Summary propositions

Healthy Ideas, Healthy Returns

9 April 2018, Uithof Utrecht

Inhoud

ScarTec Therapeutics B.V.

Founded: Nov 2016,
No equity funding to date

ScarTec Therapeutics BV, a spin-off company from the University of Twente, has developed a novel therapeutic technology named Scarless Technology. The technology is centered on a proprietary small peptide which is able to specifically block the scarring process induced by key cells so called “myofibroblasts”.

The Scarless Technology has been validated in several in vitro and ex vivo in human skin obtained from donor patients. ScarTec is dedicated to develop this technology further in order to benefit patients with scars. Recently, ScarTec has obtained funding from TTW-NWO Take-off phase-2 funding of €250.000 to develop this product.

In addition, the Scarless peptide has been tested for its efficacy in pancreatic tumor. Pancreatic tumor, the deadliest tumor type, is highly fibrotic and fibrosis acts as a barrier to chemotherapy but also induce tumor cell growth. Reduction of fibrosis may help in better penetration of chemotherapy and reduce tumor growth. The Scarless peptide was recently tested in patient-derived xenograft (PDX) mouse model in combination of chemotherapy. Interestingly, the combination treatment strongly inhibited the tumor growth by >80% and the peptide-treated tumors had lower fibrosis than untreated or chemo-treated tumors. Altogether, the Scarless peptide technology offers a topical product against skin scarring and a parenteral product for cancer therapy.

Amount of funding sought: 2,5 – 3,5 M€

X-Heal Diagnostics

Not founded yet

X-Heal Diagnostics has developed the X-halyzer technology, a patented diagnostic technology that allows specific detection of bacteria from exhaled air within one hour, directly enabling targeted treatment for patients with chronic lung diseases.

See:
https://sites.google.com/site/xhealdiagnostics/home
http://www.lifesciencesatwork.nl/x-heal-diagnostics-winner-of-the-venture-challenge-spring-2017/

X-heal Diagnostics requires an initial investment of 2 Million euro for the laboratory facilities, laboratory personnel, a maintenance engineer, a quality system, clinical validation, regulatory submission and cost of goods and investment in marketing and sales. Break-even is expected after 4 years. The gross margin is expected to be 25-30%, before taxes. After 6 years the EBITDA will be 4 Million, the value potential of the venture is approximately 9 Million euro (60% of the turnover of 15 M).

Amount of funding sought: 2M€

ScolioCase

Founded: 2017

Equity funding to date: not given

ScolioCase will allow a better treatment of a disease that presents itself in 3% of the population. The goal of the ScolioCase is to reduce suffering in children with Scoliosis, by preventing them from undergoing surgery, and stop progression of their Cobb's angle in general. This requires a systematic nation-wide screening program. By treating the disease at an early stage, a bigger chance of successful treatment is achieved and the discomfort a patient may experience throughout their lives can be reduced. Beside the benefits for general wellbeing, the ScolioCase should cause a reduction in the amount of spinal surgery performed, which will come with a financial benefit, because these procedures are far more expensive than brace treatments. Also, if the implications of Scoliosis on an individual's life are reduced, their healthcare costs later in life may also be reduced. Furthermore, a part of the profit from the ScolioCase (5-15%, depending on profits, larger profits indicate the latter) will be invested in research for Scoliosis.

Amount of funding sought: 300k€

Dia-Nose

Founded: founding anticipated in Q2 2018

Non invasive medical diagnostic device to detect disease and to monitor disease progression by sniffing a patient's feces.
Proposition consists of eNose technology (sensor) combined with self learning algorithm and data base enabling automated detection and ensuring a continuous improvement of the accuracy of the detection. Proposition offers a patient friendly, cost efficient, quicker, scalable and accurate alternative to existing methodologies, resulting in more and earlier detection of disease, allowing overall lower treatment costs, patient friendlier treatments and lower mortality rates.

Amount of funding sought: 2,9M€

Sensius

Founded: 2015

Equity funding to date: none

Sensius offers new approach to thermotherapy for treatment of cancer. Thermotherapy is the controlled heating of a tumor to approximately fortytwo degrees Celsius. It is an

adjuvant therapy solution which increases efficacy of radiotherapy and/or chemotherapy treatments up to 50%.
When treating cancer, doctors are always confronted with the trade-off between survival and quality of life. Surgery, radiotherapy and chemotherapy are the mainstay, but each has a price tag on quality of life. A prolonged life is only valuable if it is not hampered by the negative side effects of the treatment. Thermal therapy is non-invasive and has no additional negative side effects for patients.

The HyperCollar3D is our solution to bring sense in thermotherapy. In this medical device we use microwave antennas, controlled by software, for high precision heating of the tumor.
Nearby sensitive organs are fenced off from the heat. Therefore, our thermotherapy is applicable for many different tumor types in the entire body. Our patented technology is unmatched in industry.
Erasmus Medical Center has demonstrated proof of principle to treat Head and Neck cancer, one of the most challenging areas in the human body. They have treated already over seventy patients successfully.

Our customers are cancer clinics worldwide. Head & Neck cancer in Europe and the United States is the beach head market. Ten research institutes have expressed their interest in this device.
To start with thermotherapy from Sensius, clinics will have to make a single investment to buy the essential equipment. Over time, new applicators for different tumor types will become available. Besides the device, there will be a total care service package and a pay-per-patient fee on the software. The business model is tuned to make it as easy as possible to start with thermotherapy from Sensius.

Amount of funding sought: 5M€

Concord Neonatal

Founded: April 2017,

Equity funding to date: to be disclosed, 300k€ convertible loan (UNIIQ)

Every year, 15 million infants are born preterm worldwide. Preterm birth is responsible for 1.1 million deaths each year due to complications at birth, many survivors suffer from long-term disability, including learning problems, cerebral palsy or chronic lung problems.

Most preterm infants breathe insufficiently at birth, the cord is clamped immediately to not delay the respiratory support they need to survive. However, immediate cord clamping compromises the infants' cardiovascular function, which can injure its immature organs. Waiting with cord clamping until the infant has been stabilized benefits placental transfusion and more stable hemodynamics, potentially reducing complications at birth, long term disabilities and mortality.
Specialists at LUMC invented Concord, a patented delivery table that enables the neonatologist to provide urgent lifesaving care, while the umbilical cord remains intact,

keeping the baby close to mom. Concord could improve intact survival with 10% and save €47,520 during the first year for each baby to survive without major disability.

Concord Neonatal BV is a spin-out of LUMC, to commercialize Concord globally and make delayed cord clamping standard of care for these vulnerable newborns.

Amount of funding sought: 250k€

Lowering high diastolic stiffness by repurposing an old drug

Company not founded yet

At present there is no therapy for diastolic heart failure (DHF) also called heart failure with preserved ejection fraction (HFPEF). In this form of heart failure contractile performance of the heart is relatively preserved but diastolic left ventricular(LV) function is greatly impaired with slow LV relaxation and high diastolic LV stiffness. In Western societies, heart failure is currently the number one hospital admission diagnosis. HFpEF accounts for 60% of all heart failure cases and its prevalence relative to heart failure with reduced contractile performance rises at a rate of 1% per year. No single therapy was so far able to improve outcome of HFpEF patients despite multiple attempts with numerous compounds.
We previously demonstrated that high diastolic LV stiffness of HFpEF patients related to limited distensibility of their cardiac muscle cells i.e. cardiomyocytes. Distensibility could be restored in-vitro through administration of □B-crystallin, a heat shock protein. Small heat shock proteins like □B-crystallin are induced in-vivo following oral intake of geranylgeranylacetone (GGA), a drug widely used in Japan for treatment of gastric ulcers.
We recently administered GGA to morbidly obese ZSF1 rats, a classical animal HFpEF model and obtained the following results:

- Five weeks of GGA oral intake was well tolerated without any side effects.
- At sacrifice, small heat shock proteins like □B-crystallin and HSP27 were overexpressed around the cardiac myofilaments responsible for cardiomyocyte distensibility.
- Isolated cardiomyocytes of GGA treated animals had restored cardiomyocyte distensibility.
- In-vitro administration of □B-crystallin or HSP27 to isolated cardiomyocytes of GGA treated animals no longer affected cardiomyocyte distensibility because of the preceding in-vivo association of □B-crystallin with the cardiac myofilaments. This provides proof of concept that the previous induction of □B-crystallin was responsible for the restored cardiomyocyte distensibility.
- In-vitro administration of protein kinase A or G, which phosphorylate cardiac myofilaments, resulted in similar improvement in cardiomyocyte distensibility in GGA treated obese ZSF1 and lean ZSF1 rats. This implies a potentiating interaction on cardiomyocyte distensibility between GGA and existing drugs acting on protein kinase G such as phosphodiesterase 5 inhibitors (e.g. sildenafil) or soluble guanylate cyclase stimulators (e.g. vericiguat).
- Deterioration of diastolic LV filling kinetics and lung congestion were not observed in the GGA treated rats.

The foregoing findings provide an important inroad to a novel treatment for HFpEF, which is considered by many cardiovascular physicians to be the largest unmet need in modern cardiology.
Further exploration of the use of GGA in HFpEF requires:

- Alignment with European and American regulatory authorities for use of GGA in HFpEF.
- Execution of a phase II clinical trial using GGA in HFpEF

Amount of funding sought: 2M€

Cyclomics

Company not founded yet

We invented Cyclomics, a technology that enables sequencing of single circulating tumor DNA (ctDNA) molecules at near 100% accuracy. This is accomplished by a three-step process consisting of capturing, copying and concatenation of the original double-stranded ctDNA molecules (patent filed). The resulting DNA products can be sequenced using portable single-molecule sequencing instruments (e.g. nanopore MinION). In addition, we have developed a computational software package to perform detection and reporting of cancer mutations in the ctDNA sample based on a proprietary consensus calling algorithm. We have reached proof of concept on 6 blood samples from patients with head and neck cancer (HNC), demonstrating that Cyclomics enables recurrent cancer detection at single molecule sensitivity. We aim to apply Cyclomics for early detection of recurrences for a wide range of cancers based on ctDNA obtained from 'liquid biopsies'.

We have demonstrated that Cyclomics can detect TP53 mutations at single-molecule resolution. Furthermore, we observed no mutations in >20,000 WT measurements, indicating a very low false positive rate. A Cyclomics TP53 assay was tested on patients with head and neck cancer. We found that Cyclomics can reliably and sensitively detect mutations in the entire TP53 gene and be used as a complementary or replacing test for diagnostic imaging (CT/MRI) of head and neck cancer recurrences.

Amount of funding sought: 1M€

Face Reality

Company founded in 2017, investment to date: €175.000

Face Reality is building the classifier for facial perception of the subconscious mind.
Face Reality can bridge the gap by combining science on the psychology of perception of the face by quantifying facial features based on 6 factors attractiveness, competence, dominance, intelligence, warmth, trustworthiness.

We deliver software that validates on the basis of a face (input), which first impression that face gives (validation) and how that impression can be influenced (functionality) and which

landmarks belong to the desired impression (output). Other applications can use this output via an API to sell their business to the end customer.

The score can then be adjusted to one or more axes as desired. The algorithm then determines the desired landmarks for the adjusted first impression based on the desired score.
How?
Face reality has the technology to both identify the best landmarks and score faces.

1. We train neural networks to classify faces.
2. By scoring over a million of faces through landmarking them and let them be rated.
3. We do that for six scientifically proven distinctive facial perceptions.

The face is analyzed biometrical and 'landmarks' are determined, these landmarks are the basis for the comparison with the reference database in which the first impression is expressed in a score on six axes

Level of development/validation:
Table 1: Overview Industry, problem & solution

Industry	**Problems**	**Solution**
1. Cosmetics /Plastic surgery	• No insights regarding the effect of treatment/surgery on perception • Face morphing based on experience instead of data • Low customer awareness about impact facial morphing	• API which scores the faces based on reference database which tells something about how the face is perceived • Morphing advice via API based on scientifically validate tech. • Visual which shows the facial perception score to a customer

2. Matching (HR, Recruitment, Casting, Dating)	• Efficiency in selection
	  • Selection procedures are time consuming
	• Effectivity of matching
	  • Decision based on feelings instead of data and science
	  • Number of persons which can be
		• Machine learning/database API where you give upload data and give the option based on type of person you are looking for
		• Decision will be based on millions of faces and analyze very quickly

	analyzed is low	

3. Advertising	• Efficiency in model selection
	  • Selection procedures are time consuming
	• Effectivity of model selection
	  • Decision based on feelings instead of data and science
	  • Cultural difference in perception not taken in to account
		• Machine learning/database API where you give upload data and give the option based on type of person you are looking for. API can tell how people perceive certain faces in other parts of the world and cultures so advertisers can adjust the ideal perceived face based on their target audience
		• Decision will be based on millions of faces and analyze very quickly

Product

We already can score faces by using the scientifically validated prototypes. But that is only the beginning. We will build a classifier with millions of faces and ratings from carefully segmented users. So our AI will be able to finetune a face to specific landmarks that are significant for specific segments.

Our AI will be able to finetune faces for each marketing campaign and every segment, for specific recruitment and successful dating. The end product will be an API which generate information coming from the scoring and landmarking API. The Face Reality API can be linked to the Morphing API to besides scoring also morph the face based on a certain wishful input.

Figure 4 gives an overview of the API.

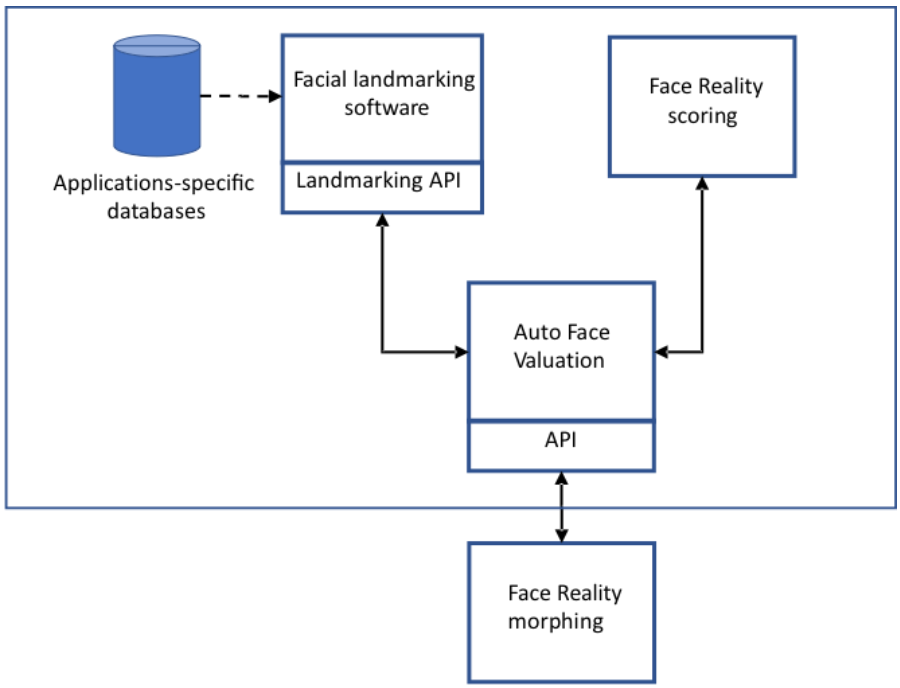

Figure 4: Face Reality API

Product development stages & markets
Since the MVP (stage 1 solution) (see above) will focus on the scoring of faces based on landmarks and will be used in each case by N=1 or 2 (e.g. cosmetic surgeon and client or recruiter and candidate), the first market to focus on will be the cosmetic surgery market. The solution provides a score before and after which can be interpreted by e.g. an surgeon (the professional). The amount people (data) which are needed to significantly say something about how faces score is less compared to the next stage, how faces are perceived by others (stage 3), here for a database of at least N=1.000.000 is needed to say something about the significant perception of faces displayed to consumers (advertising market). So the first focus market for the MVP will be the cosmetic market since the MVP fits best in this market and time to market will be far less compared to other potential MVP's for other markets. The proper development of the first stage will also be important to develop the API for stage 3, the advertising market.

Amount of funding sought: 2-3M€

Objectifying clinical spasticity scales

Company not founded yet

Spasticity is a common neurological sign of central nervous system damage and occurs after a stroke, paraplegia, or MS. Spasticity is defined as a velocity-dependent increase in muscle activity due to hyper-excitability of the tonic muscle and / or tendon stretch reflex. Spasticity hinders the coordination of movements and can lead to stiffening of joints and pain. The treatment of spasticity is diverse, from non-invasive to surgical intervention. The choice for treatment is mainly based on 2 clinical scales: the Modified Ashworth Scale and the Modified Tardieu Scale. The therapist passively stretches the spastic muscle and assesses the muscle tone during the measurement. The degree of resistance encountered

and the joint angle at which resistance increase are subjectively translated into a score on both scales. It has been shown that the reproducibility and inter-rater reliability of both scales is moderate. This hampers the determination of appropriate treatment and obtaining a reliable follow-up.
The input for the therapist can be objectified by using relatively simple sensor technology. The resistance can be registered with the aid of a force gauge and the joint angle can be determined with a combined accelerometer gyroscope sensor. By processing the data with a smart algorithm, an objective score can be obtained on both scales. Several studies have shown that sensors with an accelerometer-gyroscope combination can determine joint angles reliable. In addition, such sensors can determine the "angle of catch", the joint angle where the resistance suddenly increases during stretching of the muscle.
The aim is to develop a handy instrument with which the scores on the existing clinical scales can be objectified. The clinical tests are, as usual, carried out manually. The instrument is, for example, attached to the patient's wrist and the tester uses the instrument to move the elbow in case of a spastic m. Biceps. During the movement, the instrument registers the resistance and the joint angle. The instrument will consist of the aforementioned sensors. The synchronized data is ideally sent wirelessly to a computer, tablet or smartphone. Using an algorithm, the data is converted into a scale score on the Modified Ashworth Scale and to a score on the Modified Tardieu Scale. A test can be done in a few minutes.
In interviews already conducted with 10 national experts in the field of assessing the severity of spasticity, it emerged that there is a great need for such an instrument. In addition, a set of wishes and requirements was drawn up based on the interviews. Analyzing the aforementioned clinical scales in this way contributes to the development of a more well-founded treatment plan and offers the possibility to concretise the effectiveness of a treatment.

Amount of funding sought: 50k€

Single Cell Discoveries

Company not founded yet

Single Cell Discoveries is a startup that will perform single-cell sequencing experiments & data analysis. It will spin out of the existing, not-for-profit facility in the Hubrecht Institute, the Netherlands. This facility was opened in October 2016 to deal with the rising demand from local academic groups to perform single-cell experiments. Since then, demand (both local and international) has grown so much that the facility has reached a point of saturation. Clients are experiencing slow turnaround times and usually indicate they would also need help with data analysis.
As a solution, Single Cell Discoveries will offer not only the experimental platform for single-cell sequencing but will also consult on experimental setup and offer data analysis. We have developed an own protocol for single-cell sequencing (SORT-Seq) that is easily scalable and allows our clients to perform the first step of the experiments in their own lab without them having to buy any additional machines to do single-cell sequencing. For data analysis, we rely on custom algorithms that are built to analyse single-cell sequencing data. In other words: we will provide a one-stop solution for those interested in single-cell sequencing. Other than a few in-house facilities (located in different countries) that are restricted to

local groups, there are currently no places that offer such a complete service. Our founders have a combined experience of 9 years in the field of single-cell sequencing and have worked with approximately 20 different academic institutions in 6 countries. Building on this experience we will be able to help our customers perform the single-cell sequencing experiments that best matches their biological question and quickly get them the data they need.

Amount of funding sought: 150k€

Mirabilis

Founded: yes, date not given

Equity funding to date: not given

Heart failure is a serious clinical disorder that represents the primary cause of hospitalization and death worldwide. Cardiac hypertrophy – pathological enlargement of the heart muscle - is the principal risk factor for the development of heart failure and lethal arrhythmias. A complex web of interconnected signalling pathways and microRNAs has been implicated in cardiac hypertrophy. Specifically, microRNAs play a key role as regulators of gene activity and cellular function.

By counteracting the amount and activity of a single microRNA in the heart, microRNA-199b, we have demonstrated that it is possible to prevent, delay and even reverse heart disease in robust animal models of disease (rodents and recently pigs).

The current project proposal, designed by academic and commercial parties, consists of the execution of a mandatory safety/toxicology assessment of a chemically and pharmacologically optimized microRNA-silencing compound, MRB-8001.

To this end, an Organisation for Economic Co-operation and Development (OECD), federal Drug Administration (FDA) and European Medicines Agency (EMA) recommended two-species preclinical safety/toxicology dosing strategy is envisioned to expose mice, pigs and non-human primates to escalating doses of MRB-8001 followed by extensive pathological and toxicology analyses. Our ultimate aim is to obtain regulatory approval and test safety, effectiveness and tolerability of the experimental oligonucleotide in a Phase 1a dose-escalation study in patients suffering for heart failure.

Our proposal opens a window of opportunity for large R&D investments and returns for pharmaceutical companies dedicated to cardiovascular diseases and biotech companies focused on the development of RNA therapeutics.

Amount of funding sought: 2M€

SENSIP

Founded: Nov 2016

Equity funding to date:

The problem: Methods for bacterial detection and testing generally rely on microbiological techniques. Although bacteria can be identified in a sensitive manner, the current techniques are typically slow, expensive and require analysis in a laboratory. In recent times, faster tests have been developed based on PCR and sequencing methods and mass spectroscopy (e.g. MALDI-TOF). However, the latter techniques are not often used for routine testing.

The solution: SENSIP's technology enables the rapid detection (15 minutes) and identification of pathogens and small molecules through an easy to use cost effective detection device.
This will allow test results to be made available for faster decision making in situations where time is critical (e.g. sepsis). Furthermore, the technology is portable and we plan to further develop it for point-of-care applications (e.g. urinary tract infection).

Technology: SENSIP's patented platform technology consists of biomimetic sensors (e.g. based on surface imprinted polymers (SIPs), molecular imprinted polymers (MIPs)) and a thermal analysis device. It is at TRL4. SENSIP's device can be used to detect a wide range of molecules bacteria, proteins, viruses and small molecules.

Markets: The device has big potential to be applied in different sectors, for example, health, food (e.g. dairy), animal care and water.

Status: SENSIP is a spin-off from Maastricht University and is currently being founded.

Team:

- Dr Mary McCarthy (Brightlands Maastricht Health Campus) will act as CEO in the early stages. She has 20 years of industrial experience in the chemical industry in R&D, technology transfer and venturing.
- Prof Dr Thomas Cleij is the Dean of Sciences (Maastricht Science Programme) at Maastricht University and is a co-inventor of the SENSIP technology.
- Prof Dr Bart van Grinsven is assistant professor at the Maastricht Science Programme.

We seek funds (500k€ for 18 months) in order to bring the technology to TRL5 and 6. A number of target applications have been defined with the associated timelines/milestones.

Amount of funding sought: 500k€