CreSolution Biotechnologies Business Plan

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1. Executive Summary

The Republic of China, Taiwan is infamously known as the “Kingdom of Dialysis”, with an overwhelming high number of its population suffering from Chronic Kidney Disease, especially in Central and Southern Taiwan. As a team based in Southern Taiwan, this is an extremely important problem and thus decided to pursue this area of research. Chronic Kidney Disease (CKD) is a disease where the kidney begins to lose its function over time, and cause the accumulation of uremic toxins inside our body which is harmful for the human body. Unlike other treatments for the disease that focuses on treating the side complications of uremic toxin accumulation, CreSolve will tackle the problem from the root - the accumulation of uremic toxins.

Oh My Gut project is a leading and innovative solution to slow down uremic toxin accumulation in Chronic Kidney Disease (CKD) patients. In particular, CreSolution will be focusing on slowing down p-Cresol accumulation in the body, which research has shown to be associated with cardiovascular disease in hemodialysis patients and also induces the deterioration of Chronic Kidney Disease (CKD). Quantifying uremic toxins are uncommon in healthcare providers due to its exorbitant prices. Therefore, company proposes two products: a CreSolve and CreSense.

The creation of a CreSolve using engineered *Escherichia coli* Nissle 1917 in order to provide a safe and effective way to target the p-Cresol accumulation inside the body. Our engineered *E.coli* are able to take in amounts of p-Cresol precursor, tyrosine, and turn it into a useful product. To further complement CreSolve, it is also equipped with CreSense that is user-friendly and customizable..

The main objectives of our products are to lower the risk of Chronic Kidney Disease (CKD) patients getting complications such as cardiovascular disease as well as providing an early screening kit for quantifying the amount of p-Cresol in patient’s blood. Although the products have two different potential markets, but the company put faith in the establishment of both our drug and device can be a huge help in the fight against uremic toxins.

2. Business

2.1 Company Description

Brought together by a synthetic-biology competition known as the International Genetically International Machine (iGEM) Competition created by the Massachusetts Institute of Technology (MIT), the project Oh My Gut is the brainchild of a team of cross-disciplinary students from the National Cheng Kung University (NCKU), whom are interested in using synthetic biology as solutions for the removal of accumulating uremic toxins in Chronic Kidney Disease (CKD) patients. The Oh My Gut project will represent the core asset of this start-up company, **CreSolution Biotechnologies**.

2.2 Mission Statement

CreSolution Biotechnologies’ mission is to develop an affordable non-invasive removal method of uremic toxins in Chronic Kidney Disease patients with high effectiveness to help reduce the risk of CKD patients acquiring other health complications due to the accumulation of uremic toxins in their body. Besides, aiming to foster

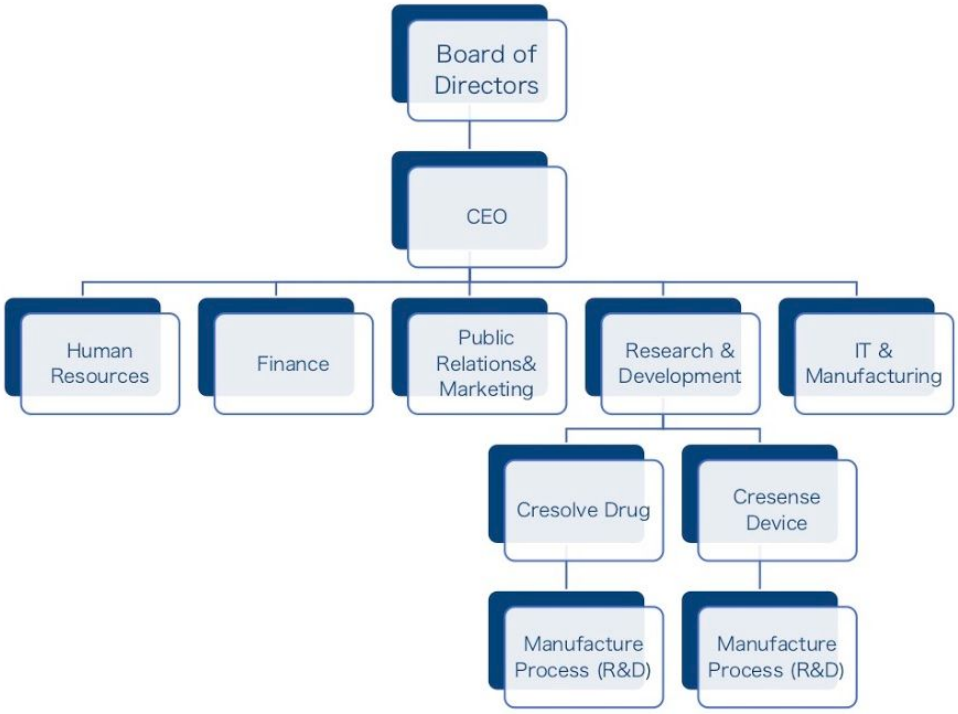
interdisciplinary research within a conducive environment and utilize various platforms to bring products to market efficiently as an investment of company future expansion to the healthcare platform.

2.3 Location

The headquarters and research centre of Cresoloution Biotechnologies will be located in Tainan, Taiwan.

2.4 Company Structure

CreSolution Biotechnologies will be a spin off from the National Cheng Kung University (NCKU) and the 2019 iGEM NCKU Team whose research team will be led by the principal investigator of the 2019 iGEM NCKU Team. The board of directors will consist of the acting principal of NCKU, investors and the 2019 iGEM NCKU Team.



2.5 Products and Services

Research[5][6] regarding the effects of uremic toxins on Chronic Kidney Disease patients have been going on for several years, and there has yet to be a preferred method for quantifying and reducing the uremic toxins in CKD patients. CreSolution Biotechnologies aims to be a leading pioneer in this area of research and market segment, and hence Project Oh My Gut will be consisting of two products:

1. Project Oh My Gut - CreSolve Living Therapeutics

CreSolve is a living therapeutic drug which primarily consists of a type of engineered *E.coli* Nissle 1917 (an FDA approved probiotic) that is able to turn the precursor of *p*-Cresol, tyrosine, into a useful product, *p*-Coumaric acid that possesses anti-inflammatory effects.

2. Project Oh My Gut - *CreSense* Sensing Device

CreSense is a blood p-Cresol quantification device that can measure the p-Cresol level in the human blood plasma via blood separation and living bacteria bio sensing techniques. It will consist of the sensing device itself, microfluidic sensing discs and living bacteria refills, which will be shipped together in the device packaging. As an addition, a cloud database will also be complementary and free of charge for CreSense operators to access patient/test subject diagnosis results.

The technology inside CreSense allows for a tiny amount of blood sample needed to be extracted from the test subject and placed inside an one-time only microfluidic sensing disk (manufacturer supplied). The disc will then undergo centrifugation inside the CreSense device, separating the plasma and the blood cells. The blood plasma will then enter a reaction chamber, where it will react with our specially engineered *P.fluorescens* and allow the device to detect and quantify the amount of p-Cresol in the blood plasma. The results will then be directly uploaded to an encrypted cloud database which the hospital or healthcare provider can only access. The system diagnosis log book will also be uploaded onto the cloud which CreSolution Biotechnologies can access to provide comprehensive customer support and device software calibration as well as optimization.

CreSense will only have a monthly subscription fee based on the usage of the microfluidic sensing discs, living bacteria refills and a basic warranty fee, which covers maintenance and other services.

Approval of Science

Laboratory experiment has been ongoing since April 2019 under the supervision of the principal investigators of 2019 iGEM NCKU Team and are supported financially by the Diamond Biofund and the university. This project was inspired by [4] paper , which uses *E.coli* Nissle 1917 as a synthetic living bacterial therapeutic for human metabolic disease phenylketonuria. Inspired by this research paper and more internal further research, Project Oh My Gut adopted the strategy of using *E.coli* Nissle 1917 as the chassis for CreSolve living therapeutic drug.

Methods of action

CreSolution Biotechnologies will be the party taking over the preclinical testing after all the construction along with preliminary functional test is completed and the iGEM 2019 competition ended. The aforementioned party will also proceed to animal testing in a designated laboratory space within the university campus and partner with a local pharmaceutical manufacturer to start production of the living therapeutic drug for clinical trials.

Proof of scalability/safety

To determine the scalability of our products, manufacturing process development will be carried out after the first phase of clinical trials are completed and be supported financially by funding phase 2.

CreSolution Biotechnologies will also seek to reinvest certain part of gross profit in R&D to widen the capabilities of the CreSense device by including other forms of accurate uremic toxin detection and quantification, as well as expanding the current line up of CreSolve living therapeutics that can reduce multiple types of uremic toxin or for other medical-related purposes.

The safety concerns related to large scale industrial manufacturing of the products will be regulated according to the safety standards established by the relevant government authorities. Bio-safety will be heavily enforced and regulated as part to maintain the standard of quality of our research and our living therapeutic drug. Multi-layered safety designs will be in place to ensure that our living bacteria refill for CreSense will not breach the stringent bio-safety rules that are already set in place.

2.6 Patents & Trademarks

The names: CreSolution (company), CreSolve (Living Therapeutic Product) and CreSense (Diagnosis Device) mentioned in this document will be trademark protected to maintain exclusivity usage of the names.

CreSolution Biotechnologies will be filing for patents to both Project Oh My Gut products (CreSolve & CreSense). This matter had been discussed with the Intellectual Property Organization of Tainan regarding to the protection of technologies developed in Project Oh My Gut to ensure exclusivity and protection during research and early marketing phase. CreSolution Biotechnologies will apply for patent protection towards the *E.coli* Nissle with TAL concept and the CreSense device.

The approximate Taiwanese patent for biotherapeutic drug in invention patent is $225.78 (not including yearly fee) whereas for the p-Cresol device, utility patent costs $193.52 (not including yearly fee). The applied patents will have a protection lifespan of 20 years. The application of patents in other selected markets i.e. the United States, India, China etc. will also be carried out within a 5-year period.

For further information, please refer to the **Milestones** section.

2.7 Pricing

The payment method for CreSolve Living Therapeutic Drug will be in the form of direct payment. As the products can not be directly sold to the targeted end-point consumers (CKD patients), hospitals, health care providers, pharmacies etc. will represent the potential buyers for CreSolve and CreSense products. Payment agreements for CreSolve Living Therapeutic Drug will depend on the negotiated contract terms with pharmaceutical product distributors of each market places.

The CreSense Diagnosis Device will be distributed directly through CreSolution Biotechnologies and the collaborating pharmaceutical product distributors, where payment will be based on a device-leasing and material-subscription structure. The leasing contract will require an upfront, refundable down-payment upon the ending of the leasing term, whereas the monthly subscription fee will be comprised of a basic warranty fee which covers maintenance and the acquisition amount of the microfluidic disks and bacteria refills.

For further information, please refer to the **Finance** section.

2.7.1 Unique Selling Proposition

The living therapeutics drug, CreSolve has the potential to be one of the first living therapeutics to be marketed in Taiwan that is specific only for tackling p-Cresol accumulation, which is surprising as most people are not aware of the detrimental effects of accumulating p-Cresol within the human body. CreSolve will be a cheap and effective life-improving therapeutic for CKD and even End-stage Renal Disease (ESRD) patients.

The detection device, CreSense is designed to be a cheap and efficient method to detect p-Cresol in the human blood plasma, as well as having the ability to be fully customizable to accommodate for other forms of uremic toxin detection. The device will be distributed along with an easy-to-understand guide book for quick mastery of device usage. An online forum will also be set up for customers / operators to share experiences, report bugs or ask questions between the manufacturer (CreSolution Biotechnologies) and other device operators. As a default option, the device diagnosis results and error log book will be sent to an encrypted server within our facility where it can be processed and automatically identify if there are any errors / misread in the device.

2.7.2 Minimum Viable Product

CreSolve is a drug that will have the engineered bacteria strain encapsulated within an enteric capsule, which will allow the drug to be dissolved within the intestines. Since CreSolve is a living therapeutic drug, it is required by law to have CreSolve gone through a number of clinical trials before it can be consumed by consumers. As such, CreSolve cannot be classified as a minimum viable product until clinical trials are successfully completed and proven useful as well as approved by the FDA. Oh My Gut team have interviewed a nurse in charge of dialysis patients in Chia Yi Chang Gung Memorial Hall, and she told us that usually patients will avoid injection since many elders are afraid with needle injection while capsule will be a better option. Another viable option is a chewing jelly.

As for CreSense, a working prototype has been constructed and has successfully performed an initial trial by utilizing goat blood (stand in to human blood) to evaluate the functionality and efficiency of both of the microfluidic disc and the centrifugal system in separating blood into blood plasma and blood cells. The sensitivity and accuracy of the photo-resistance sensor has also been evaluated in the initial trial. From the successful initial device trial, it can be concluded that:

CreSense	
Amount of blood put in microfluidic disk (cc)	20 cc
Centrifuge speed	3000 rpm (10 minutes) for blood separation and 600 rpm
Output	in mg/L

Table 1 Device Specification

2.8 SWOT Analysis

a. OMG CreSolve Living Therapeutic Drug

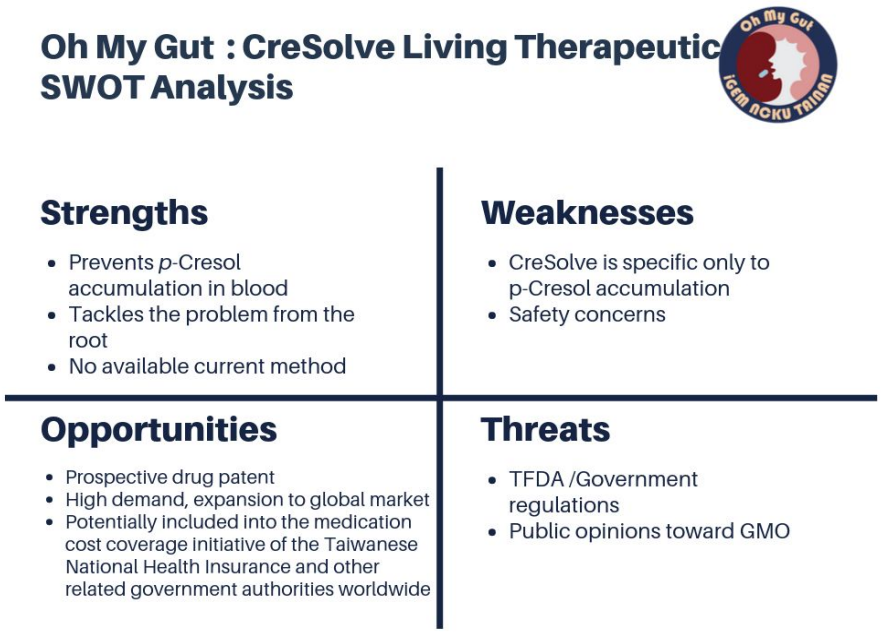


Fig. 1 SWOT Analysis of CreSolve

b. OMG CreSense Sensing Device

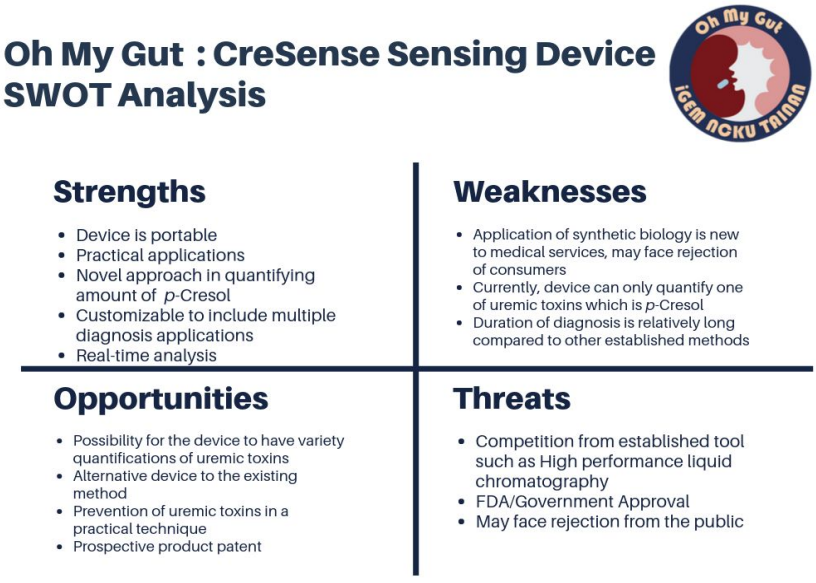


Fig. 2 SWOT Analysis of CreSense

2.9 Risk Assessment

	The risk and the likeliness (1-10)	How to avoid the risk?
External factors:		
Economic factors	6	Competitive pricing for CreSolve can be implemented to embrace the different economical background of our customers (CKD patients) as well as calling for CreSolve to be covered by every national health insurance programmes and private insurance companies .
Political factors	8	Government approvals are influential and adherence to regulations to meet or exceed the standards / requirements are essentials to have the approvals of US FDA and other similar government entities worldwide.
Social factors	8	Education towards the society about GMO and synthetic biology is important to gain the trust of consumers and build consumer confidence in such products.
Technological factors	7	All of the team will always have seminar and chances given to learn new inventions so we will not be left out.
Development of the industry	8	Optimizing the customer feedback routes by having various methods to allow customers to engage with the manufacturer as well as providing their feedback or experiences while using the products. CreSolution Biotechnologies plans to establish its own healthcare center where the CreSense device will be exclusively operated while actively developing various kinds of living therapeutic drug regarding CKD and other diseases.
The market & customers	5	A full understanding of consumer needs and comprehensive market analysis have been carried out before the initiation of Project Oh My Gut. The company, CreSolution Biotechnologies will be the entity taking over Project Oh My Gut and will carry out further research and expansion to other global

		markets.
Competition	7	To be able to compete in the global therapeutic market, CreSolution Biotechnologies and its shareholders will be investing strategically in the R&D department as well as in technologies that will streamline the daily operations of the company. The company debt accumulated will be paid off in total to attain a better financial status and further research on the products as well as their manufacturing process will be funded solely by the positive cash flow generated.
Internal factors:		
Organization & human resources	5	Participation in team building seminars and company leadership boot camps may be essential for a startup company to foster healthy relationships and gain crucial skills and knowledge into the operation of a company. Personnels and employees will be provided a rest lounge as rest is important in building up morale and productivity.
Production	6	The production / manufacturing of CreSolve and CreSense products will be initially outsource to trusted manufacturers. The quality control will be handled by the manufacturers as well as CreSolution Biotechnologies. The company will also invest in manufacturing R&D to ensure that production can be as efficient and cost effective, as well as having the capability to ramp-up production when necessary without sacrificing quality.
Finances	6	Investment funding from investors will be distributed carefully into essential materials and tools at a reasonable pricing. Positive cash flow generated will be reinvested into improving and optimizing CreSolve and CreSense as well as to reduce debt that would have been accumulated during the development phase. The company structure will be streamlined to minimize operational cost.

Table 2 Risk Assessment Table

3. Market Analysis

3.1 Market Segmentation

As a startup living therapeutic company, CreSolution Biotechnologies plans to market CreSolve and CreSense in Taiwan first as a test bed for product demand, product price sensitivity, marketing cost, production cost and production ramp-up capability before entering larger markets like the United States, China and India. Further expansions to other markets like the European Union and the rest of Austrialasia will be carried out after market demand analysis have been carried out at those respective markets.

Currently, there are two conventional drugs that targets uremic toxin removal is available on the market. First of which is [3]Kremezin, owned by Mitsubishi Tanabe Pharma Corporation, KUREHA CORPORATION based in Japan. It was established in 1991 and has since kept developing their packaging. In 2018, they repackage the drug into a black granules powder form. It is sold in key regional markets like Japan, Korea, Taiwan and the Philippines but due to its hefty retail price, Kremezin is not covered by National Health Insurance of Taiwan. As part to collect more information on medications which are being prescribed to CKD patients in Taiwan, a trip to a potential customer, the government owned National Cheng Kung University Hospital took place. The conclusion the team presented after interviews with related personnel was CKD nurse , Miss Yu-Chen Kuo, she told CreSolution team, they did not apply Kremezin to CKD patients in NCKU Hospital though NCKU Hospital applied NHI covered drug called Ketosteril for their patients. Ketosteril is an essential amino acid for low protein diet CKD patients. Short background about Ketosteril , it is owned by Fresenius Kabi Germany which has many manufacturers place in each region and distributed through many regions and drug is packed in tablets.

3.2 Customers

The targeted customers for CreSolve Living Therapeutics are mainly hospitals or other health care providers with the end-point consumers being CKD patients as a doctor-prescription drug, with the aim of reducing or reverse the accumulation of p-Cresol (a type of uremic toxins) in the body. The drug will mainly be marketed and distributed by trusted distributors, and will be made available in conventional hospitals, healthcare providers and pharmacies where it can be purchased only by the doctor's prescription.

The CreSense Device will only be made available to hospitals and other healthcare providers through a leasing contract with CreSolutions Biotechnologies, which can be made directly with the company or its trusted pharmaceutical distributors.

1. Demographic Information

Chronic Kidney Disease (CKD) is divided into stages 1-5, where by stage 5 CKD can be regarded as End-Stage Renal Disease (ESRD), which CreSolve Living Therapeutics will be slightly more targeted towards. As for the CreSense Device, it will be equally suitable for any consumers (either healthy or CKD patients) who wish to undergo a p-Cresol level diagnosis test as a pre-screening or for early detection of p-Cresol accumulations.

Based on [2], the highest prevalence of ESRD patients in Taiwan usually range from people of 65 years and above but the possibility of people aged 45-64 years in getting ESRD is also unexpectedly high.

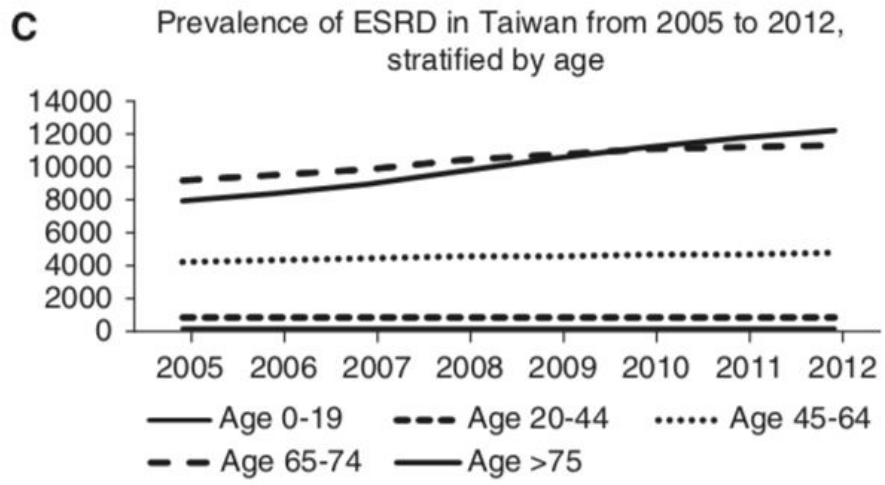


Fig.3 The prevalence of ESRD, stratified by age groups [2]

For the gender specification , from 2005 to 2012 overall prevalence of ESRD based on gender , female is higher but apparently if seen from incidence figure , males are developing more to ESRD compared to female since 2006-2012.

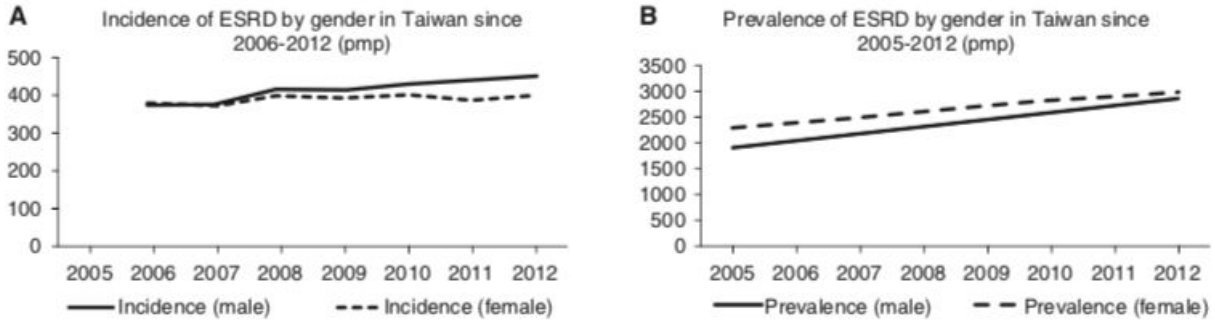


Fig.4 The incidence (A) and the prevalence (B) of ESRD stratified by gender in Taiwan 2005-2012 (per million population). [2]

To summarize, the targeted consumers of CreSolve Living Therapeutics are mostly people aged 65 and above for both genders, while CreSense is suitable for anyone who wishes to examine their p-Cresol levels in their blood.

2. In geographical terms, due to the difference in culture and eating habits, the prevalence of CKD and ESRD will differ from region to region. The pricing and the accessibility of CreSolve Living Therapeutics to the consumers will play a major role in the retail performance in markets with low prevalence of CKD and ESRD.

3. The social and economical status of people will not be a major factor since the mission of CreSolution Biotechnologies is to have CreSolve and CreSense be affordable and effective for the people who need them regardless of their financial capabilities.

4. For these past few years, ESRD patients who developed from Diabetes Melitus were increasing and based on the data [1], mostly male, senior citizens and people that have lower education towards CKD and kidney health in general are the main driving force for the increase.

5. The delivery method of CreSolve Living Therapeutics will be in the form of a capsule. The engineered bacteria will be freeze-dried and place into an enteric capsule, which will dissolve and release the bacteria when it reaches the intestines. This form of Living Therapeutics delivery is chosen due to the preference of the public in consuming medication, where the team have conducted its own surveys in NCKU Hospital and the discussion with experts during August 2019. The results are shown below:

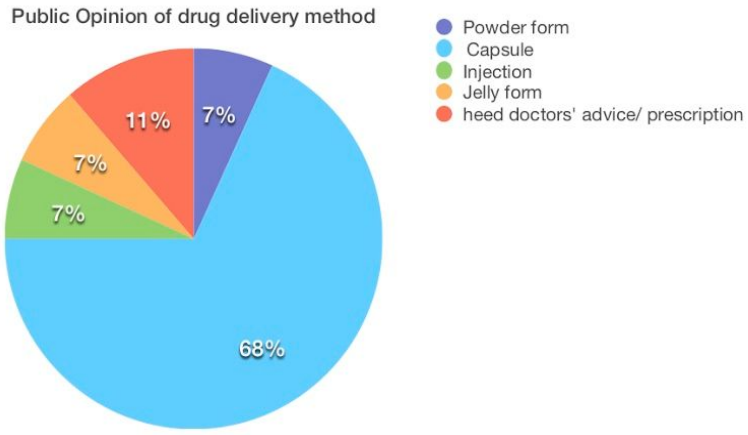


Fig.5 National Cheng Kung University Public Opinions of drug delivery method (total participants =44)

6. The lifestyle of people varies from one person to the next. According to a study in 2016 [1], certain lifestyle behaviors tend to increase the risk of people acquiring CKD. For instance, supper, bedtime snacking, smoking and lack of habitual moderate exercise may increase the risk of CKD. Research shows that usually middle-aged and older men getting CKD and reaching ESRD levels are caused by the unhealthy lifestyles stated above. (Michishita, Ryoma, et al., 2017)

3.3 Stakeholder Analysis

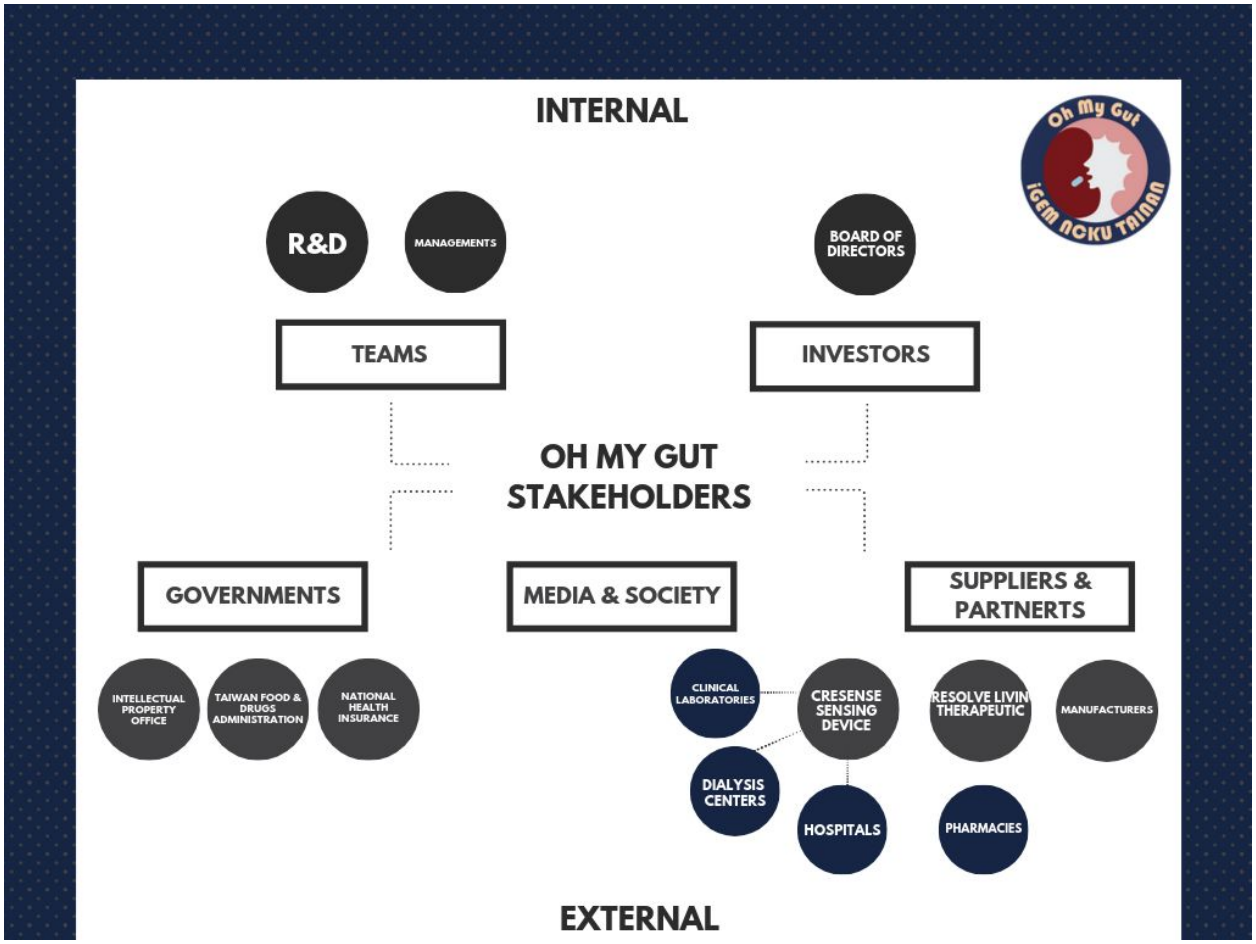


Fig.6 Oh My Gut Stakeholders

To establish CreSolution Technologies without compromising CreSolve and CreSense development, the team will start to connect with all external stakeholders and investors to further achieve CreSolution's goals and visions in the future. With a vision to provide affordable prices to engage with anyone in need of medical advice and attention, it is essential to ensure efficiency of manufacturing, lowering costs of production and preparation for ramp-up production. To enter the products in the market, pre-clinical and clinical trial phases needed to be achieved through government help and inspection. While the trial is ongoing, we will connect with all distributing companies.

Stakeholders	Interests
Team	Training update is needed to expand the capabilities of team and target to be reached.
Owners (stockholders)	Manage the project progress ,arrange all of the future plannings for company and services , contact with investors and reduce liabilities cost

Investors	Funding the project, provide new market expansion

Table 3 Oh My Gut Stakeholders' Interests

3.4 Competitors

To quote Sun Tzu, "know thyself, know thy enemy, a thousand victories." Hence, in order for CreSolve and CreSense to be successful commercially, a thorough market analysis has been carried out to identify any potential competitors. As a result, several possible competitors have been identified, but are not significant threats to the product as they are significantly different.

For CreSolve Living Therapeutics :
CreSolve is a living therapeutic drug with an engineered E.coli Nissle 1917 that is able to reduce p-Cresol production, thus slowing down p-Cresol accumulation. CreSolve is equipped with a kill switch to assure the safety of our engineered bacteria. Cresolve is able to tackle from the root with its specificity only for p-Cresol and it will not harm any other parts of the body.

Name	Year Founded	Product Description	Areas served	Product Price	Strength's	Weakness'
KREMEZIN	1991	Absorb uremic toxins and their precursors within the gastrointestinal tract, allowing them to be excreted in the feces.	Japan, Korea, Taiwan and Philippines	$7.2 / 2 gram sachet of powder	It effectiveness has been proven through several clinical trials.	Expensive and is not included in the coverage of the National Health Insurance.
Ketosteril	2009	Prevention and treatment of damages due to faulty or deficient protein metabolism in chronic kidney disease	Europe Asia, USA ,Australia	$1.05/ tablet	Proven to give nutritional effects for CKD Patients (doing low protein-diet) and is cost-effective.	Only for low-protein diet CKD patients.

Table 4 List of potential competitors for CreSolve.

For CreSense Sensing Device:

CreSense device is a novel pre-screening diagnosis device which will serve as an add-on device to our CreSolve Living Therapeutics product for healthcare providers. Currently, there is not any measurement device that is similar to Cressense in design. The device has a miniature centrifuge cleverly designed to be housed within it, which will be coupled to a microfluidic disc to separate blood plasma from blood. The diagnosis data of the blood plasma sample will then be directly sent to an encrypted online database, which is accessible to device connected and authorized for the service to ensure that the privacy of the patients are protected.

Presently, HPLC (High Performance Liquid Chromatography) is the most common way to detect and quantify p-Cresol in human blood plasma but it is often not available in healthcare service providers due to its high purchase price and high maintenance cost. HPLC was invented in 1960's, which uses the chromatographic

separation method to quantify the data with a data processor as well as a UV light emitter and receptor. The device also requires extensive personnel training prior to operating it and is ideally used in laboratory settings only.

3.5 Supply Chain

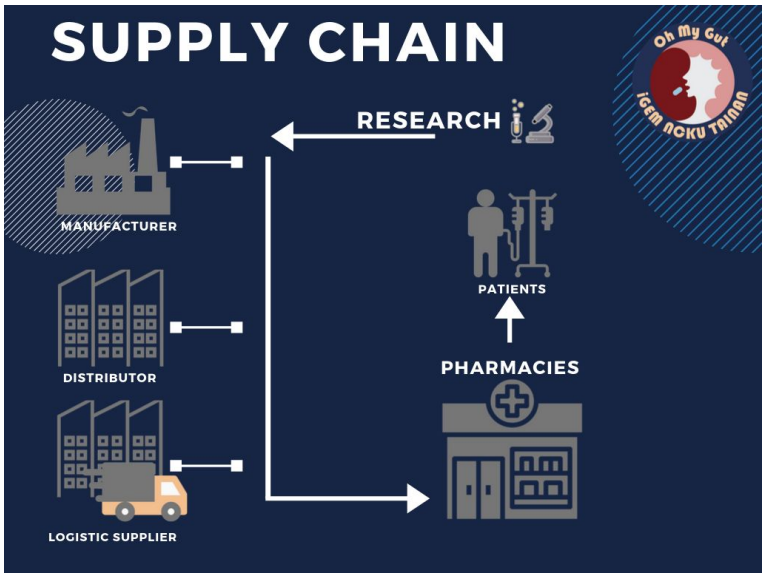


Fig.7 CreSolve's Supply Chain

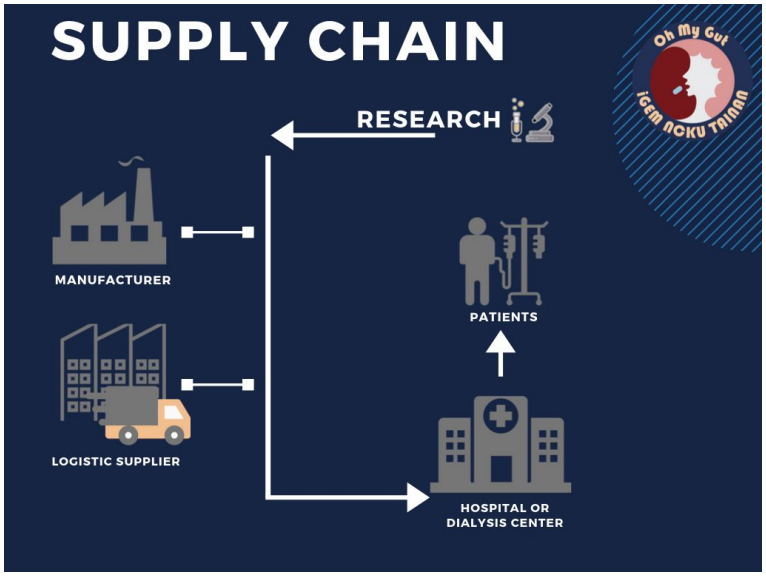


Fig.8 CreSense's Supply Chain

Currently, neither the CreSolve nor CreSense have been approved by the Food and Drugs Administration since both of them contain Genetic Modified Organisms (GMO) which is a major challenge for us. CreSolution will file

for patent protection to ensure our assets are being protected from plagiarism and obtain the required safety approval for usage and sales in the market simultaneously.

3.5.1 Marketing

For CreSolve, it is planned to collaborate with multiple trustworthy and experienced pharmaceutical distributors to aggressively push CreSolve into the market at a compelling price point. In this collaboration, CreSolution Biotechnologies aims to harness the experience of marketing professionals in the distributor companies to gain reputation and market share with the living therapeutic product across multiple markets of different countries. Promotion periods and bulk purchase discounts are options that can be negotiated to achieve brand and product recognition during the early phase of product introduction. Moreover, by outsourcing the product marketing, the company can save cost on employing marketing experts and advertising, as well as the time needed to build relationships with crucial customers, like hospitals and other healthcare providers.

For our CreSense, we will employ a similar tactic by having the distributors we are collaborating with promoting the device to the healthcare providers. Besides that, we will also have a small team set up to actively promote our device by attending conferences on diagnosis technologies and demonstrate the device as well. Unlike our CreSolve, which we aim to generate positive cash flow for the company within a 5-year period, the CreSense will be temporarily leased out (5-year period) to healthcare providers as a proof of concept and for future device calibration and improvement. As such, we will market our device as a supplement to our CreSolve, whereby the only cost the healthcare providers have to pay is a refundable down-payment and the operating cost (electricity, bacteria refills and microfluidic sensing discs).

Apart from that, CreSolution Biotechnologies will attempt to get coverage from major healthcare insurance providers, albeit it national or private, around the world for the consumption of CreSolve and the use of our CreSense to promote the use of both of the products.

3.5.2 Packaging

The packaging design will be further discussed upon when CreSolve enters phase 4 clinical trial. The CreSolve capsules will be filled into a bottle made of plastic, while the number of capsules per bottle will be further determined by basing on the recommended dosage of the product when the clinical trials are about to be concluded.

For the CreSense, it will be packaged into a cardboard box and styrofoam holders, which consist of the device itself, a power cable, 25 microfluidic disk, bacteria refills(freeze-dried) and an operating manual. An online manual will be also available with more languages and an online forum will be developed to troubleshoot bugs and common issues.

3.5.3 Distribution

The CreSolve will be distributed by collaborating distributors from factory to healthcare providers and pharmacies in markets across the world where usage and sales are approved. The purchase and consumption of the product can be only through a doctor's prescription.

On the other hand, the CreSense will be distributed directly by CreSolution Biotechnologies from factory to customers via employing the services of existing couriers as a fragile equipment, of which the cost will be consumed totally by the company.

As for the logistical requirements for the products, temperature and humidity control will be key to the well-being of the products, with the temperature tolerating range pre-notified to the distributors and couriers as well as being listed on the respective packaging. The tolerable temperature range of the

products are expected to be at around 4 degrees celsius and room temperature, while the humidity range will be determined during testing phase.

4. Finances

4.1 Product Cost and Retail

4.1.1 CreSolve

Aligning with our company's mission, the CreSolve is targeted to be an affordable oral-based medication for CKD patients whom are expected to have other additional long-term expenses. As the CreSolve, its related manufacturing process and supply chain do not have a definite cost being quoted as of today, hence the following prices listed below will be rough estimates, by just considering the projected profit margin of 8% for the first 5 years of sales. The profit margin may be adjusted accordingly if necessary within the projected product lifespan.

Materials/Expenses	Quantity	Cost per unit	Cost
Lab Use LB Preparation			
Lab One-time use tools			
Water & Electric Bill	12 months		
Manufacturing Outsourcing Cost	-	TBQ	TBQ
Retail,Marketing & Advertising			
Logistics			
Operating cost, Tax & Miscellaneous			
Est. Total			$104.90

Table 5 CreSolveCost Estimation

Title	Amount
Est. Product Cost	
Profit Margin	8%
Est. Retail Price	

Table 6 CreSolve Retail Price Estimation

4.1.2 CreSense

For our CreSense, we will be employing a device leasing strategy, where our customers (hospitals, healthcare providers, etc.) will only need to pay a refundable down payment. The down payment will be totally absorbed if the device encounter sabotage and misuse-lead mishap or malfunction. The leasing contract will be at least 5-8 years, with device maintenance being complementary along the leasing period. A subscription fee will be imposed per month on the device customer and operator, which consists of a basic warranty fee, TESTING DISC and BACTERIA REFILLS usage. The estimated down payment and basic warranty fee are listed below..

Title	Amount (USD)
Est. Down Payment	$800
Est. Basic Warranty Fee (per month)	$100

Below is the list of our total costs that will be used in the device:

Component	Quantity	Cost per unit	Cost
Arduino Uno	2	$5.16	$10.32
NodeMCU ESP8266	1	$10.87	$10.87
Electric speed controller	1	$17.74	$17.74
Brushless motor	1	$14.51	$14.51
Light sensor (tsl-235R)	1	$4.35	$4.35
Filter	1	$16.77	$16.77
Casing	1	$16.12	$16.12
Screws	4	$0.24	$0.24
Sensor holder	1	$6.53	$6.53
Lithium-ion battery	1	$9.80	$9.80
Total			$104.90

Table 7 Cost of components for CreSense.

NOTE : The stated cost of $104.90 is a rough price , the cost may be reduced to an estimated of $50 per device, if the manufacturing process and supply chain is being optimized to a high production capacity and components bulk purchase.

4.2 Funding

The funding of this project will be divided into 3 phases and will be used for the operational cost and invested into 4 main divisions.

Funding Phase	1	2	3
Therapeutic R&D Division	$18,000,000	$20,000,000	
Device R&D Division	$14,000,000	$14,500,000	
Therapeutic Product Manufacturing Process R&D Division	$3,500,000	$10,000,000	
Device Manufacturing Process R&D Division	$3,000,000	$8,000,000	
Therapeutic & Device Manufacturing			$32,500,000
Marketing & Advertising			$12,000,000
Patent Application	$5,000,000		
Operating Cost & Paychecks	$7,000,000	$7,000,000	$7,500,000
Total	$50,500,000	$52,500,000	$52,000,000

Table 8 Funding Phase and Amount Distribution

NOTE: The stated costs above are an estimation based on the data we have collected, it may vary or change in the future. The currency used is the United States Dollar.

4.2.1 Therapeutic R&D division

The funding for therapeutic R&D division will be used to acquire common lab equipment and apparatus (i.e. tips, eppendorf, etc.). The bulk of the funding will be used for pre-clinical and clinical trials.

4.2.2 Therapeutic Product Manufacturing Process R&D division

The funding for this division will mainly be used to improve the efficiency of therapeutic product manufacturing in order to lower the cost of production and have the ability to mass produce as well as ramp-up production when needed.

4.2.3 Device R&D division

The funding for this division will be used to acquire materials to be tested before being used to assemble the sensing device as well as to produce a more eco-friendly version of the microfluidic sensing disc. Equipments and machineries for the development of the device and sensing disc will be acquired to aide development. Certain part of the funding will also be dedicated to laboratory safety to prevent mishaps and workplace accidents. A minor part of the funding will be used to build the CreSense Cloud Services and employ the use of Amazon Web Service [10] or Microsoft Azure [11] to host the internet cloud service which CreSolution Biotechnologies seeks to provide.

4.2.4 Device Manufacturing R&D Division

The funding for this division will be used to research the assembly process and set up a supply chain to assemble the sensing device, microfluidic disc and Living Bacteria Refill to ensure an efficient assembly process to reduce manufacturing cost and possess the ability to ramp-up production when necessary.

5. Milestones

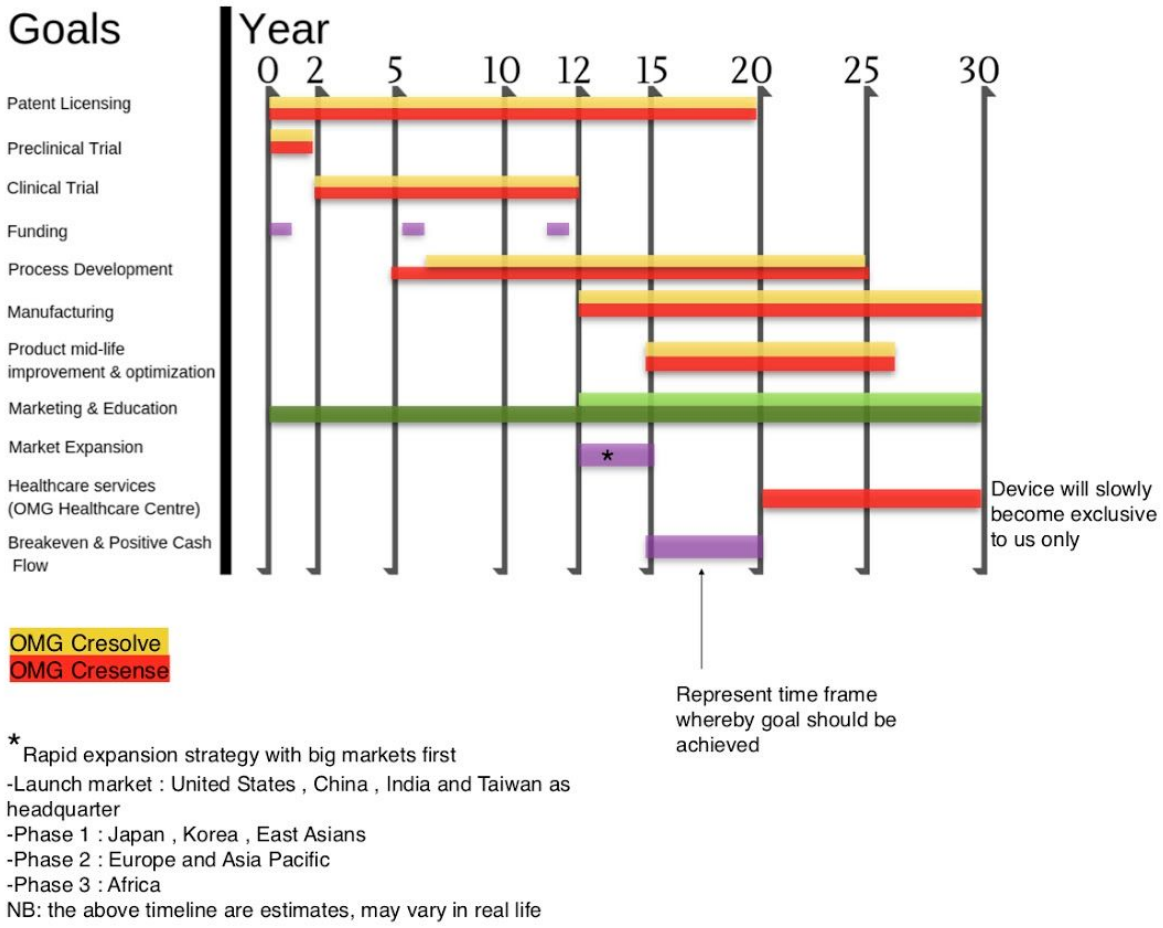


Fig.9 Oh My Gut Milestones

In the 20-year patent licensing period, pre-clinical tests and clinical trials will be carried out under the guidelines of the United States Food and Drug Administration (FDA) and will be carried out in Taiwan. while optimizing our products in expanding various of uremic toxins drugs and measurements.In addition , education about GMO to make public knows and aware of GMO uses. . While 5 years after our start-up company began , we will be starting to build healthcare services specialized for CKD patients , partnering with doctors , medical device companies to make OMG exclusive clinic. Last 5 years of the licensing patent , we will be having clinic with our exclusive device available , a research platform for entrepreneurs to make their ideas happen by the help of our service, and source of CKD patients analysis data . In addition, education about GMO to make public knows and aware of GMO uses.

6. Futures

6.1 Expansion

The future direction of CreSolution Biotechnologies can be divided into 4 sub-divisions, which are Living Therapeutics Division, Medical Diagnosis Device Division, Cloud Services and Healthcare Provider division.

For the Living Therapeutics Division, the framework and technologies established by Project Oh My Gut will be carried on into the development of new products which targets different market niche / disease. These established framework and technologies will be improved and optimized alongside the development of related Living Therapeutic products. The aim of such investment and innovation is to reduce the cost as well as improve the effectiveness of the Living Therapeutic products.

For the Medical Diagnosis Device Division, CreSolution Biotechnologies will allocate a certain portion of gross revenue to expand the functionality and enhance device sensitivity of CreSense that can not only measure p-Cresol concentration in the blood but also other uremic toxins or biomarkers in one device. The company also aims to develop a non-invasive approach to accurately quantify the levels of such substances.

CreSolution Cloud Services will be introduced to incorporate the power of the internet to the field of medicine. This Cloud Service will be targeted to healthcare providers to store vital information (diagnosis and other medical records) of a customizable and tailored profile of each individual with up-to-standard encryption protocols. The services of this division will include universal medical record accessibility for any collaborating healthcare providers, global demographic & statistics, epidemic detection and alerting system, common knowledge exchange, online surveys functionality and AI-powered data processes.

The aim of CreSolution Healthcare Provider division is to increase the accessibility of our products and services (CreSolve Living Therapeutics and CreSense Sensing Device) by establishing our own healthcare provider platform, i.e clinics and diagnosis centres.

CreSolution Biotechnologies aims to expand the area served to cover most of the countries around the world, starting by the introduction into the United States, China and India, which represent the largest market in the world. Further expansion will be focused on the European Union and other Asia Pacific countries.

6.2 Vision Statement

To become the leader in employing the power of synthetic biology and genetic engineering to enhance current therapeutic methods as well as innovate new approaches to treat diseases and other medical conditions. We aspire to change the public's perspective on GMO synthetic biology and genetic engineering, meanwhile providing

such solutions to improve and extend the lives of people by setting up an affordable healthcare platform to increase the accessibility to **ANYONE** who requires medical advice, attention and products.

6.3 Business Goals

The short-term goal for Project Oh My Gut is to successfully accomplish clinical trials and have the patents granted as soon as possible. After which, product marketing can be carried out to build a customer base and the brand itself. CreSolution Biotechnologies will also be actively taking part in conventions, seminars and conferences to improve brand recognition as well as charity programmes to improve brand reputation. The company will take on a public engagement and education role to promote the use of living therapeutics in treating disease and increase the knowledge and confidence of the public on the idea of synthetic biology and genetic modified organisms as a whole.

The long-term goals for CreSolution Biotechnologies are to expand CreSolve and CreSense into larger markets as well as adapting the technologies and frameworks established by the 2 products into treating other types of diseases and detecting other forms of uremic toxins or even bio-markers. The company will also seek to improve other services which it offers (i.e. online cloud storage and processing database) as well as starting its own healthcare provider division that provides conventional healthcare services to the public and exclusive cheap uremic toxin diagnosis test with CreSense Sensing Device.

As for the financial aspect, CreSolution Biotechnologies aims to breakeven after 5 years of product introduction to the market and will start to reinvest in improving the products and services, develop and market CreSolution Cloud Services as well as disburse dividends to investors at the 6th year point. The company intends to be debt free at the 20th anniversary of the company by allocating a huge portion of the net profit into debt repayment and further R&D cost will be funded internally forward there on.

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