MBA Entrepreneurship
Vilnius University Business School

**MBA ENTREPRENEURSHIP PROGRAMME**

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***THE REPORT ON EXPERIENTIAL ENTREPRENEURSHIP PROJECT***

# *Development of business model of locally-acting anesthetic medication product and clinical research*

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**Vilnius**

Introduction.

The following report presents a short summary on creation of the business model of locally-acting anesthetic medication product BUPIPRO and it's clinical research

**Problem/opportunity**

Perianal symptoms are very common, approximately 3% of the population in the Western world develop these symptoms each year (Johanson JF, 1990). The first option for most patients is over-the-counter medication from the pharmacy, and only about 1/3 will see their family physician (Jakubauskas M, 2020). Even then 2/3 patients will be prescribed locally acting medications. American Society of Colon and Rectal Surgeons (Davis BR, 2018) and European Society of Coloproctology (van Tol RR, 2020) recommend the use of locally acting medications as one of the first choices of treatment as a safe option.

Lidocaine, short acting local anesthetic is universally used for most of these medications. However, the duration of action is approximately 1-3 hours, so symptoms quickly return. Bupivacaine, local anesthetic of the same pharmacological group, a generic medication with up to 5-6 times longer-action, is widely and routinely used in anesthesia, and has never been used as a component for such medication.

There is large number of medications (at least 54), currently widely used in the world and thus many competitors. However, none of the medications use long-acting local anesthetics and no company has data to support this. The data on most of the medications is of low quality and outdated [4]. Introduction of a new, long-acting product with clearly documented advantages in the duration of effect and better symptom control should be easy and the message of the product very clear. Current market for hemorrhoids in the world is stated between 560 to 900 million USD (it includes medical devices also) (https://www., 2022).

A customer profile was used to identify characteristics of possible customers (see Figure 1). The customers have few jobs to be done:

1. The patients have to relieve the pain that they are having
2. The prescribers want to relieve the pain of their patients and to provide the best treatment and get the best satisfaction from their patients
3. The pharma companies want to earn the most possible money by selling the medications.

The pains experienced by the customers are:

1. For patients – pain, time off work, many daily applications
2. For prescribers – their patients in pain, all medications are the same, limited quality evidence
3. For pharma – large competition of similar medications; limited quality evidence, one medication similar to the other

The gains by the new product could be:

1. For patients – quick and long acting, effective medication, with less need for multiple applications,

2. For providers – effective and safe medication to prescribe, with clearly proven and well-described benefits

3. For pharma – clearly better product with good quality evidence – easier to sell

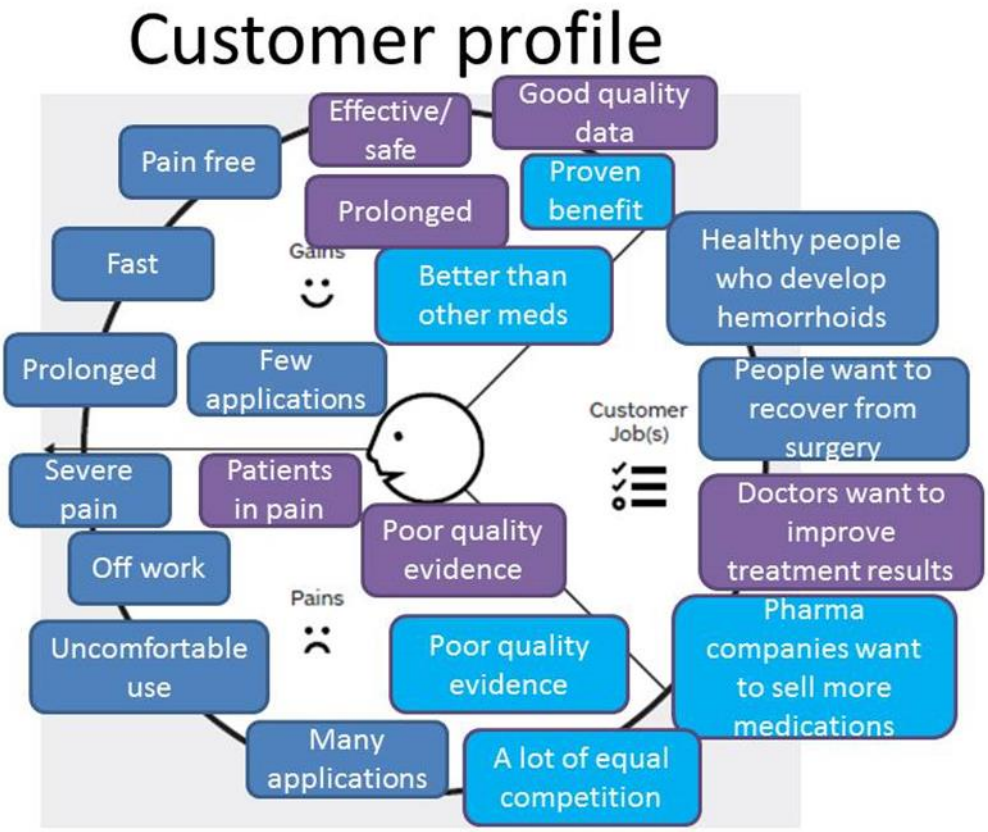


Figure 1. Customer profile of Bupipro

**Value proposition**

The value map represents the product we offer (Figure 2). It is, in essence, a composite patented medication (patent is essential to avoid easy copying by competitors) with proven prolonged duration of action and high-quality publication evidence to support the superiority over the common competitors.

The main pain relievers are:

1. For the end-user: to relieve pain, reduce number of applications, reduce costs by reducing the amount of medication use.

2. For the prescriber: reduce repeated visits, reduce the number of unhappy patients.

3. For the pharma company: Clearly better (with good evidence) than competition

The main gain creators:

1. For the end user: the medication provides improved healing, improved quality of life, reduces pain for longer, requires less applications per day

2. For the prescriber it improves the results of the treatment

3. For pharma: it provides good-quality data.

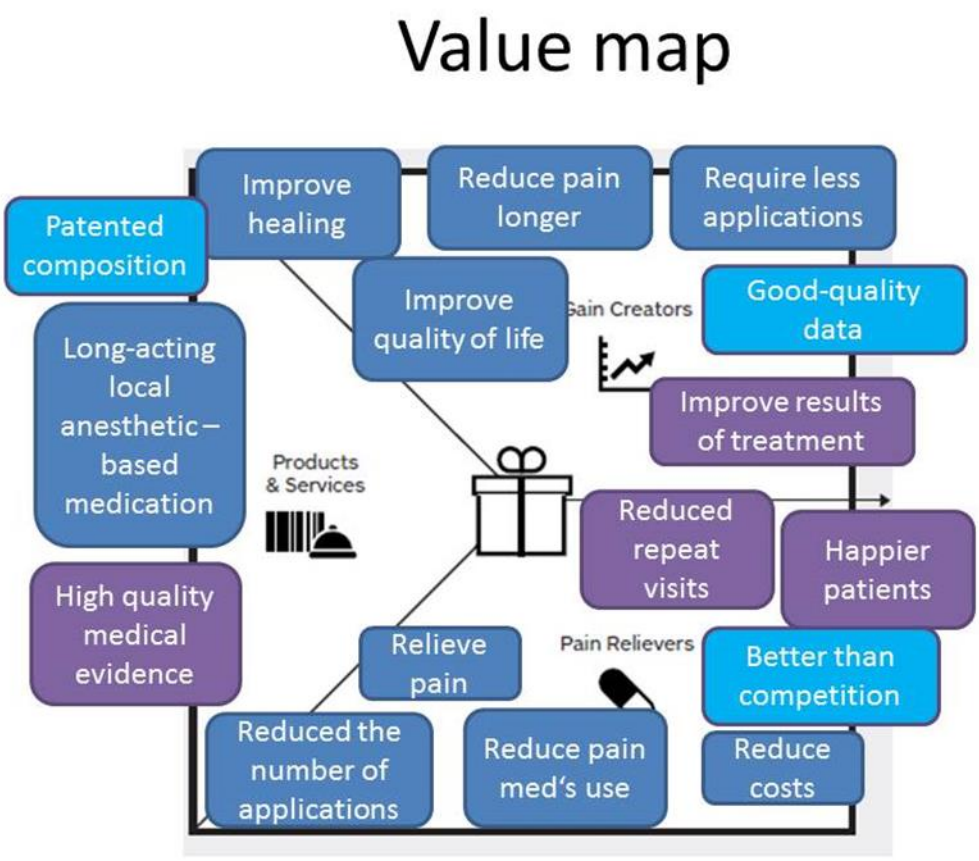


Figure 2. Value map for Bupipro

Testing the value proposition is the essential part of the hypothesis generation process. Bland D et al (D.Bland, 2020) suggests testing interventions, in order to evaluate, whether the assumptions, we make in creating value proposition are correct and if not – how far we are from the truth.

Some of the questions regarding the patient preferences in hemorrhoidal disease have already been extensively scientifically studied – there are multiple "patient reported outcome" sets – the characteristics of hemorrhoids treatment, that patients consider to be the most important, and they have been tested and validated by the colorectal community (Sara Z Kuiper 1, 2021). Pain, itching and protrusion are three most commonly described symptoms, that are of the most importance to the patients by three of the scores, and bleeding and soiling are two additional symptoms, mentioned by

one of the scores. Thus the proposed medication would take care of at least two of the three crucial symptoms of pain and itching by acting as a local anesthetic.

Bupipro is a medication, and, as such, it is impossible to perform it on a small “low grade field test”. However, we could hypothesize, that it is possible to create a minimum viable product (MVP) – Figure 3.

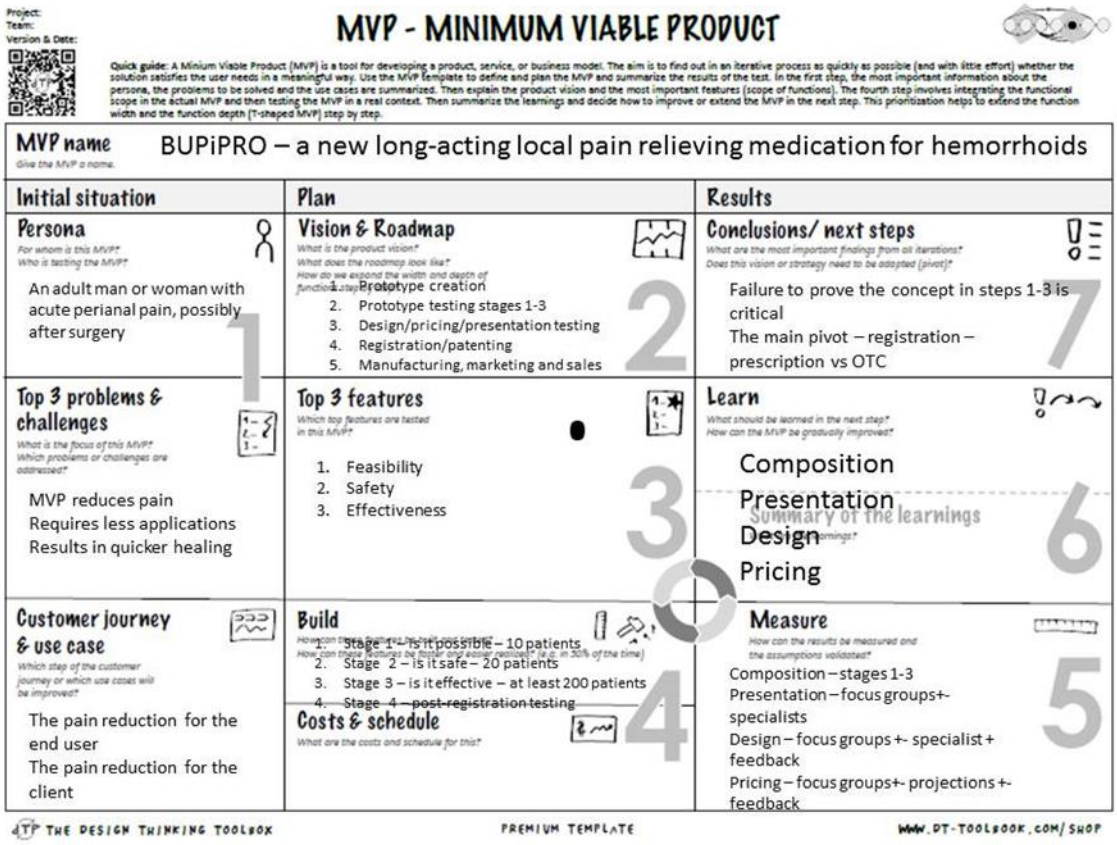


Figure 3. MVP of Bupipro

Several trials have to be performed for the product, they are represented in Figure 4. In addition to the ones, mentioned in the figure, the focus groups of patients could be used to identify the best presentation of the product, the design of the box and evaluate the pricing.

Testing of the medication is significantly different to testing the value proposition of a startup, since it is a heavily regulated industry and it is not possible to be performed easily and without appropriate approval. However, in essence the concept of testing is similar, and each testing round should in essence return the learning card, which would provide the answers to the questions of each tests and maybe a possibility to pivot.


Figure 4. The testing cards for phase 1-3 trials of the product and the learning card explain your statement of a value

**Business model**

Figure 5 presents the Economic layer of the tripple-layers business model canvas [5] of the suggested company.

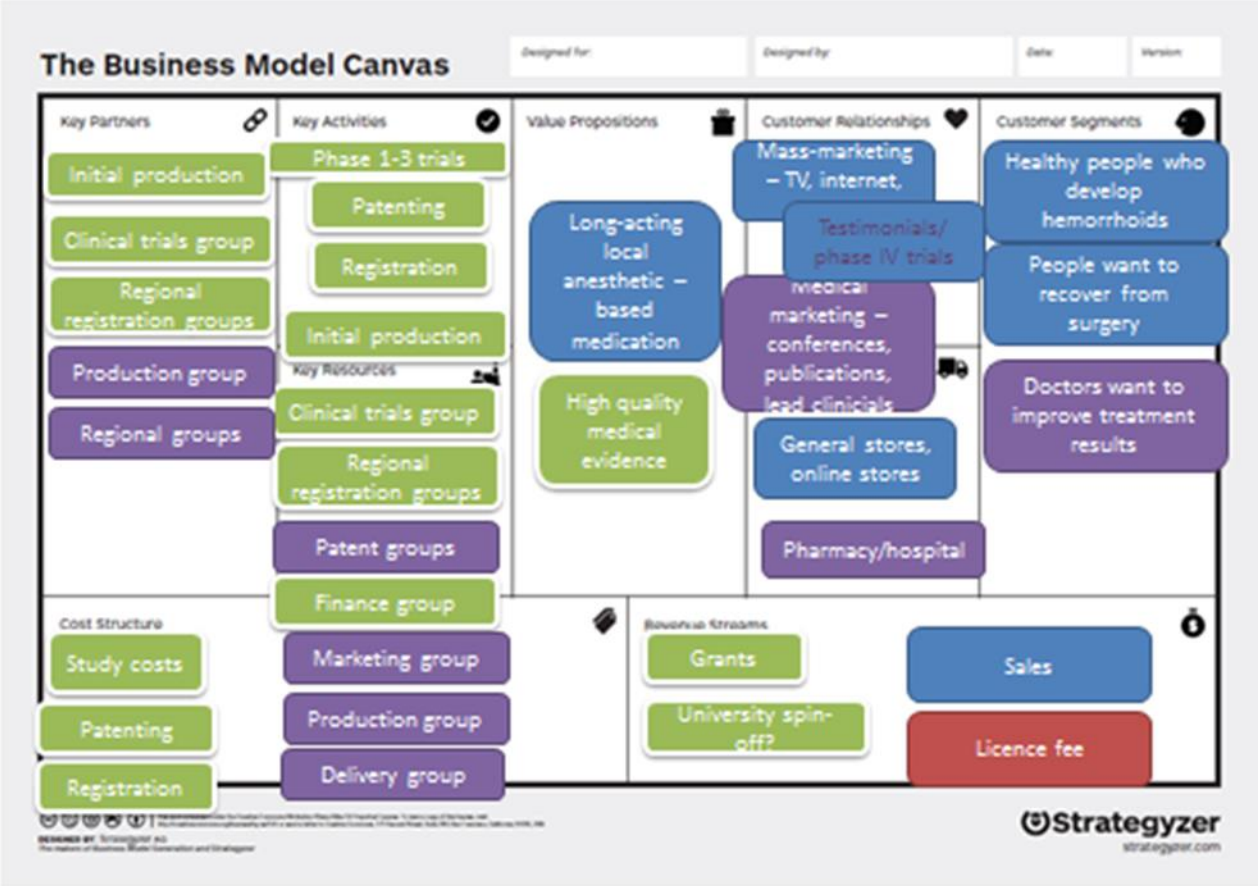


Figure 5. Economic layer of the Tripple layer Business Model Canvas

Value proposition, as mentioned, consists of creating and patenting the long-acting local- anesthetic based medication, with high-quality evidence of effectiveness and improved duration of action. The customer segments for this company would be either patients, who require this medication due to new onset of disease or the patients after proctological surgery. They are represented in the blue squares. The relationships with the patients could be achieved via mass-marketing over TV and internet and publications. If the medication is over-the-counter (OTC), the outlet could be the internet sales, general stores and pharmacies, based on the country.

Another important customers are doctors, who would want to have a medication, that would improve the weel-being of their patients quickly and effectively. They are represented in the violet squares. The relationships with doctors would be paramount, if the medication is registered as the prescription medication. Marketing in such an instance should be through medical conferences, publications, interaction of lead clinicians. The sales for these customers would occur through prescriptions and pharmacies .

Green boxes represent the vital, essential points – they have to happen for the whole project to be viable. Key partners have to come together: the partners, who will help manufacture the test product

and placebo for tests, Clinical trials group has to participate to perfom the first phases of clinical trials, as well as partners with experience in the registration of medication have to join. Key activities are initial production of the test and placebo batch, phase 1-2 trials have to be performed, the medication has to be registered and patented. Key resources are the expenses for the primary manufacture, and the resources for the first two phases of the clinical trial. If initial trials are successful, the patenting and registration have to be performed with their relative expenses.

Production, study and registration costs are initial important costs for the initial company period. After this, the decision on further action has to be taken: the medication could either be produced, marketed and sold with the respective activities and costs and risks. The other possibility would be to sell the product to the existing pharmaceutical/medical company, who would acquire the licence to sell and market the medication.

Initial revenue streams could be related to co-operation both with the Vilnius University and with the University hospital, which has clinical trials unit. Both of these organizations are interested in creating spin-off companies, and such co-operation would reduce the prices for clinical trials and for research team.

**Go-to-market plan**

Target market: Large population, who develop perianal symptoms (3% per year) and are able to afford locally acting ointment would be the target market of the end product. Large international markets, such as the US (333 mln) people and EU (446 mln) people would be the primary areas, where the medication could be marketed. However, the market, at which the sales will be targeted, depend on the product, which we are planning to sell and upon the licence, at which the end product will be sold. There are three options for the end user:

1. The patients, who suffer from the symptoms – they are the end user, if the medication is over-the-counter - registered

2. The prescribers, who prescribe the medication to the patients – if the medication is licensed as a prescription medication. The prescribers are also target audience for marketing even in the medication being over-the counter, since their recommendation may lead to end-buyer's choice to pick our product. The marketing could be aimed at patients, but also towards the pharmacists and wide range of medical doctors and nursing staff, working in the fields of general/colorectal surgery, gastroenterology, internal medicine.

3. The pharmaceutical companies – they could be the end-buyers, if the product is a licence to manufacture a well-tested and well performing medication. There are many competitors in the market - at least 54 companies selling different medications, which are, currently widely used in the world.

Product market fit: None of the medications currently use long-acting local anesthetics and no company has data to support this. The data on most of the medications is of low quality and outdated [4]. Introduction of a new, long-acting product with clearly documented advantages in the duration of effect and better symptom control should be easy and the message of the product very clear. This could differentiate our product for the end-user of our choice:

1. The patient – they would get the long acting medication (8hrs), that would give them pain relief for a long enough time to sleep at night or do their work- which no other medication currently is able to achieve. Marketing here should be directed towards the patients or their relatives, and should be wide-ranging, since the disease is common. Prescribbers could be targeted here also by presenting the high-quality data through professional communication in meetings, conferences and workshops.
2. The prescriber – they would get a product, different from everybody else in the duration of action; possibly more satisfied patients (if the pain after procedures would be reduced). The super-users could be adopted, who could spread the message to the wider medical and prescriber community about the benefits of the new medication
3. The pharma company – they would get a licence to sell high-quality proven product, based on high-quality published data, that would clearly distinguish the product form competitors and that would allow them to expand their company portfolio and offer more medications to the same end-users or prescribers. The search for potential buyers could begin when the stage II trials are promising, and the search should involve the team, early investors and advisory board, so that it would be possible to identify potential suitors.

Pricing strategy: There are few possible pricing strategies – markup pricing, which includes production cost and profit margin estimation. However, this method requires the data about the variable costs and expected sales volumes. However, it has significant drawbacks, - it ignores the current demand, it does not consider competition and it is usually difficult to estimate the exact sales. The other pricing method is called Perceived value pricing method. It is a market-oriented method, as the price is based on the consumers' perceived value of the product. Thus, consumers' views on price are given priority. Perceived-value method matches with consumer orientation, it also considers indirectly competitors' offers and it is more realistic than any other method. Here perceived value can be taken as base, with adjustments in costs and objectives. However, it is practically difficult to measure perception of the market, as the method is based on the trust. All the limitations of marketing research are applied in this case too. Competitive parity method could be used in saturated markets, is based on the competitors' pricing. The price can vary – it can be equal to competitors, lower or higher, depending on the company's goals. This method is applicable when costs are difficult to measure and competitors' response is uncertain. Such pricing brings uniform pricing in the industry.

On the other hand, such pricing is one-sided, only competition factor is on the primary customer. If the decision to sell in pharmacies will be taken, the markup pricing considered and the costs, qualities, services, and consumers' perception of value are ignored. In the case of Bupipro, a combination of pricing methods could be used, but again the choice will depend should form the baseline of price, and then value-based pricing could be used to increase the returns of the company. Competitive parity method could be used in the beginning to increase the market penetration and decrease competition. If the pharmacy company would be the final customer, the pricing could take into account the sales that the medication can generate over the lifetime of a patent and percentage from the sales could be calculated, e.g Prepration H, the biggest seller in the US, has a market share of 78 mln USD. If the licence for the medication in the US would take up 10 years and the medication would be expected to generate the sales of 10% of preparation H sales, the licence for the US market could be 3900000. Since the market in Europe is larger, than in the US, and other world markets are growing significantly, the global license could be sold for 10-12 mln USD.

**Competitor analysis**

About 4.4 % of the global population suffers from hemorrhoids and the prevalence rate is growing very fast. The global hemorrhoids treatment market is expected to grow at a Compound Annual Growth Rate (CAGR) of 5.8% over the forecast period (2021-2028). The hemorrhoids market is currently at 0.98BN USD.

The American segment is the largest regional market segment for the global hemorrhoids treatment market. The rising prevalence of hemorrhoids due to lifestyle change and the adoption of sedentary habits is fueling the market growth in this region. According to research by NIDDK, 1 out of 20 Americans have hemorrhoids and 10 million new cases appear each year. Moreover, well-developed healthcare infrastructure and active government support will further boost market growth. The European segment is the second-largest segment, however, when combined to EU, the market is the largest. The rising geriatric population and prevalence of lifestyle disorders are generating demand for hemorrhoids treatment. Moreover, well-developed medical infrastructure and active medical research backup are positive market factors in this segment. The Asia-Pacific is the fastest-growing market segment. The rapid development of healthcare infrastructure and the growth of the pharmaceutical industry are driving the market growth in this region. Moreover, the patient fall is also increasing with the increase in awareness about the disorder. The other segments viz the Middle East and the African segment are expected to witness moderate growth over the forecast period.

59 medications for hemorrhoids are listed on the drugs.com (https://www.drugs.com/condition/hemorrhoids.html). The major global companies playing a key

role in the hemorrhoids treatment market are : Abbott Laboratories, AstraZeneca plc, Bayer AG, Boehringer Ingelheim GmbH, Boston Scientific Corporation, CONMED Corporation, Cook Medical, GlaxoSmithKline, Olympus Corporation, Pfizer Inc., Takeda Pharmaceutical Company, Taro pharmaceuticals Inc., Teva Pharmaceutical Industries Ltd, Astra Zeneca, Glenmark Pharmaceuticals are the major companies operating in Global Hemorrhoids Treatment Market.

No company in the world is using bupivacaine as local anesthetic component of the local medications, it is mostly lidocaine, benzocaine, dibucaine – these are all short-acting locally used medications. Other medications have steroid components (anti-inflammatory) and vessel-contracting agents. Recently, PP-110, and Israely developed medication, was recently awarded a US patent, takes two approved active ingredients (pramoxine 1% and phenylephrine 0.25%) and puts them into an innovative delivery system. When applied, the gel leaves a thin film to ensure long-term contact of the active ingredients with the affected tissue. This ensures the longer-term action of the medication, and, thus improves the duration of action. In an open-label study, PP-110 (in gel and wipes form) was provided to some patients once daily, while other patients received Preparation-H Extra Strength per label instructions, three to four times per day. Patients using the PP-110 gel reported statistically significant better results in the three most prevalent clinical parameters relating to common symptoms of hemorrhoids — pain, bleeding and itching — compared to patients treated with Preparation-H (https://www.israel21c.org/new-hemorrhoid-treatment-bests-preparation-h/)

This clearly shows, that prolonging duration of action of medications is well reported by the patients and may provide objectively better outcomes. However, the study was open-labelled, thus, prone to significant bias, and thus has to be reproduced in double-blind randomized settings.

**Project team**

The team is currently composed of two founders, and the search for the third one is ongoing.

Tomas is the CEO of the company, responsible for project creation, medical testing, search for investors/team members and advisory board. He has significant experience in clinical trials, medicine, treatment of hemorrhoids and practical medical fields. I have affiliation with the Vilnius University and Vilnius University hospital, who are interested in innovation and new product development. The hospital has available setup for all stage clinical trials and sufficient patient population for the trial recruitment.

Brigita is the COO of the company, responsible for the daily operation of the company and its office, financial flows, also participates in planning and execution of all activities of the company. She has more than 25 years of middle and senior-level managerial experience, and is currently a real-estate investor.

The third team member will be someone, who has significant experience in the early stage Pharma product development/registration in Europe or in the US.

We are also looking for advisory board members, who could assist us in finding investors/partners for minor share in the company. They would act as mediators and help open doors to potential investors/partners down the road.

Possible risk and its management:

1. The risk of insufficient project management competence of the project team

The project is planned by the three main partners, who each will have significant experience in their respective fields and who could complement each other. The financial planning was performed using existing datasets, so financial expenses are accounted for in real-world scenario.

2. Negative/inconclusive studies

The risk is high, as the final goal is to create the very effective and well working composite medication. However, bupivacaine and it's properties are already very well-tested and proven in medicine, although, not in the field of hemorrhoids medications.

Even if this medication does not prove to be significantly superior to other medications, it could still be used as an alternative to existing medications with the appropriate marketing strategies by the companies, willing to enter the new market. Also, it is possible, that this medication may become more applicable in other disciplines, where local anesthetic formulations are used, e.g. wound care, dental care and others.

3. Increased expenses for studies/registration/patenting – this may happen despite the adequate calculations and reasonable overhead calculations, provided below. The increased costs/expenses would be communicated with investors immediately and all possibilities to avoid unnecessary costs would be used.

**Financial projection and key metrics**

Income statement is presented in table 1.

| | **Year 1** | **Year 2** | **Year 3** | **Year 4** |
|---|---|---|---|---|
| Revenue | 0,00 € | 0,00 € | 0,00 € | 10.000.000,00 € |
| **Cost of Goods Sold** | 0,00 € | 0,00 € | 0,00 € | 10.000.000,00 € |
| Gross profit | | | 0,00 € | |
| **Total expenses** | 300.000,00 € | 700.000,00 € | 1.000.000,00 € | 1.000.000,00 € |
| Income before Tax | -300.000,00 € | -700.000,00 € | -1.000.000,00 € | 6.000.000,00 € |
| **Income Tax** | 0,00 € | 0,00 € | 0,00 € | 900.000,00 € |

| | | | | |
|---|---|---|---|---|
| Net Income | -300.000,00 € | -700.000,00 € | -1.000.000,00 € | 5.100.000,00 € |

Table 1. Income statement

Key activities/deliverables are presented in table 2.

| | **Year 1** | **Year 2** | **Year 3** | **Year 4** |
|---|---|---|---|---|
| **Activity** | Setup<br>Phase 1 trial | Investor search<br>Phase 2 trial<br>Patent application<br>Phase 3 trial - beginnning | Investor search<br>Phase 3 trial<br>Other application avenue studies | Phase 3 trial results available<br>Patent application<br>EU/FDA registration application |
| **Deliverable** | Safety/feasibility | Early efficacy/ dosage<br>Patent application | Successful recruitment in phase 3 trial<br>Potential pharma investor term sheet received | Phase 3 trial publication<br>EU/FDA registration<br>Agreement with pharma investor signed |

Table 2. Key activities/deliverables

Investment plan is presented in table 3.

| Stage | **A (years 1-2)** | **B (years 3-4)** |
|---|---|---|
| Amount needed | 100.0000 | 2.000.000 |
| Ownership willing to give | 10% | 40% |
| Post-money valuation | 1.000.000 | 5.000.000 |
| Requirement for the investor | Early stage pharma investing experience | Exit to large pharma experience |

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