BUSINESS PROPOSAL

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SYMEMCO THERAPEUTICS

Symemco
Therapeutics

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Mission and vision statements

Mission statement

Our company aims to create a therapeutic drug to target the neuroinflammatory pathways associated with mild to moderate stages of Alzheimer's disease (AD) by genetically engineering Escherichia coli (E. coli) to produce high yields of pterostilbene.

Vision statement

Symemco Therapeutics' main goal is to delay the progression of mild to moderate AD, to extend the time a person living with AD can maintain their independence in their daily lives. We plan to implement anti-inflammatory therapies to treat AD and ultimately extend this application of synthetic biology to a range of neurodegenerative diseases.

Our main aims

Here at Symemco Therapeutics, our current main aims are:

- Create an AD therapeutic targeted to identified neuroinflammatory pathways.
    - By utilising the compound pterostilbene, we are working towards targeting the NLRP3/caspase-1 inflammasome pathway, not currently a target of currently available AD therapeutics.
- Ensure our product maximises accessibility.
    - We intend to manufacture pterostilbene in a cost-effective manner to ensure financial accessibility for stakeholders and also encourage production of multiple methods of delivery to cater to all patients needs.
- Implementing a multidisciplinary approach to AD therapeutics.
    - We are focused on bringing a multidisciplinary group of individuals together, from computer science, genetics, bioengineering, biochemistry, biomedicine, global health, and medicine backgrounds, to gain diverse perspectives and evaluations in all aspects of our company.

Market Problem

Currently, more than 55 million people are living with dementia worldwide, with nearly 10 million new cases each year (World Health Organisation, 2021). With this predicted rise in cases we have identified six key limitations associated with the AD therapeutics market.

These problems in include:

(1) Costs surrounding Alzheimer's Disease:

In general, it is estimated that the average cost of bringing a drug to the market is £1.1 billion. This includes costs of funding spent on clinical trials, including failed trials, and money raised from investors (London School of Hygiene and Tropical Medicine, 2020). More specifically, the cost of developing a drug for Alzheimer's Disease (AD) from non-clinical stage up to FDA approval is currently stated at £4.7 billion (Cummings et al., 2018), with the total cost of dementia (a term for a range of neurodegenerative diseases that are inclusive of AD, where AD makes up 50-75% of all dementias) in the UK currently being estimated at over £34.7 billion a year (Alzheimer's Society, 2020). Furthermore, the process of the clinical stages of drug development for AD are estimated at £35.9 billion, with stage three clinical trials being the most expensive (Cummings et al., 2021). This makes AD treatments and care an extremely costly endeavour, exceeding many other therapeutic areas in the therapeutic market, and is expected to continue to increase to more than £846 billion due to our ageing population (Wong, 2020).

(2) Lack of AD physiology targeting therapeutics:

Currently on the market, there are a range of drugs to treat the symptoms of AD, but no diseases-modifying drugs targeting AD. We at Symemco Therapeutics, aim to bring a disease-modifying therapeutic to the AD market to target the NLRP3 - caspase 1 neuroinflammatory pathway, and address this problem. Neuroinflammation pathways have been evident to further the progression of AD, but there are currently no drugs targeting these neuroinflammatory pathways (Pascoal., 2021). Drugs, such as Aducanumab, were used to target amyloid-beta (AB) plaques, typical of AD, however, there were controversies surrounding its effectiveness (Langreth and Matsuyama, 2022). Subsequently, Aducanumab was removed from the market, but the basis of the compound is still currently being explored by several companies, including Eisai Co. who is developing a drug under the name lecanumab. Overall, the lack of disease-modifying drugs on the market means that there is a continual need for emerging therapeutics to address problems with the Alzheimer's therapeutics market.

(3) High risk levels:

Biotech companies have the potential to make significant returns when posing a safe and effective product. However, there are huge risks surrounding the uncertainty of the product

actually making it to the market due to high research and development (R&D) costs and strict drug regulatory body approval (Murphy, 2022).

Most biotechnology companies acquire a patent to protect the novelty of their product, allowing time to recover expenses used on R&D and establish their product amongst competitors. However, once their patent expires, companies risk financial stability as they are reliant on the product being successful so they can secure regulatory body approval and sell it on the market.

In order to approve their drug, companies have to go through regulatory bodies. In the UK, this consists of a five step process including discovery, preclinical research, clinical research, the Medicines and Healthcare products Regulatory Agency (MHRA) review and MHRA post-market safety monitoring (Miller, 2021).

Companies are reliant on the success of a drug reaching the market, to account for the estimated £1.1 billion cost of bringing a drug to the market as mentioned previously. However, even if the drug reaches the market, companies need to make sales and a profit, which can depend on a multitude of factors including the consumers perception of the company and its product. For example, the US Medicare programme refused to pay for Aducanumab, a drug mentioned previously, unless patients were participating in clinical trials. Even though the drug was initially FDA approved, public perception contributed to its eventual removal from the market (Langreth and Matsuyama, 2022). After drugs are released onto the market, there is still post-market clinical monitoring, which biotechnology companies should be aware of. In general, the risks in many cases can outweigh the potential benefits and success of the company.

(4) Patient care:

AD patients experience behavioural and psychological complications alongside cognitive deterioration, therefore receiving care is imperative. Examples of this include aggravation, depression, anxiety, appetite, and sleep disturbance. These not only affect the patient, but their family and caregivers (Malaz Boustani, M., 2007). In severe cases of AD, the patient is unable to make healthcare decisions independently, therefore by targeting the progression of AD in its mild to moderate stages, we hope to enable the person living with AD to retain their independence over their healthcare choices for longer. This subsequently takes pressure off of family and caregivers.

Moreover, the current patient healthcare system has issues with accessibility and quality of care, workforce resilience and provider sustainability. For example, one in six services still fall below the required quality standard set by the CQC. Most care is funded by the NHS, which is free at point of use. In contrast, adult care is a complex combination of state-funded and privately financed care, therefore the problem surrounding adult care is the existence of a private market (The Health Foundation, 2021). There are also limitations surrounding funding for adult care due to demographic pressures, local government financial pressures, increases in national living wage, and the COVID-19 pandemic. These problems ultimately create a vicious cycle of more unmet care needs and workforce pressure and impacts on healthcare services (UK Parliament, 2022).

Market segmentation

Alongside the number of people living with dementia previously stated, as of 2021, the global market value of AD therapeutics was estimated to be £4.0 billion with a compound annual growth rate (CAGR) of 8.4% for the period 2022 to 2029 (Data Bridge Market Research, 2022). According to the same source, in 2029, the global market value is estimated to reach £7.6 billion as the global prevalence of AD increases to an estimate of 82 million by 2030 (Guerchet, M. et. al., 2020). This is also due to an increase in government and non-government organisation spending around the globe, in the AD therapeutics and diagnostics market.

In Europe, the number of people living with dementia was predicted to be 9.8 million in 2020 (Alzheimer Europe, 2019). This source also predicted that the number of people living with dementia in the wider European region is expected to reach 18.8 million by 2050. The European Alzheimer's disease therapeutics and diagnostics market was predicted to be £2.5 billion in 2022, growing at a CAGR of 4.76%, thereby reaching a value of £3.2 billion by 2027 (Market Data Forecast, 2022).

Within the UK, the number of people living with dementia in 2020 was approximately 900,000 and is expected to reach 1.6 million by 2040 (Wittenberg, 2019). Also according to Wittenberg (2019), the total cost of dementia in 2019 was £34.6 billion and is set to reach £94.1 billion by 2040, an increase of 172%.

Furthermore, within AD there are different stages which can be broken down and classified differently as shown in Table 1.

Table 1. Showing the different stages of AD and a brief description of what occurs at each stage in terms of the amyloid plaques and Tau proteins. (Alzheimer's Association, 2022)

Stages based on symptoms	Amyloid plaque stages	Tau Braak stages
Mild or Early: Symptoms are generally mild and not always easy to notice. Common symptoms may include problems with memory, speed of thought, perception or language.	**A**: Plaques present in the base layer of the frontal, temporal, and occipital lobes.	**Braak I-II**: (I) Tau proteins are centred around the transentorhinal region then (II), Tau pathology becomes more densely packed.
Moderate or Middle: Symptoms become more apparent and the person will likely need more assistance with daily tasks.	**B**: Amyloid plaques progress to the majority of isocortex regions.	**Braak III-IV**: (III) Tau pathology moves into the entorhinal region and low levels of Tau can be seen in the CA1 of the hippocampus. There are no or only mild changes seen in the isocortex (early symptoms of AD can be seen) (IV) There are increased levels of Tau in the entorhinal region and CA1 hippocampus, however, there is no detectable brain atrophy and the pathology does not meet the current requirements for a formal neuropathologic diagnosis of AD.
Severe or Late: People will eventually need full-time care and support with daily tasks and personal care. Many symptoms can cause difficulties, however the most prominent symptoms include altered perception and physical problems.	**C**: Amyloid plaques become densely packed in all affected areas.	**Braak V-VI**: Tau can be found in almost all areas of the hippocampus and isocortex region (symptoms are apparent).

We are specifically targeting AD in its mild to moderate stages, as literature has suggested that pterostilbene binds to the ATP hydrolysis site on the NLRP3 inflammasome, and thereby prohibits the NLRP3 inflammasome's mechanism of action within neuroinflammation related to the mild stage of AD (Chen et al., 2021). Within the UK, the number of people living with mild to moderate stage dementia was estimated at 373,000 in 2019, and is expected to increase to 524,000 by 2040 (Wittenberg, 2019). People living with mild and moderate AD account for

around a third of the total number of people living with AD in the UK. Globally, 10 million people are diagnosed with AD each year, of which 50.4% are mild stage AD (Yuan et al., 2021).

Taking all of the above into consideration we were able to define our total addressable market (TAM), serviceable available market (SAM) and serviceable obtainable market (SOM). Initially, we aim to market to our SOM which is one percent of all mild to moderate cases of AD in the UK. This is shown in Figure 1.

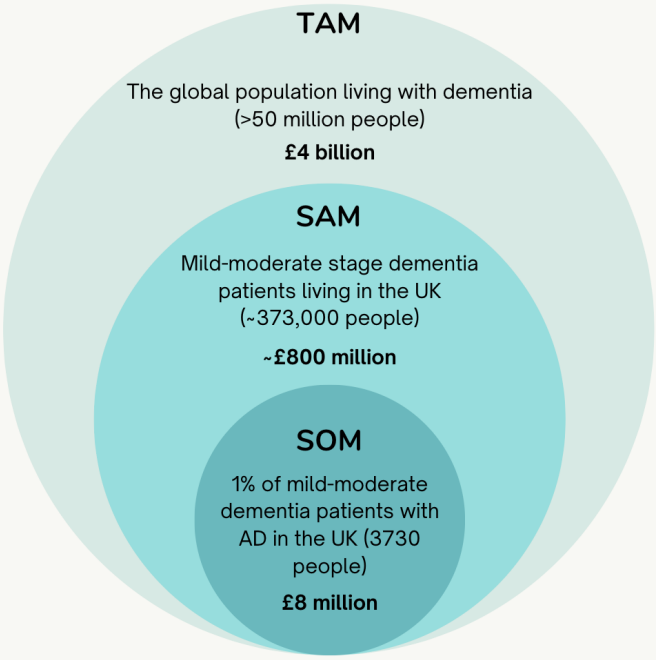

Figure 1. A depiction of our TAM, SAM and SOM based on the market segmentation research and the stages of AD detailed in Table 1.

Our solution and unique selling point

Our Solution

Our goal is to produce a disease-modifying therapeutic, thereby targeting the pathophysiology of AD. Distinctly, we aim to delay the progression of mild to moderate AD by focusing on the NLRP3 caspase-1 neuroinflammatory pathway, allowing the exacerbation of Aβ-plaque disposition. In turn, this reduces the phagocytic activity of microglia, and is a promising target in the AD therapeutics market.

Currently, there are no other therapeutics available on the market that are disease-modifying or specifically target neuroinflammation associated with AD, making our approach unique in comparison. Moreover, we intend to produce our therapeutic and determine the therapeutic

dose of pterostilbene through a novel biosynthesis pathway in our genetically modified *E. coli* bacteria. We aim for this biosynthesis method to optimally manufacture high yields of pterostilbene for therapeutic use.

Additionally, we aim to make our product as cost-effective as possible in various ways. Firstly, creating an economy of scale allows us to increase our revenue over time as production output increases with the development of our business. Additionally, we intend to use reputable manufacturers and suppliers of high quality, sustainable materials and equipment to limit costs associated with replacing lower quality materials, and to minimise our environmental impact at all possible points. Furthermore, to optimise workforce efficiency, we intend to directly supply to our proposed end users as opposed to supplying to companies that then sell to the end user, as hiring middle people can increase costs.

Furthermore, we intend to make our product accessible to the fullest extent through prioritising scalability to meet the demand for AD therapeutics, caused by the ageing population and projected rise in AD cases. This will be achieved throughout the company, from making our website and product details accessible to those that experience visual or reading difficulties, (including dyslexia and colour blindness) to making our drug in multiple administration options to ensure we cater to a range of patients and their preferences. We have considered all possible methods of delivery and intend to finalise our decision regarding which methods we will continue with at a later stage.

Within our work, we must act responsibly and safely due to our work with genetically engineering *E. coli* falling under the term genetically modified organism (GMO). We will submit all the relevant details to the Department for Environment, Food and Rural Affairs (DEFRA) in order to gain approval for marketing, trialling, and releasing our GMOs in the UK and EU. Equally, we plan to create a marketing strategy that involves educating consumers and the general public about GMOs, reducing stigma surrounding their use and highlighting their benefits. Subsequently, we will be able to address how the market will perceive our product, to maximise revenues when our product enters the market.

There are problems surrounding manufacturing processes and its environmental impact which we aim to address. We strive to power our potential manufacturing premises through renewable energy sources, including solar panels on the roof of our buildings, and reduce our waste by sourcing recyclable components at all possible stages, including in the building of our factories where viable. All efforts will be continually reviewed to identify areas which could be

improved and we plan to keep informed about all government regulations surrounding the environment as they are continually updated.

Symemco Therapeutics seeks to relieve the problems surrounding improper care of AD patients, as there is a demanding level of care needed due to the symptoms AD patients experience. We plan on doing this by making our therapy accessible to AD patients at care homes whether they are privately funded or not by partnering up with different companies to distribute our product on a large scale nation-wide and globally. By delaying the progression of AD, symptomatic progression will be delayed. This will also have a positive knock-on effect on caregivers which face turmoil and stress looking after AD patients.

The risk levels associated with the biotechnology market are difficult to address due to its volatility. However, at every step of our drug development, we aim to create detailed analysis and effective adaptations to our long-term plan and approach to ensure the progress and forward movement of our company goals.

Unique Selling Point

There is currently no disease-modifying drug available on the market targeting AD however many drugs are undergoing research or in the clinical stages of drug development. Thus, Symemco therapeutics aims to be one of the first to enter the market at this stage or entering when there are potentially only a few other competitors. We are also targeting AD using the polyphenol pterostilbene which is currently used as a food supplement. We aim, through genetically engineering *E. coli* to produce higher yields of pterostilbene, to be the first company to produce pterostilbene relevant for therapeutic use. Its manufacturing methods are not currently regulated, thus, the purification in food supplements is not quality assessed. Additionally, our novel biosynthesis method is effective in comparison to extraction methods used to obtain pterostilbene from natural sources such as grapes, peanuts and blueberries.

Intellectual property

In the UK, the Intellectual Property Office (IPO) is the official regulatory body responsible for intellectual property rights (Intellectual Property Office, 2022). The benefits of this include maintaining market share and position.

On average, it takes up to five years for a patent to be granted, according to patent attorney Dr. Sara Holland. To successfully acquire a patent, Symemco Therapeutics endeavours to develop

an inventive product, per IPO guidelines, and will ensure that work we intend to patent will be out of the public domain.

We decided it is best to patent our biosynthesis pathway, which uses an inhibition system to increase Malonyl-coA, as well as the four modified enzymes that we are using within our biosynthesis pathway - vVROMT, RGTAL, vVSTS and AT4CL- as they are not patented to produce pterostilbene. We aim to have five patents, with four of them being the individual enzymes within the pathway and one being the synthesis pathway as a whole, which will all fall under the category of a utility patent.

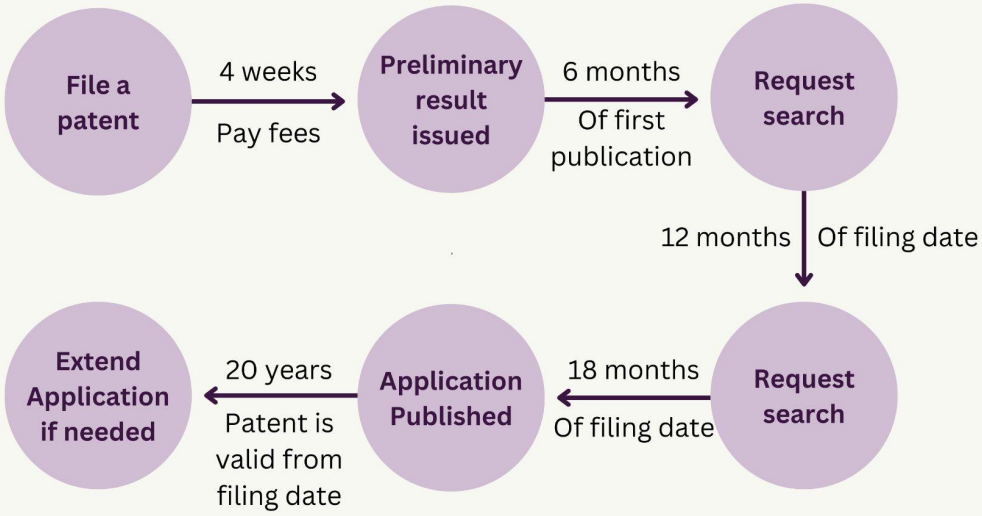

Figure 2. A timeline of the patenting process from filing the patent until receiving the patent.

In our discussion with Dr. Sara Holland, she noted that within 12 months of filing our patent we may request, through the Patent Cooperation Treaty, international patents to the countries we see fit to benefit our business. Following this, there is a 30 month period where it is prohibited to file an international patent for our invention. Thus, we aim to file within 12 months of filing our UK patent.

Due to the nature of iGEM being open source, filing for a patent is not achievable within our iGEM timeline, as information about our product is public domain. Once the competition concludes after October 2022, we aspire to file our patents.

Patent Licensing of our Pterostilbene Producing *E. Coli*

Intellectual property that is licensed may be used to develop another company's business or product in return for a fee. (Kerr and Melvin, 2020)

Third-parties that use our licensed patents are usually done (Kerr and Melvin, 2020):

- In accordance with the rights granted
- In a set time frame
- In exchange for royalties
- Subject to confidentiality clauses

Distributors, such as McKesson in the USA and Arrowedge Ltd., in the UK are examples of companies that Symemco Therapeutics would aim to licence their innovation to. Our company desires to engage with these organisations at national and international conferences and entrepreneurial events, to gain publicity and raise interest in the use of our product. It is important as the distributors named are some of the largest, highest-quality, and most influential distributors of pharmaceuticals in the country.

Within the future goals of Symemco Therapeutics, we aim to establish our product globally. Obtaining a licenced patent of our pterostilbene producing *E. Coli* would allow us to manufacture and distribute our product on an international scale, potentially via third-parties to attain greater revenue and benefit more patients.

Licensing strategy

A licence agreement is a contract that is negotiated and agreed upon between two parties in which the licensee is able to use the intellectual property owned by the licensor (Murray, 2021).

Common agreement conditions include (Murray, 2021):

1. Exclusivity (regions in which the product can be sold and duration limit).
2. Payments (royalties).
3. Subsidiary Licensing (if the licensee can or can not allow someone else to sell or use the product).
4. Limitations (number of sales).
5. Sub-agreements (disclosure and confidentiality).

Using a licensing agreement and implementing our licensing strategy means we would be able to manufacture and distribute our pterostilbene producing *E. Coli* through companies under

agreed conditions. This can increase our revenue by receiving royalties as well as help us expand by agreeing upon which regions our product can be sold and/or distributed.

Market analysis

A comprehensive market analysis was completed to develop a full understanding of the current market and its projected trajectory, and how Symemco Therapeutics would fit into this. We have analysed our company's own strengths and weaknesses through a SWOT analysis before conducting more analysis of the market we intend to enter using the techniques PESTLE analysis and Porter's five forces.

SWOT analysis

In Table 2, we have investigated the internal (strength and weaknesses) and external factors (threats and opportunities) that impact Symemco Therapeutics through the SWOT analysis method. From this analysis, we have developed strategies to address any weaknesses and threats, and apply our strengths and opportunities.

Table 2. A SWOT analysis and strategy summary of Symemco Therapeutics.

	Strengths	**Weaknesses**
	1. Easy to source equipment and *E. coli*. 2. Targeting AD neuroinflammation (as opposed to Aβ-plaques) as it was found to play an extremely important role in AD pathogenesis (Liu, Wang, Sun, andPeng, 2022). 3. Lack of direct competitors. 4. Reduced drug-drug interaction as pterostilbene is a natural compound. 5. Novel therapeutic (converting a supplement into a therapeutic and new AD therapeutic target). 6. Strong academic and technical support network. 7. Our company will only have	1. AD pathophysiology is under research. 2. The project is still at its early development. 3. Lack of cash flow. 4. Long financial recovery due to high R&D costs. 5. We are entering the biotechnology market which is highly volatile.

	rights to our intellectual property.	
Opportunity 1. Symemco Therapeutics can expand to treating other neurodegenerative diseases. 2. Pterostilbene could be used to target multiple diseases. 3. No drugs on the market targeting neuroinflammation in mild to moderate AD.	SO strategy - Symemco Therapeutics plans to diversify our product through exploring different diseases that pterostilbene has the potential to target. As there is no current market for pterostilbene therapeutics, we face a lack of direct competitors. Therefore, this creates the opportunity for Symemeco therapeutics to enter a new market. The potential growth associated with this would facilitate the research and development (RandD) costs of our therapeutic, and increase our company recognition to make our product more accessible.	WO strategy - By partnering up with suppliers and locally producing our product, we aim to reduce distribution costs and increase the scope of buyers through these partnerships. This will allow our product to reach the market faster. Through building a team of experts in the field at Symemco Therapeutics, we hope to continually research AD pathophysiology to tailor our development strategy to ensure reliable data is produced from clinical trials.
Threats 1. Healthcare acceptance of our drug entering the market. 2. Stigma around using GMOs in therapeutics. 3. Our cost could initially not be as competitive as other AD drug companies. 4. Emerging drugs from clinical trials treating neuroinflammation in AD.	ST strategy - Symemco Therapeutics will utilise the potential of pterostilbene to develop treatments for a range of diseases such as Parkinson's Disease and other neurodegenerative diseases such as dementia, cardiovascular diseases, cancer and inflammation. In later stages of the company, we hope to become an independent manufacturing and wholesaler company. By directly supplying to consumers, the price of the product will decrease, benefiting our consumers and increasing the scope of accessibility of our product.	WT strategy - Symemco plans to destigmatize GMOs by creating awareness about GMO's and their benefits. This will not only help us in market competition, but it will also allow consumers to be more engaged without products. We will also adhere to strict clinical trial requirements to ensure our company remains reputable. Through the novelty and uniqueness of our product, we aim to emphasise this to gain investors to assist in our RandD costs and overall cash flow.

Pestle analysis

After completion of the SWOT analysis, we decided to research the external environment that surrounds Symemco Therapeutics. We chose to utilise the PESTLE analysis tool that considers a range of aspects (political, economic, societal, technological, legal and environmental) that

need to be tracked to get a widespread view of the market we are planning to launch our therapeutic into. Table 3 below shows the PESTLE analysis, where each of the six components are explored.

Table 3. PESTLE analysis of the current environment surrounding Symemco Therapeutics.

Political	● The UK has been heavily focused on public healthcare quality and funding, especially recently due to the effects of COVID-19. Steps are being taken to address the current problems surrounding the NHS, including staffing and improving the quality of patient care, particularly due to pressures of a growing and ageing population (National Health Service, 2020). ● Due to the rise in inflation, NHS workers are demanding higher pay which will cost the NHS millions (Seddon, 2022). Inadequate funding of the NHS raises issues of where funds will be prioritised to. ● The financial pressures faced by the NHS raise fears its operation methods are outdated and calls for privatisation have been made. This is something that is continually debated with pros and cons for both sides. Privatisation has been accelerated during COVID-19, with the government outsourcing to private firms such as Serco and Capita for key roles during this period (Wrigley, 2020). ● With a political stability index of 0.47, against a world average of -0.07, the UK can be considered a politically stable country (The Global Economy, 2020). ● Biotech companies normally pay corporate income tax and other business taxes, and tax associated with employees (Stern and Setser, 2020) , however, there is a VAT zero rate for drugs and medicines issued by an appropriate practitioner (UK Government, 2020).
Economic	● The impact of the Ukraine invasion is expected to slow the economic growth of the UK despite the growth post-pandemic and the implementation of the 'Living with COVID' plan (PWC, 2022). ● The UK is currently facing inflation with rates estimated to reach 11% by the end of 2022 - the highest it's been in 40 years (Gooding, 2022). However it's then predicted to fall to 4% percent in 2023, and then 1.5% in 2024' (Clark, 2022). ● In the 12 months leading up to June 2022, consumer price index (CPI) rose by 9.4%, increasing from 9.1% in May (Gooding, 2022). ● AD and other forms of dementia can pose extreme economical strain on the UK healthcare system, costing the UK £34.7 billion a year (Alzheimer's Society, 2020) ● Similarly to 2020, the share of GDP allocated to healthcare expenditure was 11.9% in 2021. The total healthcare expenditure in 2021 was

	estimated at £227 billion, this includes government and non-government spending. This is largely due to the growth in services created as a result of the pandemic (Cooper, 2022). ● Alzheimer's is severely underfunded in comparison to cancer, heart disease, HIV/AIDS and even COVID-19 (Weaver, 2021), however, there are a range of organisations that raise money for AD funding including Alzhiemr's DIsease Association which raises $3.1 billion annually (Alzheimer's Association, 2020).
Social	● Approximately 55 million people have dementia, with over 60% living in low- and middle-income countries (World Health Organisation, 2021). ● In the UK in 2019, there were over 850,000 people with dementia (Alzheimer's Society, 2020). ● Outcome of Alzheimer's Disease affects more than just the patient. Family members and care takers often experience extreme feelings of stress (Grabher, 2018). ● Direct consumer advertising links more strongly to older patients, exposing them to our product (Feldman, 2021).
Technological	● There have been global advancements in using artificial intelligence but there is still an ongoing demand in the AD sector for technology including diagnostics, treatment and intelligent assistive technology for AD patients (Dahlke and Ory, 2020). ● Organ-on-aChip (OoC) is rapidly advancing and is becoming an alternative to animal testing (Ma, Peng, Li, andChen, 2021).
Environmental	● The UK manufacturing is moving towards a lower carbon footprint (with the automotive manufacturing footprint falling its lowest). ● The UK published a 25 year-strategy in which it passed a domestic law for net zero greenhouse gas emissions by 2050 (UK Government, 2021). ● In the 25 year plan, the UK government aims to achieve clean air by good industrial practices and establishing a strict regulatory framework (Department for Environment Food and Rural Affairs, 2021).
Legal	● The Intellectual Property Office is the official UK body responsible for intellectual property rights. ● UK Research and Innovation (UKRI) acts as a framework for good management in trials of medicines for human use which is in place (The Medical Research Council, 2022). ● Associations such as the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) exist that represent pharmaceutical companies around the world to allow for the effective and efficient flow of our products across the globe (International Federation of

	Pharmaceutical Manufacturers and Associations, 2022).

From this PESTLE analysis, we identified that due to the COVID-19 pandemic, the UK healthcare has emphasised improving the quality of healthcare in the country. However, due to the current inflation being experienced in the UK, the NHS will have to pay more for healthcare and staff, putting less money in the improvement in healthcare, resulting in greater underfunding for healthcare catered towards dementia. As a consequence of this, families and caregivers are facing extreme financial strains to provide support and care for patients living with AD because of elevated costs. This does not only pose a strain on families and caregivers, but also on the UK government to spend more money on dementia care, an underfunded sector in healthcare. Thus, focusing on targeting the sector of AD therapeutics can relieve economic burden on healthcare providers, as well as patients' family members and caregivers, and satisfy high demand for a preventative therapeutic for AD.

Porter's five forces analysis

To further develop our marketing analysis, we used Porter's five forces to identify five competitive areas surrounding our company. These were also used to refine the strengths and weaknesses considered in our SWOT analysis. The five forces analysed by this method are: threat of new entrants; threat of substitutes; bargaining power of buyers; bargaining power of suppliers; rivalry among existing competitors.

Table 4. Porter's Five Forces analysis of the market environment surrounding Symemco Therapeutics

Porter's Force	**Force Description**	**Force components**
Threat of new entrants	*The threat imposed on Symemco Therapeutics by new competitors in the same market.*	**Market accessibility:** From drug discovery to market, it takes 10 years on average with clinical trials taking 6-7 years of this time (Pharmaceutical Research and Manufacturers of America, 2015). On average, it costs between £825 million to £1.12 billion to bring a drug to market (Wouters, 2020). Subsequently, market accessibility can be difficult without proper research and sufficient funds. This means that any competitor looking to enter the same market as us will have to follow the same process which can limit some companies if they fail to pass certain stages in the drug development pipeline.

		Barriers to entry: High R&D costs can limit a company's ability to penetrate the market, with limited investors it is likely funds will not be met in order to pass this stage. Moreover, all new drugs must be approved by regulatory bodies, which can differ depending on location. This can mean different things depending on the body responsible. In the UK, the MHRA is the relevant regulatory body responsible for approving therapeutic drugs, in the US it is the Food and Drug The Administration (FDA). At Symemco Therapeutics, we aim to produce high yields of pterostilbene through our optimised manufacturing processes as this is more cost efficient than manufacturing low quantities. This also acts as a barrier of entry for new entrants to the market who will have to match the quantity we already supply, in order to achieve the same cost advantage of us. Very strict government policies surrounding health and safety of drugs exist. For a drug to be approved it has to show substantial safety and efficacy at phase 3 clinical trials (Food and Drug Administration, 2021). These include the FDA in the US and the MHRA in the UK. FDA takes 6-10 months for approval (Food and Drug Administration, 2022) and MHRA takes around 5 months (Medicines and Healthcare products Regulatory Agency, 2020). A new entrant will have to comply with all regulations and policies which can further act as a barrier to entry.
		Access to distribution channels We aim to build strong networks with our distribution channels which can disrupt the process of a new entrant coming to the market as they would be competing with us as an already established relationship. We aim to do this to increase the costs of a new entrant using the same distribution channels.
		Switching costs In order for a new entrant to the market to directly compete with us for our customers, a low switching cost will have to be sought. Alternatively, a significant advantage over our therapeutic will need to outweigh the associated costs with switching suppliers of the AD therapeutic.
Threat of substitutes	*The threat that occurs*	**Number of substitute products available** There are currently 126 agents in the Alzheimer's disease (AD) clinical

	when other companies start producing substitute products or services in the same market.	trial pipeline, with 82.5% intending to be disease-modifying (Cummings et al., 2021). There are therapies directed toward tau proteins, inflammation, synaptic plasticity, and vasculature, now in phase 2 clinical trials (Tan, 2022). In the last three years, four molecules have shown significant effects on clinical endpoints in phase II or III clinical trials (i.e., slowing of cognitive decline). Among these four molecules, three are anti-amyloid immunotherapies: aducanumab, donanemab, and lecanemab, responsible for a significant clearance of cerebral beta-amyloid deposits (Villain, 2022). However, Biogen withdrew its marketing authorisation application for the FDA approved aducanumab drug (Alzheimer's Europe, 2022). In conjunction with this, no disease-modifying drugs to treat AD are currently available on the market that specifically target neuroinflammation, so any direct substitute of our therapeutic is unknown at this stage.
		Buyer propensity to substitute We aim to be the sole supplier of our novel therapeutic initially, before our patent expires. This means that buyers will not have the option to choose another supplier, thus cannot consider switching. However, as more drugs become available on the market and our patent expires there will be more suppliers that our buyers could consider switching to. Therefore we must maintain customer loyalty through excellent customer service and reliable supply chains.
		Relative price performance of substitute For drugs to treat symptoms of AD, prices in the UK have a wide range. Per year: Donepezil = £9.12, Memantine = £19.20, Memantine (Alzhok®) = £698.16, Rivastigmine = £564.72, Gatalin XL = £478.80, Galantamine = £889.20 (Burn andWakeling, 2018). Our therapeutic is currently priced at £14,815.27 based on the formula Total Cost/Units. We intend for the novelty and disease-modifying component of our therapeutic, not currently available on the market, to be used to justify the initial cost aforementioned.
Bargaining power of buyers	*The pressures that consumers can put on companies including, increasing*	**Number of customers** In terms of patients as our end consumers, there are over 50 million people with dementia worldwide as of 2020 (Guerchet, M. et al., 2020). This large number of potential customers ensures customer service and product quality are paramount in what we achieve from our therapeutic. Additionally, being a potentially impactful therapeutic for a large number of people increases the pressure of producing a high quality drug that is appropriately priced to be as accessible to as

	product quality, decreasing product costs and improving customer services.	many of these people as possible.
		Differences between competitors Once our therapeutic is on the market and other companies are also able to offer similar disease-modifying AD therapeutics, we aim to maintain a high standard of quality and optimum product price to ensure healthcare providers continue to purchase our therapeutic. We also intend for our continued research and development investments into AD therapeutics will ensure our product is one of the best options available for patients.
		Price sensitivity Price is influenced by the overall market state or market state within the area of disease market (Mattingly, 2012). Gross (net) margins average are 71% (26%) for manufacturers, 22% (3%) for insurers, 20% (4%) for pharmacies, 6% (2%) for pharmacy benefit managers and 4% (0.5%) for wholesalers (Sood et al., 2017). We strive to ensure we are up to date with market trends to ensure our pricing is competitive for our consumers. Additionally, as we intend to market to the NHS, we need to ensure we are sensibly pricing our therapeutic. If regulatory bodies deem our therapeutic is overpriced they can disapprove of the drug and also advise the NHS against purchasing our therapeutic completely, this is something we should try to avoid.
		Buyer's ability to substitute Currently, there are no other disease-modifying AD therapeutic on the market so buyer's availability to substitute is low. However, as progress is made within the AD field, more disease modifying therapeutics will begin the drug development pipeline. Furthermore, compounds already in the process can gain approval before or around the same time as we intend to get our drug approved. This means there are more substitutes available, however we are unaware of the exact numbers so will have to presume and plan based on the assumption that substitutes will be available to the buyer by the time we enter the market.
Bargaining power of suppliers	*The pressure created by suppliers, which comes in the form of reduced quality,*	**Number and size of suppliers** There are hundreds of suppliers of laboratory materials and equipment in the UK alone. One supplier, Sigma Alrich, is a large global company that provides chemicals for laboratory use, and are dominant in their market. Larger suppliers generally have better stock and more investment into their products and staffing which could affect the product quality and delivery, however smaller suppliers may

	reduced availability of their product or service and increased prices.	hold a competitive advantage through partnerships. This is all something to consider when choosing suppliers of our raw materials in the future.
		Uniqueness of each suppliers product If a supplier has a monopoly of a particular product then they are able to fluctuate prices to their own accord due to their customers being unable to source the product from an alternative supplier. Therefore, we aim to use products that are less unique, keeping raw material costs to a minimum as pricing has to be more competitive within a larger competitive field.
		Availability of substitutes for the supplier's products High availability of a particular product means that supply is good, and as long as supply is in surplus of demand, prices tend to be kept to a minimum and different suppliers are more competitive. However, as demand exceeds supply, prices increase along with the bargaining power of suppliers. As a company, we intend to source materials that are reliably available and of good quality and will continually explore options with regards to which supplier can offer the highest quality product for the best cost.
Rivalry among existing competitors	*The competition that currently exists in the market Symemco Therapeutics intends to enter.*	**Number of competitors** There were approximately 670 pharmaceutical companies in the UK as of 2019 (Statista Research Department, 2021). These are potential competitors as they target the same end-users, supplying symptomatic AD drugs to healthcare providers in the UK. Globally, the neurodegenerative therapeutics and biotechnology market is dominated by the following companies: Biogen, Pfizer, Novartis, Sarnoff Corp.,Tera Pharmaceutical, UCB, Hoffmann-La Roche Ltd, Acadia Pharmaceuticals Inc., Lundbeck A/S and Boehringer Ingelheim International GmbH (The Business Research Company, 2021).
		Diversity of competitors Our competitors come from a range of industries: pharmaceutical companies, biotech companies, Alzheimer's disease research companies and neurodegeneration research companies all with the shared goal of treating AD. Although there are many companies working towards the shared goal of an AD therapeutic there are many pathways and potential areas of interest that are being targeted by

		each company. These competitors are also globally active, with currently 180 countries/territories contributing to AD research (Dong et al., 2019). This means that there is an opportunity for us to form partnerships with competitors, sharing a common goal, but having different approaches and knowledge can benefit the AD market as a whole. Specifically, we have already considered a partnership with a diagnostics company, BetaSense to provide a complete diagnostics and treatment plan for AD patients.
		Industry concentration The UK pharmaceutical markets top 5 companies and their market shares in 2018 are as follows: Pfizer (8.2%), Novartis (6%), GSK (5.3%), Merck andCo (5.2%) and Bayer (4.6%) (Mikulic, 2020). The five firm concentration for this industry is 29.3%; a low concentration and competitive. AD therapeutics hold approximately 2.4% of the global therapeutics market, and the drug, Donepezil, is leading the market with a global market share of 68.4% in 2021, according to Future Market Insights (2022). Bringing a novel disease-modifying therapeutic, we aim to join these top companies and our unique selling point provides us with a competitive edge to do so.
		Industry growth Alzheimer's therapeutic sales have expanded at a CAGR (compound annual growth rate) of 6.5% between 2017 and 2021. This is due to an increase in use of drugs such as Donepezil and increased use of biomarkers in AD diagnosis. Between the years of 2022 to 2032, the industry growth is expected to expand at a CAGR of 9.3% (Future Market Insights, 2022). With the current need of a disease modifying drug for AD, there is competition within firms trying to be the first to emerge in this area. After the FDA approval of Aducanumbab, Biogen's stock price increased by 38.8% within the day, and other companies have seen similar trends (Brennan, 2022). This has shown to investors and the general public alike that there is demand for a new treatment. We hope this industry growth will aid in our journey to seek funding and commercialise our therapeutic.
		Brand loyalty Within most markets, consumers prefer to buy known brands over cheaper alternatives of a similar quality. This is no different in the pharmaceutical industry even though regulations ensure generic products are medically equivalent to the branded product. It is essential that we complete and market our novel therapeutic before our patent expires so that we can be the initial sole suppliers of our

		therapeutic and gain this brand loyalty.
		Barriers to exit Due to the high fixed cost of pharmaceutical manufacturing contractors, government regulations, strategic interrelationships and having a specialised workforce, there are barriers to exit the biotech sector. Therefore, there is continued investment in research and a lack of businesses leaving the industry before reaching profit making stages. We understand that these high fixed costs will mean profits from our therapeutic will likely not show until years down the development pipeline, therefore is it vital we have additional revenue streams to support the funding leading up to marketing the drug and continuing once the drug is on the market.
		Switching costs High switching costs prevent customers moving to another brand. Within the pharmaceutical industry, end users tend to stick with a brand they have used before (brand loyalty) and pay a premium. According to Janssen 2020, patients are 17.75% more likely to pay premium for painkillers and 12.35% more likely to pay premium for antibiotics if they consumed the identical product in the previous month in the Swedish prescription drug market. We envision similar trends will still be in place when our drug comes to the market so aim to be the first company to bring the drug to the market to gain brand loyalty and keep customers loyal, thus switching costs should only pay a small role in maintaining customers.

Competition

The application of pterostilbene as a therapeutic to target the NLRP3/caspase-1 inflammatory pathway associated with AD progression is currently not available on the global market and, within the UK specifically, there are no clinically approved drugs that target neuroinflammation. We hope to fill this gap in Alzheimer's therapeutics by focussing on disease modifying medication.

All of the competitors in the table below that supply approved AD medicines for the UK market are well established companies, and the current medications used by healthcare providers have been around for a long time. However there is limited progression and development of new AD therapeutics that target the neuroinflammation and stagnate the progression of AD in

patients with mild AD. The last approved AD therapeutic in the UK was memantine in 2002 (Alzheimer's Society, 2021). Eisai and Biogen are companies that are currently working and in clinical trials for a drug similar to ours, under the disease modifying biologic class, targeting amyloid beta plaques associated with AD.

In addition to current AD therapeutics we have to consider other manufacturers and/or suppliers of pterostilbene. This includes Merck and Sigma Aldrich who are leaders in the supply of compounds for a range of scientific purposes. They directly compete with our production of pterostilbene, however there is also the opportunity for partnership as reputable suppliers to many health care providers.

Table 5. Some of Symemco Therapeutics competitors, how they compare to us and the potential for partnership

Type of Competitor	**Name**	**Analysis**	**Benefits**	**Limitations**
Direct - AD therapeutic	Eisai Ltd/ Biogen Inc	➢ On May 10 2022, Eisai completed the rolling submission to the US FDA of a Biologics licence Application (BLA) under the accelerated approval pathway for the investigational anti-amyloid beta protofibril antibody, Lecanemab. ➢ Lecanemab targets early Alzheimer's in patients with confirmed presence of amyloid pathology in the brain, treating mild cognitive impairment (MCI). ➢ Current stage is Phase 3 confirmatory Clarity AD clinical trials involving 1795 patients and is estimated to conclude in	➢ A partnership with Eisai could lead to shared knowledge and resources surrounding development of a disease modifying AD therapeutic, enhancing the scientific research being conducted.	➢ Limitations include the controversy surrounding the original AD therapeutic named Aducanumab due to its accelerated approval by the FDA (Reuters, 2022).

		fall 2022. This trial will verify the clinical benefit according to the FDA. Following the results of this trial, Eisai may be able to submit for full approval of Lecanemab to the FDA during fiscal 2022.		
Direct - Therapeutics supplier	Sigma pharmaceuticals Plc	➢ Suppliers of galantamine to the NHS. Sold as Reminyl XL 8mg capsules for oral administration since 31 October 2008 (National Health Service, 2015). This capsule is an acetylcholine inhibitor that works by enhancing the intrinsic action. ➢ This company also supplies the NHS with memantine 10mg/ml oral solution (sugar free). This is a glutamate receptor antagonist, reducing the amount of glutamate in the brain, that is used to treat the symptoms of dementia in Alzheimer's disease. This medicine helps the symptoms that affect thinking, such as memory loss and confusion. (Michael Stewart, 2022)	➢ They have direct trading relationships with suppliers including GSK, Pfizer, Reckitt Benckiser and Bauer Healthcare (Sigma, 2022). ➢ We can propose a potential partnership when our product has been patented to establish a distribution service to pharmacies and the NHS within the UK as well as expanding globally.	➢ It is one of the biggest independent pharmacy wholesalers in the UK. It has been established for over 35 years and also has globalised through its export service therefore it may be difficult to partner with them as a startup.
Indirect -Producer of	Agroceutical	➢ Grows daffodils - the natural derivative of	➢ There is potential to partner up to	➢ A direct manufacturing

natural derivative of galantamine	Products	galantamine - in the black mountains. The high altitude is responsible for the high yields of galantamine in the daffodils compared to elsewhere. This company provided the daffodils to pharmaceutical companies to be crystallised and formed into prescription tablets/capsules. (Pharmaceutical Technology, 2019)	manufacture and distribute our product within the UK as they are manufacturing and distributing a compound from a natural product on a large scale, similarly to ourselves.	competitor as they produce a high yield of a different drug for AD treatment. ➢ A limitation they have results from their product being farmed, conditions throughout the year tend to affect the yield and space is a limiting factor and not something that can exponentially increase.
Direct - Therapeutics supplier	Rosemont Pharmaceuticals	➢ This company is a supplier of many AD therapeutics, specialising in oral solutions for ease of administration on elderly, stroke and dementia patients. ➢ They provide oral solutions of memantine hydrochloride, rivastigmine rosemont, donepezil hydrochloride and galantamine, all of the currently available treatments for AD patients.	➢ Partnering with Rosemont Pharmaceuticals opens up the opportunity for varying formulas of our pterostilbene to be produced, aligning with our goals to increase the accessibility of our therapeutic to suit a range of needs.	

Direct - manufacturer and supplier	Merck/Sigma Aldrich	➢ You can currently purchase a solid 10mg version of pterostilbene from this company, it costs £222.00 (Merck, 2022), however this is not a therapeutic, simply the compound.	➢ Partnering with a global supplier like this can increase the distribution of our product and expand past being a UK distributor. ➢ Their customer base is worldwide with offices in 53 countries and regions. ➢ They are a well established company with a well regarded reputation, they supply many compounds in a range of different quantities and states	➢ They are a well established company with a well regarded reputation, they supply many compounds in a range of different quantities and states.

Partnership

As part of our considerations of a long term development plan we have investigated the possibility of forming partnerships which is required for the expansion and development of Symemco Therapeutics. We reached out to BIOINX®, a company focused on commercialising materials and bioinks for 3D bioprinting and biofabrication. Part of the range of products they offer include the inks required for building a blood brain barrier (BBB), of which they considered supplying to us. This is something that is vital to the research and development of our therapeutic and could be applied to other therapeutics developments in the future. In return we would sell the model of the BBB, an additional revenue stream for ourselves with a proportion of the profits going to BIOINX®. We hope the partnership would increase the customer base for both businesses as we merge therapeutics with biomaterials.

Strategies and plans

To develop a range of strategies needed for Symemco Therapeutic to successfully take its next steps, we divided the project to analyse components individually. This section covers our 7Ps of marketing, our marketing strategy, regulatory approval body plan, product classification, route to market strategy and supply chain plan.

7 P's

The 7 P's of marketing is a model that allows us to identify and define key issues which could affect the marketing of our product. Identifying and finding solutions to these key issues allows us to smoothly market our product. Below are the 7P's of Symemco Therapeutics.

Product

Our product, pterostilbene, is used to stagnate the progression of mild to moderate AD through targeting the NLRP3/caspase-1 pathway associated with neurodegeneration. Pterostilbene allows the exacerbation of Aβ-plaque deposition and reduces phagocytic activity of microglia. As a result, neuroinflammation is a promising target for AD, which our therapeutic aims to down-regulate.

An advantage of our product is that pterostilbene has limited drug-drug interactions, making it safe for individuals to take who are also on other medications. Moreover, our therapeutic is disease-modifying by targeting the neuroinflammation pathway on contrats to current AD therapeutics on the market which relieve symptoms of the disease, which is a novel aspect of our therapeutic. These key factors combined give our company a competitive advantage and contribute to our company's vision.

Price

After a patent is approved and clinical trials are complete, the price of our product will heavily depend on the funding and sponsorship we receive. Our product's price is determined by taking into account research and development and the funding we require to reach a profitable and sustainable stage of our business.

As outlined in our cost analysis, the cost of our treatment per unit will equal to £14,815.27 initially, in which we will be able to reduce costs once our business is profitable and have formed partnerships to help expand and diversify our company.

Promotion

We aim to sell our product to wholesale suppliers to begin with to reach healthcare providers within the UK, private and public, such as the NHS to implement our therapeutic within the

healthcare system. In order to reach the NHS, we aim to target the NHS Hospital Trust such as such as St. George's University Hospital London which has a leading cognitive neurology and dementia department and Imperial College Healthcare NHS Trust which has a specialist dementia care team, and then expand to the rest of the trusts such as the Community Health Trust. NICE assesses the cost of the drug in which there are negotiations of price with the NHS and a decision is made by NICE if the NHS should pay for the drug or not. Once agreed upon, the drugs should be available by the NHS within three months of NICE's funding (Collins, 2020). To establish our company to reach such healthcare providers, we are planning on networking by joining multiple entrepreneurial events across the UK and Europe, allowing us to present our therapeutic and introduce our brand to members of pharmaceutical companies and healthcare providers such as doctors. Additionally, we aim to join neurodegenerative related conferences where we could network with medical providers and biotechnology companies. The AAIC (Alzheimer's Association International Conference) has established its conference dates for 2023, April 17-20. We intend to explore joining related conferences that will provide us with the opportunity to network in medical and biotech sectors above the scope of the UK.

It is important to consider patients' perceptions of our product. There is a negative connotation to using GMOs as therapeutic means, especially within AD treatments. Investing in spreading awareness about the safety and benefits of GMOs will destigmatize the use of GMOs in therapeutics and providing the relevant information regarding the mechanisms and efficacy will ensure healthcare providers and patients are well informed about the product. We would implement this through handing out leaflets and brochures, and spreading awareness online through sponsoring advertisements on social media applications.

Place

We aim to initially target the UK, due to the main healthcare provider, NHS, being free at point of use, so we can reach a larger portion of the UK population that is not restricted by their ability to pay for healthcare. This makes our product more accessible to everyone in the UK, not just for those who are able to afford healthcare. As a prescription based medication, some costs will be involved, however with our target market being aged over 65, on the NHS, prescriptions for anyone over 60 are free, therefore this is at no cost to the patient directly. Despite the ageing population being a global issue, the strain on the NHS and health and social care services within the UK highlights the need for solutions that are local before spreading globally. Therefore, in the future, we aim to branch out to the rest of Europe and USA initially to target the ageing population within those regions.

In addition, to make our product increasingly accessible to patients, we plan to have our product available on our website (not for purchasing) where users can interact with our product virtually, learning and understanding the mechanism of our therapy and its purpose. This can help us reach healthcare professionals, patients and their family members without the need for multiple visits to hospitals and pharmacies.

Packaging/Physical appearance

Our goal is to use sustainable packaging made from recycled cardboard, making it more environmentally friendly and easier to recycle. Moreover, we intend on implementing an easy and comfortable route of administration to ensure customer ease. As part of initiative for inclusivity, we aim to make our packaging by using our company colours that are colour-blind friendly, easy to read fonts as well as emboss the packaging in brail to support patients that are visually impaired.

Process

We plan on supplying our therapy to pharmacies and healthcare providers, of whom will then be responsible for prescribing our drug to the patient. Transportation of our drug is straightforward as the drug does not need to be kept at a particular temperature, mitigating the need for specialised methods of transportation such as temperature controlled appliances. For the pharmacist prescribing our drug, we aim to make this process easier; our estimated expected shelf life of 2 years ensures our product is safe and effective for an extended period so that regularity of having to dispense the drug to patients is limited. During the process of supplying and dispensing our drug, IT support will be available to contact regarding any questions or concerns that pharmacies or healthcare professionals may have. Guidance on administration will be given out by our recommendation as well as reviewed by NICE, guiding the healthcare professionals within the UK of the recommended dosage, side effects, and information relevant to the drug.

For patients themselves, questions regarding the drug can be answered by their doctor or through our online feedback system which can be found on our website. Once the drug is prescribed, patients are able to report back to their doctor of progress and side effects, like with any prescription medication and we will maintain regular contact with medical professionals so that we are able to make alterations where necessary and improve our product for future use based on the user feedback. Overall this process will ensure we are delivering a high quality product with the patient's interests at the forefront of our development.

People

We plan on partnering up with pharmaceutical companies in various locations worldwide in order to distribute our product internationally at a low-cost. Moreover, partnering with diverse companies allows for increased brand recognition globally, resulting in increased production and greater sales due to the accessibility of our product.

Having spoken to BIOINX®, a bioprinting company based in Belgium, they suggested a future partnership in which they would supply a 3D printed blood brain barrier (BBB). This would allow us to test how permeable the BBB is to our therapeutics, further helping our proof of concept. Through our meeting with the Head of Finances at BetaSense, they were open to a partnership allowing our AD treatment at Symemco therapeutics to be used in conjunction with their AD diagnostic tool to provide a multi-faceted improvement for AD patients.

Through our research, we have found companies that could pose as a potential partnership such as Agroceutical Products in which we can partner up with them in terms of manufacturing and distributing our product nation wide and to the NHS. Pharmaceutical companies that supply AD therapeutics to the NHS such as Sigma Pharmaceuticals can be a potential partnership to distribute and sell our therapeutic to the NHS and possibly expand to a global level beyond the NHS healthcare system.

Market entry strategy

Before entering the Alzheimer's Disease therapeutics market, we aim to form partnerships and network with healthcare providers, namely the NHS. This will allow us to consult clinicians before deciding to bring our therapeutics onto the market, and aid us in understanding the perspective of clinicians on how we should market and sell our drug.

To aid our R&D clinical trials process, we aim to form partnerships with companies such as GSK. This can give us the opportunity to form further partnerships to distribute and market our product not only on a national scale, but globally. In exchange, we can offer competitive pricing of our therapeutic or potentially exchange shares in the company, of which details would have to be discussed. Moreover, partnerships with bigger companies can aid with financial costs involved in drug development as well as provide us with their expertise and guidance regarding regulatory approval in other countries when we plan to expand globally.

After completing our clinical trials successfully, we aim to launch our product to hospitals around the UK, supplying to the NHS, after regulatory body approval. Marketing and selling our product to a few NHS trusts that specialise in dementia, such as St. George's University Hospital London that has a strong cognitive neurology and dementia department and Imperial College Healthcare NHS Trust which has a leading dementia care team**,** and then expanding to the rest giving us the advantage of establishing our company and product whilst gaining a deeper understanding of our drug on the market before expanding globally. After establishing our product within UK hospitals, this can give us the funding and foundation needed to shift our focus onto distribution and marketing on a wider scale.

Having relative ease in obtaining patents, we will establish joint ventures with other companies to enter the international market (primarily focusing on the EU and US). Ideally, these companies have experience with the regulatory landscape, making them able to assist with the development of our product for alternative markets. Additionally, these companies may have manufacturing and distribution facilities that can be used to produce our therapeutic on a larger scale to supply the global demand.

Regulatory approval plan

In order to have our drug be distributed globally, we need to obtain approval of the regulatory bodies of the countries we plan to sell in. Within our 10 year timeline, we hope to be established in the UK, where we need MHRA approval, the USA, where we need FDA approval, and Europe, where we need European Commission approval.

MHRA (UK)

As of 2021, there are two procedures after the completion and assessment of clinical trials (Multiple Sclerosis Trust, 2021).

1. Licensing
    - 150-day assessment to grant marketing authorisation within the UK, Great Britain and Northern Ireland (Medicines and Healthcare products Regulatory Agency, 2020)
2. NICE Appraisal
    - Assess the clinical and cost effectiveness of the drug
    - Provides guidance of use to the NHS
    - Determines whether the drug should be used by the NHS
    - Full process takes a minimum of 43 weeks

Fast-track of marketing authorisation is possible if the drug has compelling evidence that benefits a public health emergency or there is a shortage of a vital drug that has been verified by the Department of Health and Social Care.

FDA (USA)

According to the FDA guidelines, our drug can be fast-tracked for approval due to the unmet needs for serious conditions in which Alzheimer's Disease falls under (American Academy of Neurology, 2022). The same source states there are four criterias that must be met in order for our drug to be fast-tracked if there are available therapies:

1. Show superior efficacy
2. Avoid serious side effects of the available therapy
3. Decrease clinically significant toxicity of an available therapy
4. Address an emerging or anticipated public health need

This scheme allows us to submit our FDA application as soon as our drug is patented giving us the ability to distribute our product at a sooner stage than expected. Moreover, due to the priority of the drug, if there were to be any risks associated within our clinical trials, the reviewers can establish that the benefits justify the risks in order to get the drug to the patient sooner (U.S Food and Drug Administration, 2022).

European Commision (EU)

In Europe, the European Medicines Agency (EMA) is responsible for approval and assessment of new drugs, however, the European Commission (EC) is responsible for the marketing approval of the drug (European Medicines Agency, 2022).

There are 4 different drug approval categories:

1. **Centralised Process**

"The centralized procedure allows manufacturers to submit a single Market Authorization Application (MAA) to the EMA. The CP is useful for manufacturers who are planning to market products in the European Economic Area (EEA) countries Iceland, Liechtenstein and Norway as well as in the EU. The centralized procedure falls under the Regulation (EC) 726/2004 and allows the manufacturers to market the products to the healthcare professional post the approval by the European Commission (EC)." (Freyr, 2022)

2. **Decentralised Process**

“Decentralized procedure (DP) is applicable for medicines which have not yet been authorized in the EU. For these medicines, manufacturers can apply for simultaneous authorization in several EU member states. The procedure falls under the Directive 2004/27/EC. In the DP, any one-member state can take the initiative of evaluating the application.” (Freyr, 2022)

3. **Natural Procedure**

“Medicines which are outside the scope of the centralized procedure or which were authorized before the creation of the EMA fall under the authorization of the national procedure (NP). It is useful for manufacturers who aim to obtain market authorization in specific EU member states. In this procedure, applications are reviewed by the competent authorities of the respective EU member state. Each EU member state has a national procedure of its own.” (Freyr, 2022)

4. **Mutual Recognition Procedure**

“In Mutual Recognition Procedure (MRP), market authorization granted in one EU member state is recognized in other EU member states. MRP is applicable only when the manufacturer has already obtained market authorization in one of the EU countries. The regulations for market authorization through MRP are established in the Directive 2001/83/EC. If an application for MRP is submitted to more than one EU country, it must be ensured that all the applications are identical. The country evaluating the application is called as the Reference Member State and is responsible for notifying the other concerned Member States regarding the status of the application.” (Freyr, 2022)

According to the EMA (2022), drugs that contain active substances to treat neurodegenerative diseases are compulsory to undergo centralised procedures. Once our drug has been approved and we have been authorised by the EC to market and distribute our drug, monitoring of our drug will take place to ensure the safety of the drug once on the market.

Product classification

We aim for our AD therapeutic to be classified as a medicinal product as it is intended to be administered to humans with the intention of modifying the pathophysiology of AD. The different classifications are shown below in Table 6.

Table 6. Definitions of some product classifications relating to our product

Class	Description

Food supplement	This is a substance or group of substances that have been concentrated and marketed in dose form to have a nutritional or physiological effect. This includes nutrients such as vitamins and minerals and the supplement can be in pill, tablet, capsule or liquid form in measured doses. Food supplements are intended to correct nutritional deficiencies, maintain an adequate intake of certain nutrients, or to support specific physiological functions. (European Food Safety Authority, n.d)
Borderline Product	This is a product that might be medical devices, cosmetics, food supplements or biocidal products but is yet to be decided. These products are called borderline products until their status has been confirmed.
Medicinal Product	Any substance or combination of substances presented as having properties for treating or preventing disease in human beings. This includes substances and combinations of substances which may be used in, or administered to, humans, either with the intention of restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action. This also includes any substance of combination that can be used to diagnose a medical condition. (MHRA, 2020)

Route to market

Symemco Therapeutics is currently undergoing lead optimisation in the drug discovery and development stage, and will continue to move forward with other aspects of this stage post iGEM. There is a standard route for all drugs to reach the market due to the strict monitoring surrounding the safety and efficacy of drugs, in which we will follow as seen below in *Figure 3*:

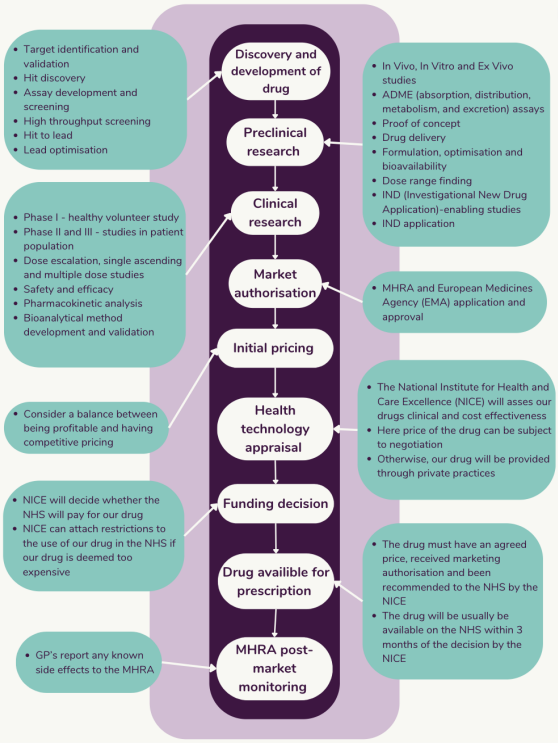

Figure 3. A Diagram showing our route to market inspired by Collins, 2020.

Supply chain

The pharmaceutical supply chain involves people, skills and information systems, regulatory, risk and compliance, transport and logistics is shown below in *Figure 4*:

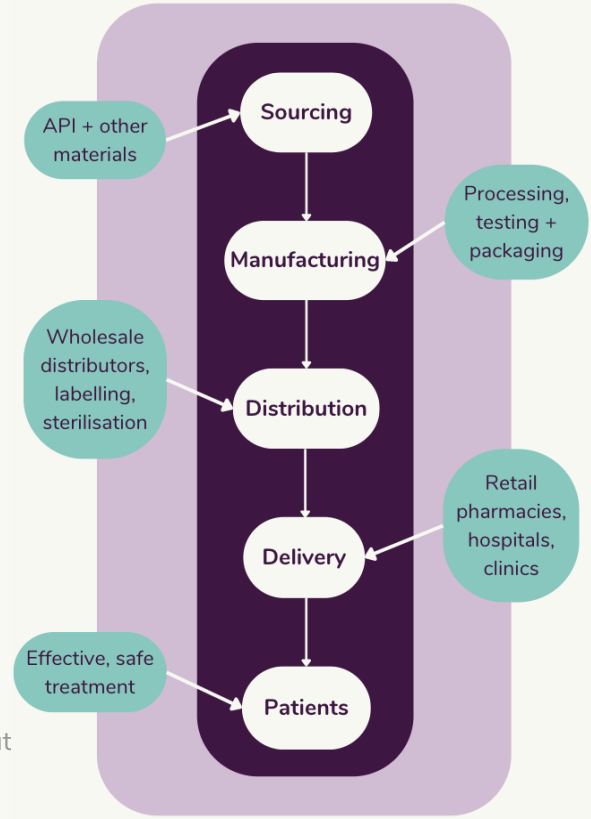

Figure 4. A Diagram showing a Pharmaceutical Supply Chain inspired by Taylor et al.(2020).

Our main aim is ensuring our supply chain continuity as this is critical for safely and effectively delivering medicines to patients, and will do so by creating a strategic and efficient supply chain plan. We will also use predictive analytics to better understand buyer behaviour and other factors that influence demand to help us tailor the production and distribution of our therapy.

1. **The current supply pipeline:**

➢ Sigma pharmaceuticals Plc are suppliers of therapeutics to the NHS. It is one of the biggest independent pharmacy wholesalers in the UK and has been established for over 35 years and also has globalised through its export service. They have direct trading relationships with suppliers including GSK, Pfizer, Reckitt Benckiser and Bauer Healthcare (Sigma PLC, 2022). This would allow us to establish a distribution service to pharmacies and the NHS within the UK as well as expanding globally.

➢ Rosemont Pharmaceuticals is a supplier of many AD therapeutics, specialising in oral solutions for ease of administration on elderly. Partnering with Rosemont opens up the opportunity for varying formulas of our pterostilbene to be produced, aligning with our goals to increase the accessibility of our therapeutic to suit a range of needs

➢ Merck/Sigma Aldrich supply many compounds in a range of different quantities and states. Their customer base is worldwide with offices in 53 countries and regions. Partnering with a global supplier like this can increase the distribution of our product and expand past being a UK distributor.

2. **Quality Assurance (QA) Overview (Petropoulu, 2018)**

➢ “QA is the parameter used to ensure prescribed medicine effectively produces the desired effect on the person taking it”.

➢ Within QA, Pharmaceutical Quality Systems (PQS) consists of parameters to help manufacturers produce a high quality pharmaceutical at levels of regulations ensuring the safety and efficacy of the drug for patients

➢ PQS in pharmaceutical products can also continue into pharmaceutical development to allow innovation and the continual improvement of our drug

➢ PQS includes:

- The pharmaceutical product is designed to meet the need and performance requirement
- The process is designed to consistently meet product critical quality attributes
- Processes, equipment, personnel and deviations are identified and controlled in an appropriate manner
- The whole manufacturing process is constantly monitored and updated to enable consistency in quality over time

3. Supply Needs

➢ Symemco Therapeutics will require the following goods from suppliers:

- L-tyrosine
- Terrific broth medium
- S-adenosylmethionine
- HPLC UV: Stationary phase
- Solutions: NaOH, ethyl acetate, methanol, mobile phases which include formic acid and absolute acetonitrile
- Centrifuge
- Photodiode array detector SPD 20A
- Packaging supplies
- Sterilisation equipment

4. Supply Timeline

➢ We will require regular, monthly deliveries of our perishable supplies in bulk and a single delivery for non-perishable items

➢ These are to be delivered by our local UK suppliers listed above by motor vehicle

5. Government Laws and Regulations

➢ An export licence to be able to export our drug anywhere in the world

➢ A for a drug manufacturer, wholesale dealer and marketing licence

➢ A for a certificate of a pharmaceutical product (unlicenced) to be sent to the MHRA

Reducing risks in our supply chain

Pharmaceutical manufacturers face unique challenges when packaging, containing, and delivering therapies. Drugs have the potential to interact with the packaging, comprising the quality of the drug and could put the patient at risk. To mitigate this, Symemco Therapeutics intends to make packaging and delivery an integral part of our research and development, as opposed to addressing this only just before introducing our drug to market.

We will also require cold storage of our product. Maintaining a secure “cold chain” during storage, handling and transportation of our therapy ensures product quality, but will also keep

our distributors and users in compliance with laws, regulations and guidelines. We will implement electronic data logging monitors to the various transportation and storage environments to maintain the correct temperature range.
We will also ensure we maintain container closure integrity (CCI). We plan to use cyclic olefin polymer (COP) vials which, unlike glass COPs, have tighter dimensional tolerances, allowing for a more consistent product.

Partnering with drug delivery contract manufacturers will offer the most relevant and high quality technology and systems to ensure the integrity of our product. For example, Patheon is one of the leading global contract development and manufacturing companies (CDMO) which could manufacture our therapeutic (Thermo Fisher Scientific, 2021).

A group of pharmaceutical and healthcare companies called Pharmaceutical Supply Chain Initiative (PSCI) would be a partner of interest. Their focus is to "continually improve ethics, labour, health and safety, and environmentally sustainable outcomes...with an aim to advance responsible supply chain practices" (Pharmaceutical Supply Chain Initiative, 2022).

Effect of geopolitical events and pandemic on pharmaceutical supply chain

The UK imported ~£1.75 billion of pharmaceuticals on average every month from the EU before Brexit, which is approximately four times more than the imports from non-EU countries. As a result, imports from outside the EU will unlikely be able to fill the significant gap created by declines in imports from the EU (Bakker et al., 2022).

Brexit also led to a change in regulatory authority, with new drug approvals and quality standards in the UK switching from the European Medicines Agency (EMA) to the Medicines and Healthcare products and Regulatory Authority (MHRA). Because of this change, pharmaceutical companies had to have duplicate quality control and release facilities in the UK and Europe, placing them at high risk of disruption in their supply chains (Roscoe et al., 2022).

To ensure a reliable supply at competitive costs due to ongoing uncertainty over European trade, we will explore onshore opportunities and local suppliers. We will also increase flexibility through greater use of outsourcing to prepare for changes in demand due to its volatility and uncertainty (Gysegom et al., 2019).

China has implemented a zero-Covid Policy which will likely exacerbate inflation issues by reducing the supply of consumer goods and raising the rates on cargo shipments from China to western ports. This will ultimately overwhelm ports in Europe with a surge of shipments once it is lifted (Karns and Coria, 2022).
In response to this, our company seeks to source raw materials and manufacturing from countries such as Vietnam and India, not limiting our supply to China only, pending the effects of the zero-covid policy in the long term.

Limiting environmental impacts

Symemco Therapeutics aims to limit the environmental impacts of our supply chain by:

1. Using greener, renewable energy resources as opposed to fossil fuels to reduce our carbon footprint, for all processes in the supply chain including transport and storage of our drug
2. Limiting pollution from packaging by investing in high performance insulation with materials that are lightweight, custom-engineered, and durable
3. Recycling and reusing our materials to reduce the processing needs of our packaging and therefore the level of greenhouse gas emissions
4. Ensuring all companies we partner with that are involved in our supply chain are environmentally conscious

Financial analysis

Fixed costs

A timeline of Symemco Therapeutics' 10-year product development process, including all fixed costs is shown in Table 7.

Table 7. Table depicting fixed costs

Stages	Start Date	End Date	Costs Associated	Breakdown of Costs
Preliminary market, business and competitor analysis	Jun 2022	Aug 2023	£11,500	As research will be ongoing, the costs for this stage will be the beginning stages of our analysis. To analyse our market, business and competitors, we must purchase reports used by clients to get an overview of the market we are getting into initially (Schwab, 2019).

Prototype Testing	Dec 2023	Feb 2024	£31,500	To test our prototype, we plan to use a blood-brain-barrier model to ensure that our drug can penetrate the brain and that its therapeutic dosage is effective. We have plans to partner up with BIOINX® on using their BBB organ on a chip, however, we will need lab space in order to carry out the testing. For this, we aim to contact King's Professors that will grant us permission to use the lab to carry out the testing.
Regulatory Approval and Clinical Trials	Dec 2023	Jan 2032	£45,000,000	CNS clinical trials cost approximately £45 million (Ledesma, 2020), where it costs £32 million for phase I, II and III, £12 million for phase IV and £1.7 million in fees to the MHRA for clinical trial registration and approval (UK Government, 2021).
Intellectual Property and Patenting	Oct 2022	Feb 2032	£19,000	There are several costs involved in patenting, including pre-filing search fees at around £450, patent application fees at around £60, official searches at around £150, examination fees at around £100, and additional fees if the pages exceed 35 (Reddie and Grose, 2021) An application for a UK patent can cost between £10,000 and £20,000 or more, depending on the complexity of the case (Reddie and Grose, 2021). A patent attorney will cost approximately £4000 (GovGrant, 2022)
Partnership Formation	Jan 2023	Feb 2031	>£500	Partnership agreements can approximately cost £500 + VAT. However,if a business lawyer was to be hired, it can cost between £200 and

				£300 per hour. Additionally, we might need to give some of our company shares as part of the partnership agreement (Contracts Counsel, 2021).
Marketing Distribution Strategy			£12,400	It's more cost effective to self-create a marketing distribution strategy, however, outsourcing a marketing distribution strategy can provide us with detailed information alongside a competitive analysis. This can be helpful long term to effectively establish our marketing strategy. The cost of outsourcing a marketing distribution strategy can vary from £8,300 to £16,500 (Team, 2020).

Staff and Administration costs

Table 8. Table depicting staff and administration costs

Category	Role in Company	Salary of Employee(s) Annually
Staff	Chief Executive Officer	£80,000
	Chief Operating Officer	£50,000
	Chief Technology Officer	£20,000
	Chief Scientific Officer	£40,000
	Executive Chairman	£50,000
	Scientists	£15,000
	Recruiters	£20,000
Admin	Hiring Costs	£3000 per hire
	Accountants	£25,000

	Bonuses	£10,000 per employee
	Admin	£8000

Variable costs

The approximations for Symemco Therapeutics' variable costs are depicted in Table 9. These are subject to change over the course of our research and development. Our total costs are shown in Table 10.

Table 9. Table depicting variable costs for Symemco Therapeutics.

Stage	Cost	Comment
R&D stage (prototype manufacturing and development)	£8,000,000	To initially develop and manufacture our prototype,we will use the resources provided to us by King's College London and iGEM. The IDT sequences are sponsored by iGEM making them free, lab equipment is provided by King's College London and lab space is free under Dr. Markiv Anatoliy jurisdiction. After our initial development, we aim to continue our R&D throughout our 10 year plan for continuous product development and research, subject to change based on our revenue and the level of investments we receive. This figure is based on the average R&D costs for pharmaceutical companies based in the UK.
L-tyrosine	>£15	100gm is £15
Terrific broth medium	>£2000	For 5kg - £2000
S-adenosylmethionine	>£33	0.5mL (32mM) is £33
HPLC UV: Stationary phase, Solutions: NaOH, ethyl acetate, methanol, mobile phases which include formic acid and absolute acetonitrile	£40,000	
Centrifuge	£15,000	

Photodiode array detector SPD 20A	£5000	
Packaging supplies	£200,000 - £2,400,000	As there are around 370,000 people in the UK with mild-moderate AD. With the aim to regularly supply our therapy to them, packaging costs £55,000 per 100,000 people, based on a monthly supply.
Laboratory space	£192,000-£ 288,000	R&D takes between 4-6 years in which it will cost £4000 per month on average to rent laboratory space
Transportation	£55,000	
Sterilisation	£23,000	

Table 10. Total variable costs and Total overall costs

Cost	Total values for variable costs	Total for all costs:
Low	£8,532,048 + (Per Unit: £2,287.41)	£54,112,948
High	£10,828,048 + (Per Unit: £2,902.96)	£56,408,948
Average	Per unit: £2,595.19	£55,260,948

Break even analysis

We created a break-even analysis to determine the number of units we need to sell to reach a point of which all costs are covered. This allows us to determine the number of units we have to sell, the price per unit, our expenses and our profits.

Per annum, 10 million people are diagnosed with AD in which 50.4% have mild AD (Yuan et al., 2021). Considering this, 373,000 patients are diagnosed with mild to moderate AD in the UK (Alzheimer's Society, 2020). If we aim to target 1% of these patients living with AD in the UK, we would need to produce our therapy for approximately 3,730 patients. To set the price of our drug per unit, we used the formula Total Cost/Units which will equate to approximately £14,815.27.

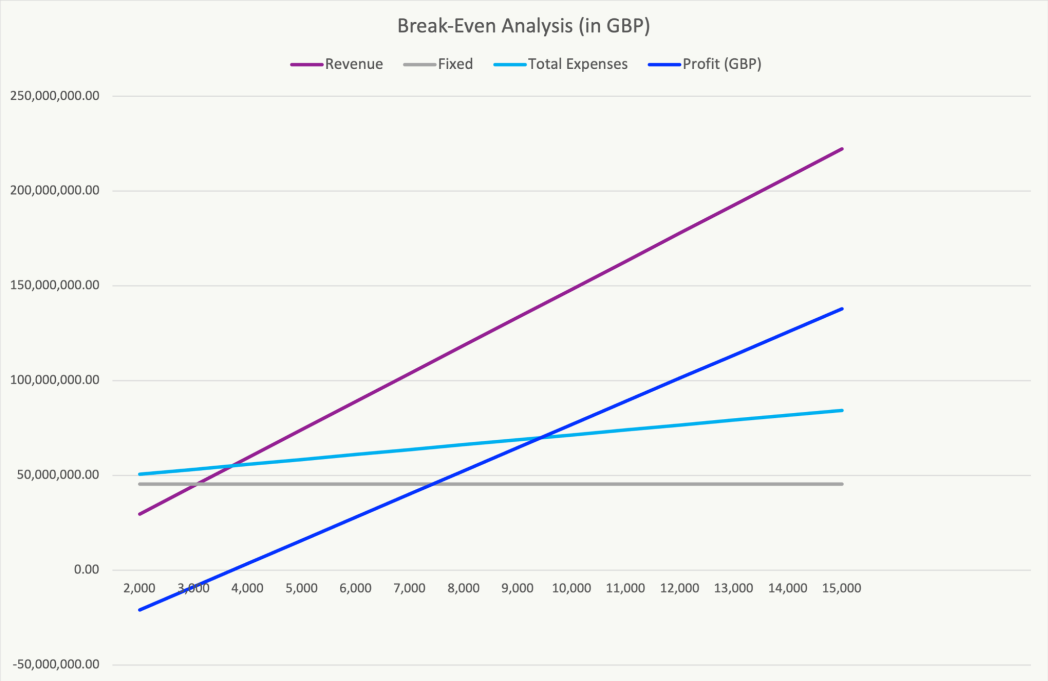

Figure 5. A chart depicting our break-even analysis including revenue, fixed costs, total expenses and profit in GBP

Gantt Chart

Our Gantt chart includes the timeline as well as the costs of our start-up 10 years from now. This includes research and development (R&D), legal operations, regulatory approval and partnership formation.

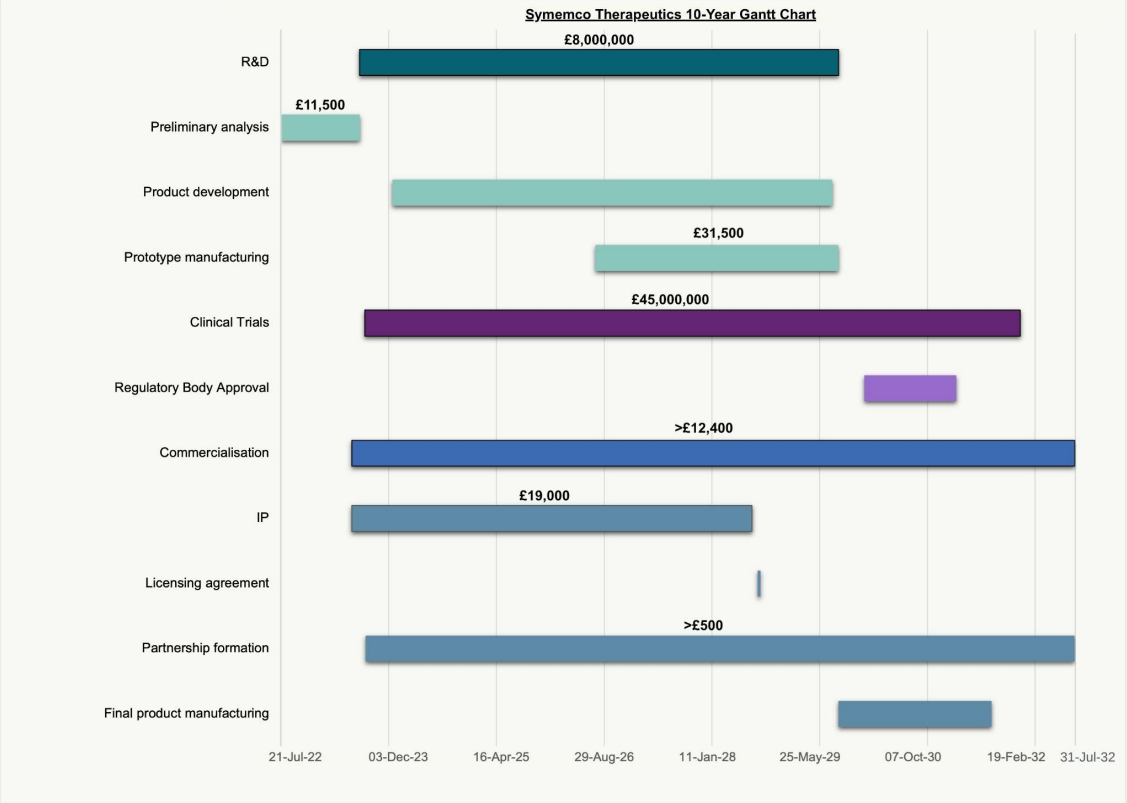

Figure 7. A chart depicting our ten year timeline starting from 21-Jul-2022 up until 31-Jul-2032 including the associated costs at each stage

Additional Revenue Streams

Blood-brain-barrier Organ-on-a-chip

As per our discussion with BIOINX®, we have the potential to sell a blood-brain-barrier (BBB) organ-on-a-chip (OoC) for in vitro modelling to companies and labs that need it. The OoC market is expected to grow around 69.4%, reaching approximately £5.31 billion by 2025 (Ozsheba, n.d.). Generally, OoC models are more cost effective than animal trials, which costs >£40,000 for a 28 day trial as opposed to buying the OoC which is sold for £18,000 by CN Bio (Staley, 2015). Selling our BBB OoC in partnership with BIOINX® can provide us with an additional revenue stream.

Experts estimate the potential of organ-on-a-chip to reduce R&D costs by 10–26%, saving costs and adding to our total revenue (Franzen et al., 2019).

AD Diagnostic

With new diagnostic tools emerging to diagnose AD at its earlier stages, we discussed a potential partnership with BetaSense to better understand the diagnosis and treatment of AD.

The AD diagnostics market is said to reach £4.28 billion by 2027. This can be part of our added revenue stream by using the BetaSense diagnostic tool to not only diagnose AD and treat it at its early stages, but also to monitor patients progress using our therapy. The added revenue stream will come from promoting the diagnostic tool alongside our drug to healthcare providers and doctors.

Selling our *E. Coli*

To help promote the use of synthetic biology within therapeutics, we intend to sell our novel pre- genetically engineered *E. Coli* with our novel biosynthesis pathway to companies and labs could widen the horizon for the use of *E. Coli* in the drug production of AD therapeutics. Furthermore, our pre- genetically engineered *E. Coli* can be further modified to target other diseases, such as cardiovascular disease, using other compounds that can be synthesised using *E. Coli*. This further promotes the applications of synthetic biology in therapeutics. Selling our *E. Coli* can also be an additional revenue stream to help us maximise our profit and reach our break even point much faster.

Funding strategy

A number of funding avenues are being considered by Symemco Therapeutics at this early stage. Funding routes such as accelerators programs, venture capitalists, angel investors, and grant schemes can provide us with funding and networking opportunities to help us establish our company as a start-up. Within our institution, we are considering the King's 20 Accelerator programme run by the King's Entrepreneurship Institute which offers nine months of support that includes networking opportunities with investors, 10 expert mentors to guide us, leadership training, and a £20,000 grant. Another accelerator programme within the UK is the Alderley Park accelerator programmes, offering a pre-accelerator programme that is two and a half days long with resources and tools to help establish a start-up, and an accelerator programme that consists of 8 weeks of 1-1 coaching and opportunities to network with investors.

There are many angel investor opportunities that Symemco Therapeutics is looking to pursue such as the Angel investment Network which allows us to pitch our business to investors. Additionally, Angels Den offers the same concept in which we pitch our business idea and open opportunities for angel investors globally to invest in our business. On a global scale, there are capital opportunities such as the Creator Fund based in Europe, which invests in many student led businesses. Within the UK, there are numerous VC firms that specialise in life sciences and biotechnology. Among the most intriguing companies are Amadeus Capital

Partners, Cambridge Innovation Capital, Epidarex Capital, NCL Technology Ventures, and UCL Technology Fund - which have a large number of medical technology startups in their portfolios, along with their willingness to invest at seed stage.

Finally, we have looked at potential grants that Symemco Therapeutics can apply to. One of them being the National Institute of Health, based in the USA, which invests more than $32 billion a year in businesses that enhance quality of life, reduce illness and disability. We are able to apply for the grant which if awarded, will help with our R&D costs. Within the UK, the most notable grants we found include Biomedical Catalyst and Innovative UK which are national funding agencies that fund innovative business in the biomedical sector as help with R&D costs and process.

Life cycle assessment

Symemco Therapeutics has carried out a life cycle assessment (LCA) to evaluate the environmental impacts associated with all the stages of pterostilbene production, to ensure we limit the environmental impact of our product. We have done a cradle-to-gate assessment, in which our life cycle includes single use technologies, reusable equipment, media, electricity, water, waste, and emissions generated during one cycle of the process (Budzinski et al., 2022).

Our LCA

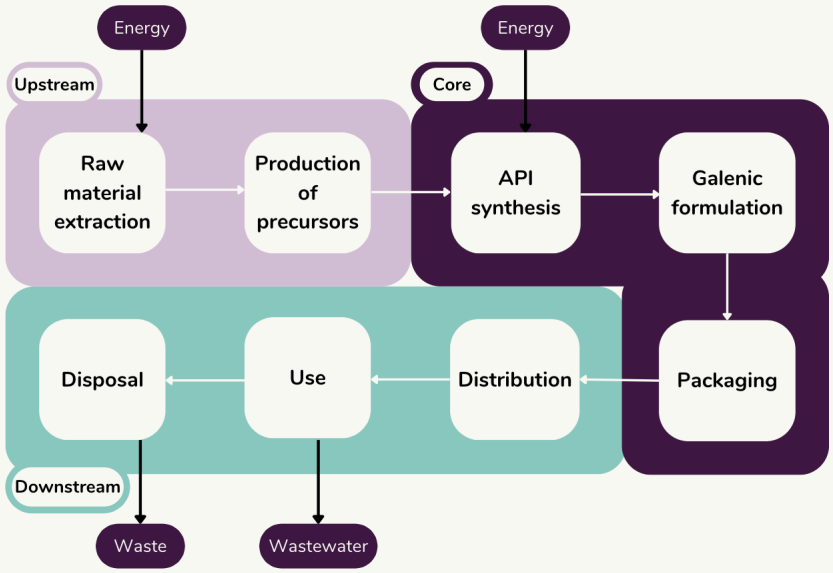

Figure 8. A diagram outlining a Pharmaceutical Life Cycle Assessment (Emara et al., 2018)

Table 11. A Table showing the processes involved at each stage of our LCA

Raw materials (L-tyrosine, Terrific broth medium, S-adenosylmethionine)	Extraction and exportation of these materials to our facilities uses energy in the form of oil and electricity
Manufacturing (HPLC UV, centrifuge, photodiode array detector)	Energy, recourse and utility consumption
Distribution	Transportation from factories to wholesalers locally and globally
Use	Sterilisation process and package production to meet health and safety requirements
Disposal	The product is ingested therefore no waste of the product itself. Factory and packaging waste

At each stage of the cycle, we have electricity and oil inputs, leading to waste and emission outputs. To combat the impact of these processes, we will use the FineChem screening tool developed by Gregor Wernet. This will estimate the resource use and environmental impacts of petrochemical production based on the molecular structure, allowing us to provide life cycle impact assessment (LCIA) metrics associated with the solvent production phase (Cespi et al., 2015). Additionally, we will implement waste, wastewater and exhaust treatment for the outputs, for example: waste incineration without heat recovery, recycling and landfilling. Most importantly, we will collaborate with LCA experants and researchers to ensure the most accurate LCA results (FibreNet, 2018).

Future growth and exit plan

As our product is a drug, we have the ability to licence our product to not only hospitals, but also to different companies such as manufacturers, distributors, diagnostics and biopharmaceuticals. After the approval of our product, we plan on protecting our work through the utilisation of IP's and patents. By licensing our product to different companies, we could expand globally and allow our product to reach different markets. Our product requires no additional costs of training healthcare staff members on the use of our product. Extra routes of revenue are generated through partnerships by selling our *E. Coli* and partnering up with companies to sell and market their products such as AD diagnostics.

Approaching and partnering with pharmaceutical companies related to our product such as Annovis Bio and Eli Lilly, allows for the chance of being obtained by them which can help us expand our product as a whole, as well as give us greater recognition amongst key players in the industry.

Risk assessment

To take full consideration of any risks involved with our project we carried out a risk analysis shown in Table 13. After assessment of the risks we analysed the current control measures we have in place and what we intend to do in the future to mitigate risks to the greatest extent.

We rated each identified risk on two aspects, the likelihood they would occur and the impact they have of the project. The numbers assigned for each risk and their corresponding rating are shown in Table 12 below.

Table 12. A breakdown of the different levels of likelihood, impact and overall risk rating used in Symemco Therapeutics risk assessment.

Likelihood	1	Unlikely
	2	Likely
	3	Most likely
Impact	1	Low impact
	2	Medium impact
	3	High impact
Risk Rating	1-2	Minimal risk
	3-4	Low risk
	5-6	Medium risk
	7-9	High risk

Symemco Therapeutics plans to review these risks continually as our project continues to develop and the risk profile expands. We intend to carry out a review of our risk assessment once a year, however as a novel company this is subject to change, and some aspects might require more frequent reviews, all dependent on the development of Symemco Therapeutics.

Table 13. A table portraying a risk assessment and risk management for Symemco Therapeutics

Risk identification	Risk assessment			Risk management	
	Likelihood (1-3)	Impact (1-3)	Level of risk (1-9)	Current control measures	Future control measures
Failure of product at pre-clinical/ clinical stages	2	3	6	Ensuring, through deterministic kinetic modelling, that we are optimally producing pterostilbene based on current literature.	Producing and applying the protocols for the regulation of pterostilbene production.
Adverse side effects	1	3	3	Thorough preliminary research into previous studies using pterostilbene, in order to ensure all side effects are assessed. Contacted authors of relevant papers to further understand the role of pterostilbene in therapeutics.	Pre-clinical trials focus on identifying and documenting the therapeutic and toxic dose, as well as side effects. Identify changes that can be made, to minimise any adverse effects of pterostilbene.
Lack of regulatory approval	2	3	6	Continual review of MHRA guidelines and requirements to ensure our product meets approval standards	Research is needed to evaluate Pterostilbene's efficacy as a therapeutic compared to a food supplement.
No deal with NHS	2	2	4	Providing an alternative treatment, that intends to be disease-modifying, which is novel to the NHS.	Approval from NICE, who can recommend our drug to the NHS. Approval from NICE shows that there is evidence to back up the therapeutic.

Quality checks	2	3	6	Ensuring our *E. coli* produces high enough yield of pterostilbene and results are reproducible and significant. Testing for a constituency of high purity of pterostilbene produced by our *E. coli*.	Carrying out more tests to model our pterostilbene in liver for metabolism Using a BBB model to ensure pterostilbene reaches the brain enough to reach the therapeutic threshold.
Low sales	2	2	4	Ensuring our funding strategy is continually reviewed. Finding alternative revenue streams alongside our minimal viable product. Developing an exit strategy.	Find ways to increase the number of additional revenue streams we have. Look into other market sectors our product could be useful in or adapted to fit in, for example the treatment of other diseases, such as cardiovascular disease based on current literature.
Mild side effects	3	1	3	Contacted authors of papers that identify side effects of using pterostilbene to evaluate the risk this poses.	Ensure standardised protocols are developed to identify side effects at the earliest possible stage.
Failure of pterostil-bene to produce desired effect	2	3	6	Optimising our *E. coli* to produce the maximum yield of pterostilbene.	Developing protocols that investigate the mechanism of action of pterostilbene in the brain.
Issues obtaining E.coli	2	3	6	Using a reliable provider of *E. coli*, on a smaller scale and production is not time sensitive currently. Ensuring orders are placed in advance of when needed to allow for any transport delays or	Considering multiple suppliers of *E. coli* and ensuring we order at suitable times and keep informed about the *E. coli* supply chain.

				supplier stock issues.	
Disposal of waste products	2	2	4	Following a standardised procedure to safely dispose of our *E. coli* and other waste materials.	Review disposal methods and research alternative methods and their environmental impact. Research into ways we could make our project more sustainable to reduce the amount of waste product.
Patent rejection	2	2	4	Developed our understanding of patents with Dr. Sara Holland from Potter Clarkson to ensure the patents we intended to file were novel and patentable.	Have a dedicated IP team, specialised in the area to mitigate rejection of patents.
Yield issues with pterostil-bene	1	2	2	Explore all sequences that could optimise the production of pterostilbene through mathematical modelling.	Outsource the production of pterostilbene.
Failure to commer-cialise manufac-turing of pterostil-bene	2	3	6	Ensuring our protocols are able to be repeated and scaled easily for commercialisation. Exploring suppliers to ensure large quantities of our required parts are obtainable.	Research other manufacturing methods of pterostilbene to use as an alternative. Outsource manufacturing to another company. Cost analysis of potential suppliers to ensure we are keeping costs of raw materials as low as possible.

Team and management

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