,00	$167.905.551.000,00	$285.960.971.000,00
EBITDA margin								94,19%	95,12%	95,68%	96,70%

Operating Cash Flow											
Cash inflow								$16.169.000.000,00	$64.780.000.000,00	$175.481.500.000,00	$295.715.500.000,00
Cash outflow	$1.371.510,00	$2.989.000,00	$3.385.000,00	$4.896.000,00	$3.385.000,00	$2.147.000,00	$3.189.000,00	$938.835.000,00	$3.162.205.000,00	$7.575.949.000,00	$9.754.529.000,00
Total operating cashflow	-$1.371.510,00	-$2.989.000,00	-$3.385.000,00	-$4.896.000,00	-$3.385.000,00	-$2.147.000,00	-$3.189.000,00	$15.230.165.000,00	$61.617.795.000,00	$167.905.551.000,00	$285.960.971.000,00

Appendix X: Estimated patent costs

Assumptions:
U.S. filing costs assumed for Japan and China.
All maintenance costs being the same as the U.S.
Highest prices given are the ones that will be incurred.

Sources:
https://patenttranslationsexpress.com/patent-translation-services/
Response from Bereskin & Parr
Response from Virtue Legal Services

Total countries	4
Total patents	25

In American USD $	ESTIMATION PERIOD										
	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033
Patentability Search	$4.000,00										
Freedom to Operate report	$8.000,00										
Filing of U.S. patent	$175.000,00	$375.000,00		$375.000,00			$125.000,00				
Filing of EU patent				$300.000,00			$125.000,00				
Filing of JP patent				$425.000,00			$125.000,00				
Filing of CN patent				$411.000,00			$125.000,00				
Maintenance fees (due 3 & 7 years after IP filing)							$2.000,00				$700.000,00
File a U.S. utility patent	$15.000,00										
File a U.S. provisional patent	$7.000,00										
File EU patent	$12.000,00										
Patent searching	$4.000,00										
Respond to examiner's report	$5.000,00										
PCT application incl. fees	$15.000,00										
English to Japanese	$2.070,00										
English to Chinese	$1.440,00										
Freedom to Operate	$2.000,00										
TOTAL	$250.510,00	$375.000,00	$0,00	$1.511.000,00	$0,00	$0,00	$502.000,00	$0,00	$0,00	$0,00	$700.000,00

Appendix XI: interview overview with different stakeholders

Number	Category	Name	Expertise/Position	Company/Institute
1	direction of the company	Paulo		
2	patient	N/A		
3	patient	N/A		
4	patient	N/A		
5	patient	N/A		
6	pharmacy	Schekeb Haschemi	Process Specialist, pharmacist	GSK; Post-Apotheke
7	Nephrologist	Miguel Bigotto Vieira	Nephrologist; Member of the American Society of Nephrology	Centro Hospitalar Universitario de Lisboa Central
8	Scientific evaluation	Can Diner	Joniur research group leader for Disposable Microsystems; Biosensors & Bioelectronics Best Paper Award;	University of Freiburg
9	Scientific evaluation/direction of the company	Filipe Quinaz	CEO, masters degree in computer engineering and pursuing a Ph.D in Biomedicine	Nuada, Criam
10	Manufacturing	Niels Harry Oelsen	Business Development & Customer Care (Partner)	Cre8tek Denmark Aps
11	Manufacturing	Alice Lee	Sales Manager	iSmarch
14	exit options	João Santos Pereira	CEO who did a successful healthtech M&A in 2020	
15	IP strategy	Andy D	Business Development Manager	Virtue Legal Services
16	Laywer/IP strategy	Tony Orsi	Managing Partner; Lead of Medical Device Group; Head of Executive Commitee	Cooley LLP
17	Laywer/IP strategy	Sabrina Morales	Business Development & Operations Manager	Cooley LLP
18	funding strategy	Andreas Wüpper	Investment Director	Fresenius Medical Care Ventures