# The Future of Personalized Medicine: iPS cell technology as a Game-Changer in drug discovery

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# Management Summary

The global burden of diseases significantly impacts individuals, families, and communities worldwide, causing physical, emotional, and economic distress. The development of effective drugs is crucial in preventing, treating, and managing diseases, reducing morbidity and mortality rates, and improving the quality of life for patients. However, drug development is complex, time-consuming, and expensive, necessitating a deep understanding of disease mechanisms, target identification, and rigorous testing. The traditional approach to drug discovery has several limitations, including low predictivity and reliance on animal models that may not accurately represent human diseases.

Induced pluripotent stem (iPS) cell technology has emerged as a promising alternative in drug discovery to address this problem. The technology has the ability to closely mimic human cells as an advantage, a feat that cannot be achieved through traditional approaches. Additionally, iPS cells can differentiate into various cell types, providing valuable platforms for disease modeling and drug testing. The technology also has the opportunity to reduce the timeline and development costs of drug discovery,  and increasing revenue generation.

This study aims to address the impact of iPS cells in drug discovery by answering the following questions:

- How does the incorporation of iPS cell technology affect the timeline of drug discovery?
- What is the impact of iPS cell technology on development costs compared to traditional approaches?
- How does using iPS cell technology influence the reliance on animal models in drug discovery?
- What are the implications of iPS cell technology on revenue generation and potential investment opportunities?

A comprehensive analysis will be conducted by reviewing relevant literature, examining case studies, and conducting expert interviews in the fields of drug discovery and iPS cell technology, in order to answer these questions. The findings of this study will contribute to understanding the financial and temporal benefits of iPS cell technology in drug discovery, aiming to improve patient outcomes, reduce healthcare costs, and advance the broad field of medicine.

The literature review has revealed that iPS cells can be valuable in reducing the timeline and development costs associated with drug discovery. Firstly, iPS cell technology offers the potential to streamline the drug development process and accelerate the timeline. Traditional drug discovery methods often involve time-consuming steps, such as screening large compound libraries and conducting preclinical tests on animal models. However, iPS cells provide a more efficient and relevant disease modeling and drug testing platform. By using iPSC-derived cell lines, researchers can more accurately predict the response of human cells to potential drug candidates, allowing for faster identification of promising compounds. This accelerated timeline can greatly benefit pharmaceutical companies, enabling them to bring new drugs to market more quickly and take advantage of patent protection, leading to increased revenue potential.

Promising results from research on Duchenne muscular dystrophy (DMD) and Parkinson's disease have raised expectations that drugs developed using iPS cells will be introduced earlier than those developed solely based on animal studies. Furthermore, iPS cell technology can potentially reduce reliance on animal testing in the preclinical phases of drug discovery. Animal models often have limitations in accurately reflecting human diseases and predicting drug responses. iPS cells, conversely, can be differentiated into disease-relevant cell types, providing a more accurate representation of human biology. Using iPS cells in early preclinical testing allows researchers to obtain more reliable data on drug efficacy and safety without requiring extensive animal studies. This reduction in reliance on animal models aligns with ethical considerations and offers potential cost savings in drug development, as animal studies can be resource-intensive.

Semi-structured interviews have revealed comparable results to the literature research. According to the participants, iPS cell technology is perceived as a promising tool in drug discovery, capable of reducing timelines and development costs while fostering increased revenue generation. Some participants believed that iPS cells could shorten the timeline by providing more relevant data on drug candidates, while others were skeptical. However, all participants agreed that iPS cells can help enhance predictivity and productivity. By incorporating iPS cells in the early stages of drug discovery, researchers can obtain accurate results, make better decisions, and identify promising drug candidates more efficiently. This early assessment helps eliminate ineffective candidates and reduce the time associated with clinical trials.

Furthermore, the participants demonstrated the potential of iPS cells to decrease reliance on animal studies in the drug discovery process. Nevertheless, it is acknowledged that iPS cell technology must undergo thorough validation before it can complete replaceme animal studies in drug discovery. Furthermore, iPS cell technology is considered expensive and complex, which presents a barrier to widespread adoption. The participants believed that if these challenges were addressed, iPS cells would hold the promising future potential to be adopted. As iPS cells can mimic the human body, they can be effectively utilized in developing improved human disease models. This ability of iPS cells can result in reduced drug failure rates, as well as the overall costs and timeline of drug development, potentially increasing revenue generation. Participants unanimously recognized the advantages of investing in iPS cell technology projects. They emphasized the significance of considering various factors, including the maturity of the technology and its desired public image, when making investment decisions. Investing in iPS cell technology was perceived as a favorable option due to its potential to address animal welfare concerns and mitigate potential issues with animal rights activists.

Participants and literature highlight the benefits of iPS cells in drug discovery, including early assessment of drug impacts on human cells, reducing timelines, and minimizing drug failures. Literature supports the efficacy of human disease models in accelerating drug discovery and reducing failures. DMD research demonstrated a two-year reduction in the drug development timeline by integrating iPS cells in the preclinical phase. Experts and literature concur that while iPS cells offer advantages in reducing animal testing, their current limitations, such as immaturity and gene expression differences, emphasize the ongoing need for animal models in drug development to ensure a comprehensive evaluation of drug efficacy and safety. Participants believed that as iPS cells usage becomes more widespread and standardized, costs may decrease. Utilizing iPS cells in the preclinical phase was seen as advantageous, allowing for cost savings by identifying promising candidates earlier. Literature suggests that implementing human disease models like iPS cells during the preclinical phase can lead to a 10-26% reduction in total development costs, streamlining the process and potentially saving significant expenses.

In conclusion, the incorporation of iPS cell technology in drug discovery offers the potential to reduce timelines and development costs while decreasing reliance on animal models. iPS cells can enhance revenue generation by attracting customers and investors due to their higher success rates and human relevance.

# Introduction

Diseases are a significant global burden that impacts people, families, and communities everywhere (Whiteford et al., 2013). They cause physical, emotional, and economic distress, often resulting in disability, reduced quality of life, and premature death (Whiteford et al., 2013). Despite significant advances in medical science and technology, many diseases continue to pose significant challenges to healthcare systems, healthcare professionals, and patients (National et al. (US), 2003). One of the most critical needs in the fight against diseases is the development of effective drugs (Kar et al., 2010).

Drugs are essential tools for preventing, treating, and managing diseases, and they play a crucial role in reducing morbidity and mortality rates (Rodziewicz, 2023). Drugs are also vital for improving the quality of life for patients and their families, reducing healthcare costs, and promoting overall well-being (Rodziewicz, 2023). However, developing new drugs is a complex, time-consuming, and expensive process that requires a deep understanding of the underlying disease mechanisms, target identification, drug design, preclinical testing, clinical trials, and regulatory approval (Disorders, 2014). Many factors can hinder the development of new drugs, such as scientific and technical challenges, regulatory barriers, financial constraints, and ethical considerations (Sun et al., 2022). Despite these challenges, there is a growing need for new and innovative drugs to address the unmet medical needs of patients with various diseases. This need is particularly pressing for diseases that have no effective treatments, are resistant to existing therapies, or are prevalent in underserved populations (Pharmaceutical Companies Can Develop More Innovative and Affordable Medicines by Refocusing Their Spending, but Government Intervention Is Needed | LSHTM, 2023).

The use of induced pluripotent stem (iPS) cells in drug discovery holds immense promise for revolutionizing the development of treatments for various diseases. By harnessing the potential of iPS cells, researchers can create patient-specific cell lines that accurately represent the genetic makeup of individuals, allowing for more precise and tailored drug testing (Inoue & Yamanaka, 2011). Utilizing iPS cells in drug discovery can enhance the development of more effective drugs for diseases, including cancer. iPS cells can model human diseases, allowing researchers to understand disease mechanisms better and test potential drugs for these diseases (Inoue & Yamanaka, 2011).

The use of iPS cells in drug discovery has multiple advantages, including decreasing the failure rate of drugs and reducing the costs associated with the traditional approaches of drug

discovery, such as animal studies (Nicholson et al., 2022). iPS cells are obtained from adult human cells like blood cells and reprogrammed in a pluripotent state, meaning they can differentiate into every cell in the human body. This enormous advantage allows the researchers to generate relevant cells for the studied disease. This technology will increase the probability of developing innovative therapeutic targets and effective drugs (Nicholson et al., 2022). By utilizing iPS cells in the early stages of drug discovery, like the preclinical phase, researchers can screen earlier the potential drugs for diseases in a more efficient method (Nicholson et al., 2022).

## Problem Statement

The traditional approach to drug discovery, which involves screening large libraries of compounds for potential therapeutic activity, has several limitations (Van Norman, 2019) (Lin et al., 2021). The lack of predictivity and translatability of preclinical models, high attrition rates, and drug development costs pose significant challenges for the pharmaceutical industry (Van Norman, 2019) (Lin et al., 2021). Additionally, the traditional approach often relies on animal models, which may not accurately reflect the human disease phenotype or response to treatment (Van Norman, 2019) (Lin et al., 2021). Therefore, there is a need for alternative methods, such as the promising technology iPS cells, that can improve the efficiency and success rate of drug discovery and provide more relevant models for human disease.

## Research Question

The research question for this project is:

"What is the finical and timeline impact of utilizing induced pluripotent stem (iPS) cell technology in drug discovery compared to traditional approaches?"

- How does incorporating iPS cell technology in drug discovery impact the timeline compared to traditional approaches?
- What is the effect of utilizing iPS cell technology in drug discovery on development costs compared to traditional approaches?
- How does employing iPS cell technology in drug discovery influence the reliance on animal models?
- How does utilizing iPS cell technology in drug discovery impact future revenue generation and potential investment opportunities?

# Background information

## Drug Discovery Process

The development of new drugs is a critical aspect of modern medicine, and it involves a complex and multifaceted process known as the drug discovery process (Disorders, 2014b). The drug discovery process is a rigorous and highly regulated process that begins with identifying a disease target and ends with regulatory approval for clinical use. It involves various scientific disciplines, including molecular biology, chemistry, pharmacology, and clinical research (Office of the Commissioner, 2018). The drug discovery process can be divided into several stages, each presenting unique challenges and opportunities for drug development (Pandey, 2023). These stages include target identification and validation, hit identification and optimization, lead identification and optimization, preclinical testing, clinical trials, regulatory approval, and post-market surveillance (Figure 1) (Pandey, 2023).

The drug discovery process is time-consuming and expensive, with an average cost of over $2.6 billion worldwide and a success rate of only 1 in 10,000 compounds (Sun et al., 2022b). despite these challenges, it is crucial and essential to developing new drugs to meet the medical needs of patients with different diseases, and it represents a significant growth opportunity for pharmaceutical companies and the healthcare industry (Sun et al., 2022b).

In the last ten years, researchers developed multiple technologies to prevent the limitation of traditional approaches, such as the induced pluripotent stem (iPS) cells technology. Using iPS cell technology is expected to lead to faster and more efficient drug development than traditional approaches (Huang et al., 2022).

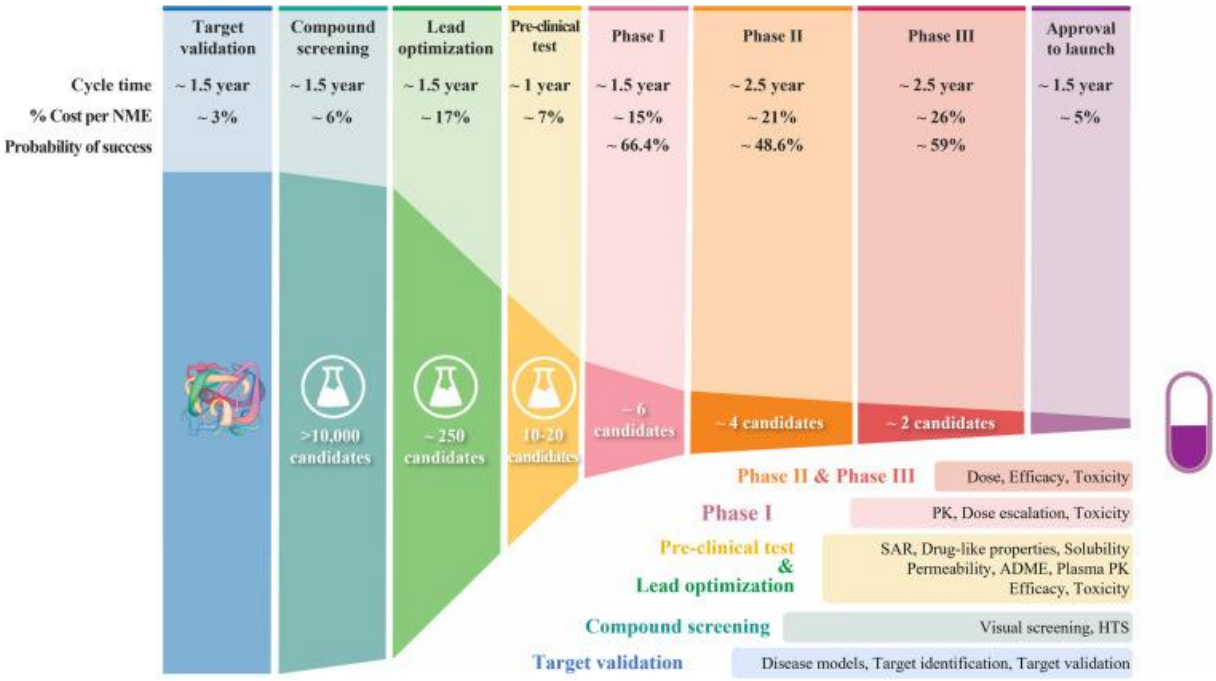


*Figure 1: The stages of drug discovery and development, as well as the likelihood of failure at each step (Sun et al., 2022b).*

## The Role of Induced Pluripotent Stem (iPS) Cell Technology in Drug Discovery

Induced pluripotent stem (iPS) cell technology has become valuable in drug discovery and regenerative medicine (Shi et al., 2016). IPS cells are somatic cells reprogrammed into a pluripotent state, allowing them to differentiate into various cell types (Medvedev, 2010). This technology has several advantages over traditional drug discovery methods, as it allows for the production of large numbers of human cells that can be used to model disease and test potential therapies (Medvedev, 2010). Generating iPS cells involves introducing specific transcription factors into somatic cells and reprograming them to a pluripotent state (Kim et al., 2011).

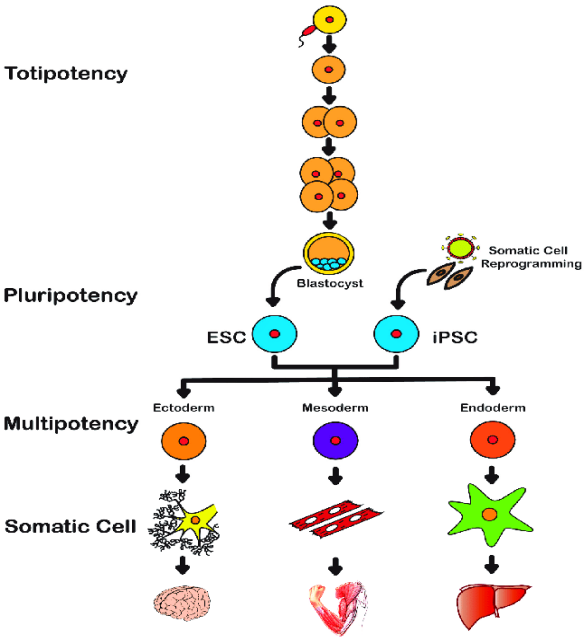


*Figure 2: Pluripotent stem cells, including embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs), have the capacity to differentiate into all types of cells, as illustrated in a representative diagram of their differentiation potential (Menon et al., 2016)*

These iPS cells can then be differentiated into specific cell types of interest by adding different and specific transcription factors, such as neurons or cardiomyocytes (figure 2) (Menon et al., 2016). This ability of iPS cells allows for

creating disease models using patient-derived cells, which more perfectly reflect the disease phenotype than traditional models using animal or cell lines (Siller et al., 2013).

Furthermore, using iPS cells avoid the ethical issues associated with using embryonic stem cells (Lo & Parham, 2009). In drug discovery, iPS cell technology has the potential to accelerate the identification and testing of potential therapies (Bashor et al., 2022). iPS cells can be used to screen large libraries of compounds for their ability to modulate disease-specific phenotypes, saving both times and cost more than traditional approaches (Paik et al., 2020). This approach has been used to identify compounds that can correct the phenotypic mutations associated with several diseases, including Parkinson's disease (Z. Hu et al., 2021) and Alzheimer's disease (Penney et al., 2019).

Additionally, iPS cells can study the mechanisms underlying disease pathology and identify potential drug targets (Nicholson et al., 2022b). In regenerative medicine, iPS cell technology holds promise for developing cell-based therapies (Aboul-Soud et al., 2021). iPS cells can be differentiated into various cell types, including cardiomyocytes, neurons, and pancreatic beta cells, which could replace damaged or diseased cells (figure 2) (Menon et al., 2016). Furthermore, iPS cells could generate personalized cell-based therapies using patient-derived cells (Chun et al., 2011). IPS cell technology has revolutionized drug discovery and regenerative medicine by providing a valuable tool for disease modeling and drug screening. The ability to generate patient-specific cells and to study disease mechanisms using iPS cells can accelerate the development of effective therapies for a wide range of diseases (Nicholson et al., 2022b) (Aboul-Soud et al., 2021).

## The Transformative Potential of Induced Pluripotent Stem (iPS) Cells in Drug Discovery

The use of induced pluripotent stem (iPS) cell technology in drug discovery has several benefits for the drug discovery process. These stem cells have emerged as a promising tool in drug discovery due to their ability to differentiate into various cell types and recapitulate human disease conditions in vitro. The paper of (Lin et al., 2021b) did mention that iPS cell models offer several advantages over traditional models, including the ability to generate patient-specific cells and tissues, which can reduce inter-individual variability and improve the predictiveness of drug testing. Moreover, using iPSC-derived models can reduce the need for

animal testing and accelerate the drug discovery process, which could lead to cost savings in the long run (Lin et al., 2021b).

IPS cells enable the development of disease-specific models; iPS cells can be derived from patients with genetic diseases or those predisposed to certain diseases. This advantage allows for the development of disease-specific models that can be used to study the underlying disease mechanisms and identify potential drug targets (Lin et al., 2021b).. For males, This is particularly relevant as many diseases, such as prostate cancer, are gender-specific and can be challenging to model using traditional methods (Rowe & Daley, 2019). By using iPS cells to develop personalized therapies, patients can receive personalized treatments for their specific disease conditions, improving treatment efficacy and reducing side effects (Rowe & Daley, 2019).

People are more likely to suffer from age-related diseases such as Parkinson's disease and Alzheimer's disease (X. Hu et al., 2020), (Penney et al., 2019b). IPS cells can be used to model these diseases, which can help to identify potential drug targets and develop treatments for these debilitating conditions (Rowe & Daley, 2019). IPS cells can be differentiated into various cell types, including those that are difficult to obtain from human donors (T. Y. Kim et al., 2019). This ability of iPS cells enables the production of large quantities of homogeneous and disease-relevant cells for drug screening and toxicity testing, reducing the need for animal testing (T. Y. Kim et al., 2019). This process is essential for patients as they are often involved in occupations that put them at risk of exposure to toxic substances (T. Y. Kim et al., 2019).

While traditional approaches to drug discovery have been effective in identifying new drugs, they often have limitations that can be overcome by using human-model diseases such as iPS cells. The paper of (Van Norman, 2019) showed that using animal tests in drug discovery is a costly and time-consuming process. Animal studies often have limited predictive power for human drug responses due to differences in physiology and genetics between animal species and humans (Van Norman, 2019). The cost of maintaining animal colonies and conducting studies can be significant, particularly in large-scale studies involving multiple animals and long-term observations. Furthermore, animal studies can be subject to variability and bias, leading to inconsistencies in results and difficulties in interpretation (Ko & Gelb, 2014).

Moreover, the use of animal studies in the drug discovery process can also lead to delays in the development and approval of new drugs (Ko & Gelb, 2014), (Van Norman, 2019). The high failure rates of drugs in clinical trials are often attributed to the poor predictive power of animal

studies. This can result in a significant loss of resources and time spent on drug development, as well as increased costs for drug manufacturers and patients (Van Norman, 2019).

Traditional drug discovery methods often rely on animal models, which may not accurately reflect the human disease condition. Obtaining human tissue samples can be challenging, particularly for diseases that affect specific organs such as the heart, and may require invasive procedures that can be risky for patients (Van Norman, 2019). Traditional drug discovery methods may not accurately reflect the disease mechanisms underlying a particular disease (Sun et al., 2022a). Which can result in the development of drugs that are ineffective or have adverse effects on patients. (Sun et al., 2022a). Traditional methods may not be able to recapitulate the complexity of the human disease condition in vitro. Which can make it challenging to identify potential drug targets or accurately predict the efficacy of a drug in humans (Sun et al., 2022a). Traditional drug discovery methods have a high drug failure rate, with only a small percentage of drugs that enter clinical trials eventually receiving regulatory approval. This can result in high costs for pharmaceutical companies and ineffective patient treatments (Sun et al., 2022a).

# Company Overview

## Mission and Background Information

*Mission of Ncardia is to enable biopharmaceutical companies to accelerate their drug discovery pipelines through the integration of human iPSC technologies*

Ncardia is a renowned biotechnology company founded in 2017 after acquiring Pluriomics. Its primary focus lies in producing and supplying human induced pluripotent stem (iPS) cells and tissue models for a wide range of applications, including drug discovery, safety pharmacology, and regenerative medicine. The company is headquartered in Leiden, South Holland, the Netherlands. Ncardia also has representatives in the United States of America. In 2021, Ncardia expanded its capabilities by acquiring Cellistic, a Belgian company specializing in cell therapy (Ncardia Home, 2023).

Ncardia's product pipeline comprises disease-specific cell models derived from iPS cells, encompassing cardiac, neural, and hepatic cell types. These models serve as invaluable tools for pharmaceutical and biotech companies to identify and validate drug candidates, evaluate safety and efficacy, and enhance the efficiency of the drug discovery process. The customer base of Ncardia includes pharmaceutical and biotech companies, academic institutions, and research organizations. Their products and services find applications in preclinical drug discovery and safety testing, disease modeling, and personalized medicine research (Ncardia Home, 2023).

The company has established strategic partnerships with numerous pharmaceutical, biotech and investment companies to expand its offerings in drug discovery. One notable partnership is with Knitici, a prominent investor that has contributed approximately 50 million euros to support advancements in the stem cell field (Veenstra, 2021).

## Organizational Structure

Ncardia is a company overseen by a board of directors led by the CEO, who is responsible for driving the company's growth and ensuring its success. Ncardia has a team admin in charge of making arrangements for meetings and travels to support the executive team. The CEO oversees several Chief Officers, including the Chief Technical Officer (CTO), who is accountable for platform development, scientific expertise, IP strategy, and the Gosselies site. Additionally, the

head of project management is responsible for organizing and reporting on projects and handling customer interactions. The Chief Financial Officer (CFO) manages financial processes and controls and is accountable for the ERP rollout. In addition to the previously mentioned Chief Officers, Ncardia has a Chief Commercial Officer (CCO) responsible for managing sales and marketing, backlog and pipeline, and new customer interactions. The Chief People Officer (CPO) manages people-related processes, recruitment, and internal company communication. Finally, the Chief Operations Officer (COO) manages Ncardia's operations and revenue and is responsible for implementing the company's strategies (figure3) (The information is obtained from CPO at Ncardia).

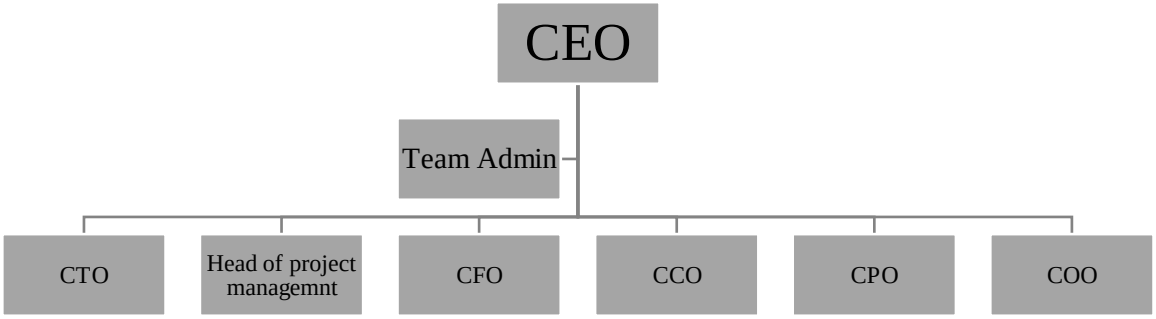


*Figure 3:The Executive team structure and functions of Ncardia*

## A Five Forces Model Assessment for Ncardia

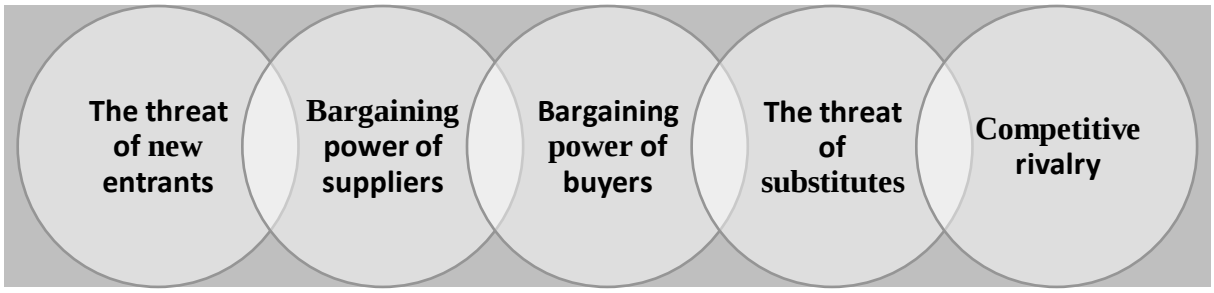


*Figure 4: the porter's five forces model*

The iPS cell industry has a very competitive environment; companies in this field should understand and analyze the structure and environment to operate correctly. The five forces model will be applied to examine the position of Ncardia in the field and be aware of the industry's challenges, limitations, and competitors. The five forces model includes analyzing

the threat of new entrants, the bargaining power of suppliers, the bargaining power of buyers, the threat of substitutes, and competitive rivalry. This analysis will allow Ncardia to evaluate the financial and timeline impact of using iPS cell technology in drug discovery. This analysis can provide insights into the financial viability and market positioning of Ncardia (information is obtained through an interview with Arjen Vaalburg, the head of Marketing at Ncardia).

**The threat of new entrants**

Ncardia operates within a specialized and innovative market, providing advanced stem cell-based technologies and services to biotech and pharmaceutical companies. As one of the early movers in this field, Ncardia enjoys a strong reputation and has fostered valuable partnerships with prominent bio-pharmaceutical firms Such as Roche. These partnerships contribute to Ncardia's competitive advantage and help establish barriers to entry for potential new players. Given the high level of innovation and expertise required, the barriers to entry in this market are substantial. Ncardia should invest significantly in research and development to stay at the forefront. Introducing new products and solutions in drug discovery will differentiate Ncardia from its competitors. New entrants must invest significantly in research and development, acquire intellectual property rights, and build a robust customer base.

However, as the market continues to evolve, Ncardia will face increasing pressure to offer customers competitive pricing and unique value propositions because the iPS cell industry is growing. Ncardia should be able to provide products with attractive pricing to customers. That can include optimizing internal processes and exploring cost-saving measures. Continuous innovation and the ability to adapt to changing customer needs will be crucial in maintaining its competitive edge. Ncardia should closely examine customers' needs, follow the iPS cell industry trends, and react quickly to changing demands. Ncardia should develop solid and practical barriers to safeguard its market position. This goal can be achieved through ongoing investment in infrastructure, technological advancements, and expanding its intellectual property portfolio. These measures enhance Ncardia's offerings and create a moat around the company, making it more difficult for new entrants to replicate its success.

Furthermore, building long-term partnerships with bio-pharmaceutical companies is a strategic approach to decrease the threat of new entrants. These partnerships can provide a steady revenue generation and serve as a testament to Ncardia's expertise and credibility in the industry. By improving these relationships, Ncardia can attract more investment, expand its market reach, and further solidify its competitive advantage.

**Bargaining power of suppliers**

Ncardia relies on suppliers such as academic institutes for its essential raw materials, including stem cells, blood cells, and growth factors. Currently, the bargaining power of these suppliers is relatively low. However, because the industry where Ncardia is operating is very innovative, the entrance of new competitors can potentially increase the suppliers' bargaining power.

To improve the financial state of Ncardia, Ncardia should build long-term partnerships with the key suppliers in the industry. Building partnerships and collaborations based on trust will allow Ncardia to have more favorable pricing, receive high-quality materials, and access the suppliers' expertise. Ensuring timely delivery of materials will enable Ncardia to save time and costs while developing induced pluripotent stem (iPS) cells. This efficiency will enable Ncardia to expedite the delivery of iPS cells to its customers, mainly biopharmaceutical companies, thereby accelerating the drug discovery process. Ultimately, this efficient process will lead to faster development of innovative drugs.

Moreover, Ncardia can invest further in research and development to explore new innovative sources of materials and technologies. By developing new innovative solutions, Ncardia can reduce reliance on multiple suppliers, resulting in significant time and cost savings. This strategy will allow Ncardia to enhance its independence, streamline its supply chain, and explore more efficient and cost-effective substitutes. By applying these strategies, Ncardia can improve its procurement process, save time and costs, and improve the drug discovery process.

**Bargaining power of buyers**

Ncardia is one of the leaders in the iPS cell industry and has higher power than its customers in deciding the prices of the products. Ncardia is operating in a very innovative and specialized market. Buyers' bargaining can differ based on multiple factors, including the size, offered alternatives, and purchasing volume. Large pharma companies can utilize more influence on the pricing than smaller ones. To address the power of buyers, Ncardia can establish a strong and long relationship with its customers.

Additionally, Ncardia can focus on supplying products of high quality to its customers, which will increase customer trust and satisfaction and reduce the probability of customers choosing other suppliers. As mentioned, Ncardia should stay at the forefront of this industry by developing innovative materials and solutions. Developing innovative products and services

will make it difficult for competitors to compete with Ncardia. That will strengthen Ncardias position as leader of the iPS cell industry as well as reduce the power of buyers to switch their suppliers.

Ncardia should always address the opportunity for customers and colossal pharma to insource iPS cell technology. therefore, Ncardia should implement an approach and closely follow industry trends. This strategy allows Ncardia to support its offerings with the specific requirements of buyers, reducing buyers' power and retaining its customer base. By implementing these strategies, Ncardia can reach a stable financial state by establishing stable revenue streams. This stability will allow Ncardia to allocate more resources toward research and development efforts, stimulating innovation and technological advancements. As Ncardia strengthens its position in the market and maintains strong customer relationships, it can expand its customer base and attract new clients.

**The threat of substitutes**

Ncardia technology has multiple potential alternatives that can replace the technology in drug discovery, including animal studies and organ-on-a-chip technology. Animal studies are one of the potential alternatives because they have shown promising results in the past. Currently, animal studies are the most used approach in drug discovery, and it is a trustful approach in the pharmaceutical industry.

Organ-on-a-chip technology is one of the most promising technologies in drug discovery. This technology allows researchers to investigate human organ systems, providing a better understanding of the drug’s safety and efficiency. Organ-on-a-chip technology is a growing technology and has the potential to replace iPS cell technology in the future. That can affect the financial state of Ncardia because some customers can choose the new technology due to its ability to mimic the human body and its organs.

In addition, artificial intelligence (AI) is one of the promising advancements in drug discovery to substitute the iPS cells technology. This technology can analyze many biological data related to drug discovery and toxicity testing. This technology has advantages such as reducing the dependence on cell line research and animal studies and reducing the usage of iPS cells. That can impact the financial state of Ncardia, as some customers can choose AI due to its high efficiency and shorter timeline.

Ncardia should address the threat of substitution by improving the proposition of its technology, iPS. Ncardia should stay aware of the latest trends in the drug discovery industry. By doing that, Ncardia can remain at the forefront of drug discovery. Following these trends will allow Ncardia to identify potential innovative and rare solutions that its competitors cannot replace.

**Competitive rivalry**

The iPS cell industry is very competitive, with multiple established players in the market. As one of the leaders in the iPS cell field, Ncardia has multiple advantages over its competitors. Ncardia has very sophisticated technology, expertise, and experience in the field. Ncardia has a strong position and reputation by constantly supplying high-quality products and services. These aspects contribute to Ncardia's competitive edge and allow it to remain at its position in the industry.

In contrast, the rapidly growing market in which Ncardia operates poses a significant challenge for Ncardia in attracting biotechnology and biopharmaceutical companies. To address this challenge, Ncardie should emphasize the importance of competitive pricing, which is important in meeting customer needs and demands. That results in enhancing its appeal to customers and having a stable financial state and attractive options in the field.

Furthermore, Ncardia should build robust marketing and sales strategies to remain at its competitive advantage position or improve it. Ncardia can emphasize its iPS cell technology through digital marketing channels such as digital platforms, especially LinkedIn, industry events, and attending conferences where the drug discovery theme is central. Ncardia should improve its competitive advantages, invest in innovative projects, establish competitive pricing strategies, and build robust marketing strategies to improve its financial state and attract new clients.

## SWOT analysis assessment for Ncardia

SWOT analysis is conducted to provide a complete analysis of the internal strength and weaknesses and external opportunities and threats of Ncardia. This SWOT analysis will provide Ncardia essential insights into its position in the iPS cell industry. Ncardia can identify opportunities for improvement and build strategies to keep its strength and explore its growth opportunity, improving its weakness and preventing threats. The analysis will allow Ncardia to explore its plans, including entering new markets, developing new services, or establishing collaborations. The analysis can help Ncardia to avoid its limitation, including its weakness and threats; improving this will allow Ncardia to grow financially. Ncardia can set its achievable goals based on its strength and opportunities. Ncardia can establish a business plan that will focus on improving its weakness, thereby ensuring that the resources of Ncardia are adequately allocated to drive growth and achieve success ( The information in this section is obtained through an interview with Arjen Vaalburg).

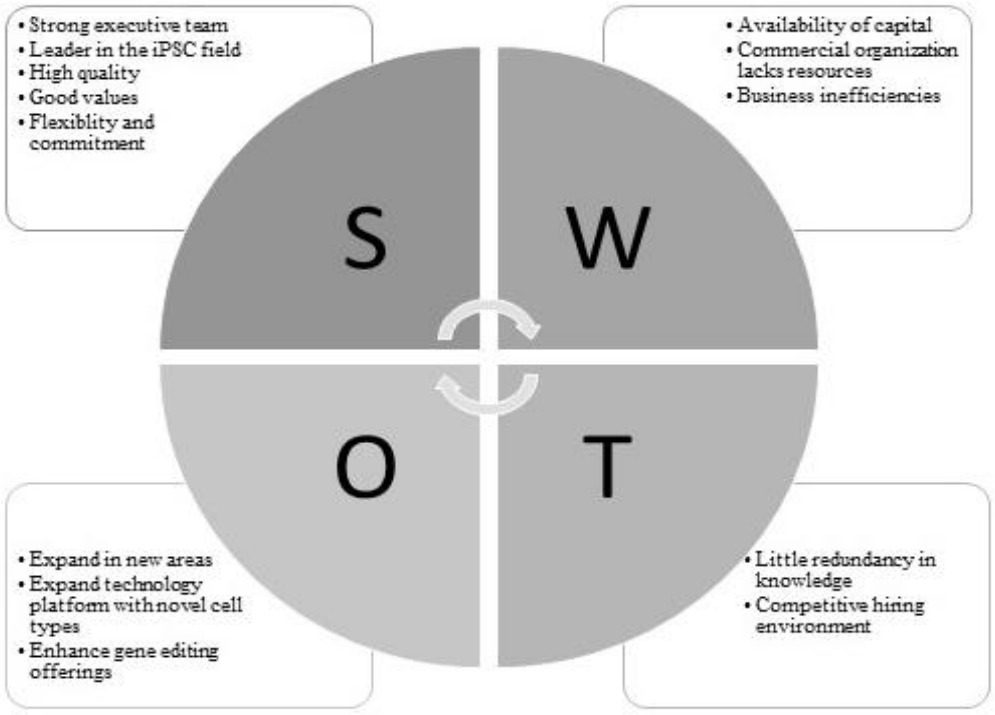


*Figure 5: Swot analysis of Ncardia*

### Strength

Ncardia has a strong executive team with several experts in the iPS cell industry. Ncardia has a clear vision, goals, and strategy. In addition, Ncardia has a team of highly skilled experts in

stem cell biology and drug discovery. The expertise allows the company to innovate and develop new products and services that meet the needs of its clients. That will strengthen the position and the financial state of Ncardia.

Ncardia is one of the leaders in the industry of iPS cells. That allows the company to establish a strong market position and gain the trust of major pharmaceutical and biotechnology companies such as Roche. Ncardia is a company that delivers high-quality services and products to its customers. The company adheres to strict quality standards and regulatory requirements to ensure its products are safe, reliable, and effective.

Ncardia's culture is built on respect, excellent communication, safety, and dedication. These values are ingrained in the company's culture, creating a positive working environment where employees feel valued and empowered. Ncardia benefits from its strategic location in vital ecosystems. The company's headquarters in Leiden, south-Holland, the Netherlands, and its presence in Belgium provide proximity to essential and famous academic institutions, research organizations, and biotech clusters. This geographic advantage allows Ncardia access to talent, resources, and collaborative opportunities. By being part of these strong ecosystems, Ncardia can leverage collaborations, access emerging technologies, and enhance its competitive position in the market.

Ncardia shows flexibility and a solid commitment to meeting customer needs. The company understands the evolving pharmaceutical and biotech industry requirements and adapts its products and services accordingly. Providing relevant solutions and responding quickly to customer requirements strengthens Ncardia's relationships with clients, fostering loyalty and repeat business. This flexibility and commitment to customer satisfaction contribute to the company's competitive advantage and long-term success.

**Weakness**

One of the weaknesses of Ncardia is the availability of capital. As a biotechnology company operating in a competitive industry, securing sufficient capital for research and development, expanding manufacturing capabilities, and scaling operations can be challenging. Limited access to capital may restrict the company's ability to invest in new technologies, hire additional skilled personnel, and expand its market presence. To avoid this weakness, Ncardia can explore

various possibilities, such as seeking external funding through partnerships, collaborations, or attracting investments from venture capitalists or strategic investors.

Ncardia may face limitations in terms of resources within its commercial organization. This weakness could include a shortage of sales and marketing personnel, leading to potential gaps in customer acquisition and market penetration. More resources for effective marketing campaigns, customer support, and sales strategies may help Ncardia's ability to reach its target audience and maximize its market potential. To overcome this problem, Ncardia can consider expanding its sales and marketing teams, investing in training and development programs, and adopting effective customer relationship management systems. This strategy will strengthen the company's ability to acquire new customers, increase market share, and improve overall revenue generation.

Inefficient business processes and scaling challenges can impact Ncardia's profitability. As the company expands its operations and customer base, inefficiencies in manufacturing, supply chain management, and other operational areas can lead to increased costs and reduced profitability. Inadequate scalability may also limit the company's ability to meet growing demand and leverage economies of scale, resulting in lower profit margins. Efficiency improvements and scalability can be achieved by implementing lean manufacturing practices, optimizing supply chain processes, and investing in automation technologies.

**Opportunities**

Ncardia can expand its business by targeting the areas of the central nervous system (CNS), skeletal, and immune cells. These areas represent significant therapeutic areas with high demand for advanced cell models. By developing and offering iPS-derived cells and tissue models specific to these areas, Ncardia can access new markets, attract a broader range of customers, and diversify its revenue streams. Expanding into these areas aligns with the company's expertise in stem cell-based technologies and provides growth and market expansion opportunities.

Ncardia's sister company, Cellistic, currently engages in activities that align with cell therapy. Cellistic specializes in cell therapy, which uses cells to treat various diseases and conditions. Ncardia can explore the expansion of its technology platform by incorporating novel cell types. The field of stem cell research is continuously evolving, and discoveries are being made

regarding the potential of various cell types. By incorporating and offering iPS-derived cells from novel and emerging cell types, such as organoids, microglia, or pluripotent stem cells, Ncardia can stay at the forefront of technological advancements and meet the evolving needs of the biotech and pharmaceutical industries. This expansion will allow Ncardia to provide innovative solutions and capture new market opportunities.

Gene editing technologies, such as CRISPR-Cas9, have revolutionized biotechnology and opened up new possibilities for precise genomic modifications. Ncardia can leverage this opportunity by enhancing its gene editing offerings. By incorporating gene editing techniques into its iPS-derived cell models, Ncardia can provide customers with genetically modified cells that more accurately mimic disease conditions, enabling more accurate drug discovery and personalized medicine research. Enhancing gene editing capabilities will differentiate Ncardia from competitors and attract customers looking for advanced, customizable cell models. Ncardia can invest in developing in-house gene editing capabilities or establish collaborations with gene editing technology providers. Training personnel in gene editing techniques and staying updated with the latest advancements in the field will ensure Ncardia remains at the forefront of gene editing applications

**Threats**

One of the threats Ncardia faces is the risk of limited redundancy in knowledge within the organization. As a specialized biotechnology company, Ncardia relies on the expertise and knowledge of its employees, particularly in areas such as stem cell research, cell culture techniques, and assay development. If crucial personnel with specialized knowledge leave the company or face unexpected circumstances, critical knowledge and skills can be lost. This threat can disrupt ongoing projects, affect operational efficiency, and hinder the company's ability to deliver high-quality products and services. Ncardia can implement knowledge management strategies, such as cross-training programs, documentation of key processes and expertise, and establishing of mentorship programs. This strategy ensures that critical knowledge is shared among team members and reduces the reliance on specific individuals.

The biotechnology industry is highly competitive, and attracting and retaining top talent can be challenging. Ncardia faces the threat of a competitive hiring environment where skilled professionals with expertise in stem cell research, cell engineering, and related fields are in high demand. Competing companies and academic institutions may offer attractive employment

packages and opportunities for career growth, making it challenging for Ncardia to recruit and retain the best talent. A shortage of skilled personnel can limit the company's ability to innovate, develop new technologies, and maintain its competitive edge. Ncardia can focus on creating an attractive work environment that fosters employee growth and development. This includes offering competitive compensation packages, professional development, advancement opportunities, and fostering a positive and inclusive company culture. Building strong employer branding and engaging with academic institutions can help attract top talent.

# Literature review

## The Impact of Using iPS Cell Technology in Disease Modeling

### Promising Outcomes of iPS Cell Technology in Familial Dysautonomia Disease Modeling and its Potential for Reducing Reliance on Animal Studies

Using iPS cell technology in research on Familial Dysautonomia provide researchers multiple advantages in understanding the underlying mechanisms of Familial Dysautonomia and selecting promising and potential drug candidates (Dietrich & Dragatsis, 2016). The iPS cells were generated from Familial Dysautonomia patients, and the cells were used in modeling the disease in vitro (Dietrich & Dragatsis, 2016). That allows the researchers to study the disease in a cell-based system that closely mimics the human and patient body, accurately representing the disease (Dietrich & Dragatsis, 2016).

Furthermore, the study showed a deficiency in the expression of a gene called IKBKAP in iPS cells of Familial Dysautonomia patients, which is responsible for the disease (Dietrich & Dragatsis, 2016). These findings emphasized the role of iPS cells in identifying the associated genes with this disease, which can be used to develop new therapeutic strategies (Lee & Studer, 2011). iPS cells allowed for a specific target for drug development, which can be challenging to identify using traditional approaches such as animal studies. That will reduce the failure rate in clinical trials, which cannot be prevented by using animal studies (Lee & Studer, 2011).

Finally, using high-throughput screening on the iPS cells of Familial Dysautonomia allowed the researcher to test thousands of compounds to identify potential drug candidates for Familial Dysautonomia (Lee & Studer, 2011). This method provides a rapid and cost-effective manner to screen for drug candidates and can be used to develop personalized therapies (Lee & Studer, 2011). This method can benefit researchers of diseases with uncommon genetic mutations that cannot be discovered using animal studies (Lee & Studer, 2011).

### Cost and Time Savings in Drug Discovery for Duchenne Muscular Dystrophy (DMD) Through the Utilization of iPS Cells

Duchenne Muscular Dystrophy (DMD) is a genetic disorder characterized by progressive muscle weakness and wasting (Venugopal, 2022). It primarily affects boys, with symptoms

typically appearing before age 6. Currently, there is no effective therapy for DMD, but some treatments can manage symptoms and slow the progression of DMD (Venugopal, 2022).

Ncardia and RegenXbio are currently engaged in collaborative research to create an innovative treatment for Duchenne muscular dystrophy (DMD), RGX-202. Ncardia used iPS- derived cells cardiomyocytes (heart muscle cells) from DMD patients in the preclinical phase of drug discovery to investigate effective drug candidates for DMD (REGENXBIO Inc., 2023). The new drug RGX-202 was effective by inhibiting a protein called myosin, which is responsible for muscle contraction. The drug also improved the strength generation of the heart muscle cells, indicating that the drug can be a potential treatment for DMD patients (Kawas et al., 2017).

Ncardia was able to complete the preclinical phase of DMD drug discovery within 4-6 months, resulting in reducing the timeline of the drug discovery process by over three years (the information was obtained during an interview with the COO of Ncardia Johan te Koppele). The drug is currently undergoing clinical trials conducted by Regenxbio, which is an essential step toward evaluating its safety and effectiveness for treating Duchenne muscular dystrophy (AFFINITY DUCHENNE: RGX-202. ClinicalTrials.gov, 2023.). This section contains information shared by Johan te Koppele, the Chief Operating Officer at Ncardia, during an interview.

Johan te Koppele (Chief Operating Officer at Ncardia):

*"The preclinical studies for DMD took only 4-6 months, potentially reducing the development process by over four years. This shortened timeline is promising for accelerating the development of effective treatments for Duchenne muscular dystrophy."*

In contrast, Pfizer's PF-06939926 gene therapy for DMD is currently in clinical trials, and the company used animal models, such as mice and dogs, to evaluate its safety and efficacy. Research on this therapy began in 2016, and the first patient was recruited for the Phase 1B clinical trial in 2018. The estimated date of completion of this phase is 2026. Although there is no available data on the drug discovery process, it is estimated that the clinical studies, including phases 2, 3 and the approval process for this drug, will take more than 15 years to complete (A Study to Evaluate the Safety and Tolerability of PF-06939926. ClinicalTrials.gov, 2023). (Appendix 2A).

Compared to Ncardia's and Regenxbio's study, using induced pluripotent stem (iPS) cells instead of animal models saved at least three years in the drug development process. This time savings not only reduces development costs but also could allow the company to introduce the drug to market more quickly, leading to increased revenue generation.

The start date of the clinical phase 1/2 began in 2023 and is estimated to be completed in 2025, making its total duration until now around four years, including the preclinical and drug discovery process. The expected date to complete the study after the approval could be around ten years (AFFINITY DUCHENNE: RGX-202. ClinicalTrials.gov, 2023.). Regenxbio's therapy, RGX-202, can have a shorter timeline of at least four years than Pfizer's therapy. This accelerated development timeline positions Regenxbio to benefit more from a monopoly and reduces the risk of failure in clinical trials. With RGX-202's promising advancements, Regenxbio can gain a significant advantage over its competitors. By shortening the timeline, Regenxbio can secure a head start in the market, establishing itself as a leading player in the field. This competitive edge allows them to enjoy a more significant market share for a more extended period, potentially resulting in higher revenues and increased profitability (Appendix 2B).

### Potential Time and Cost Reduction Through iPS Cell Approach in Parkinson's Disease Drug Discovery

Parkinson's disease (PD) is a neurological disorder that affects movement. It occurs when the cells in the brain that produce dopamine, a chemical messenger that helps control movement, begin to deteriorate and die (Beitz, 2014b). As a result, people with Parkinson's disease may experience tremors, stiffness, slowed movement, and difficulty with balance and coordination. Parkinson's disease is a chronic and progressive condition that worsens over time, and there is currently no cure. However, treatments are available to manage symptoms and improve quality of life (Beitz, 2014b).

Prasinezumab and NCT03815071 are two ongoing researchers developing drugs for the treatment of Parkinson's disease by using two different approaches. Prasinezumab was developed by the Hofmann-La Roche company using the traditional approach of synthesizing compounds to increase dopamine levels in the brain (CTG Labs - NCBI, 2023). On the other hand, NCT03815071 was developed by Allife Medical Science and Technology Co., Ltd using iPS cell technology, which allows for the generation of large quantities of human neurons in the lab for drug discovery (CTG Labs - NCBI, 2023b). In this comparison, we will focus on

these two drugs' development costs and timelines. The costs of developing drugs can vary widely depending on several factors, including the complexity of the drug, the number of clinical trials required for approval, and the regulatory requirements for drug development. While the exact costs of developing Prasinezumab and NCT03815071 are not publicly available, we can make general comparisons based on the development costs of drugs.

The traditional approaches were used in the research to develop Prasinezumab. This approach typically involves a long, expensive drug discovery process that can take several decades and cost billions of dollars. This high costs process is because traditional drug discovery methods typically depend on animal models and cell lines that may not accurately reflect the human disease and may require extensive optimization and testing to identify safe and effective drugs (Dickson, 2009). Prasinezumab, a monoclonal antibody being developed for treating Parkinson's disease, was not developed using iPS cell technology (Pagano et al., 2022). It is currently in phase two of clinical trials, which started in 2017 and is expected to be completed by 2026 (CTG Labs - NCBI, 2023). It is estimated that it will take an additional four years for phase 3 and a year for FDA approval, which means the drug may be introduced to the market between 2030-2032, according to calculations based on the study (Maguire et al., 2021). The entire development process for Prasinezumab, including the discovery process, preclinical studies, and phase 1, is expected to take over 17 years (Appendix 3A) (CTG Labs - NCBI, 2023).

In contrast, iPS cell technology has the potential to significantly reduce the costs of drug development by allowing for high-throughput screening of compounds in a human-relevant system (Rowe & Daley, 2019). This can reduce the time and resources required for drug discovery and the costs associated with animal models and optimization studies (Rowe & Daley, 2019). The drug development process of NCT03815071 seems to be relatively short. The research on NCT03815071 started in 2019, and since this date, the drug has passed the preclinical phase and shown promising results in models of Parkinson's disease cell lines (CTG Labs - NCBI, 2023b). Allife Medical Science & Technology Co. Ltd, the company developing NCT03815071, began a Phase 1 clinical trial of the drug in healthy volunteers in 2020 to evaluate its safety and tolerability (CTG Labs - NCBI, 2023b). The company completed phase 2 of the clinical trial in Parkinson's disease patients and started the recruitment for phase 3 of the clinical trials (Appendix 3B) (CTG Labs - NCBI, 2023b). The expected time that NCT03815071 will be introduced in the market is around 2028, which means that the

development process of NCT03815071 will be around 13 years based on the self-made calculation according to the study (Maguire et al., 2021).

It is worth noting that Allife Medical Science & Technology Co. Ltd used around 10 participants in their clinical Phase 1 and 2 studies, while studies of Prasinezumab involved more than 300 participants. Using fewer participants can reduce the development costs associated with each participant and ultimately reduce the overall cost and timeline of drug development. The cost per participant is around $41k, so using 290 fewer participants can save at least $12.00 million per phase (Moore et al., 2020). One reason for the shorter development timeline for NCT03815071 may be the use of induced pluripotent stem (iPS) cell technology in drug discovery and using fewer participants during clinical trials. This technology rapidly screens many compounds in a human-relevant system, significantly accelerating drug discovery. With iPS cell technology, potential drug candidates can be identified and optimized relatively quickly, thus expediting the drug development process. (Appendix 3A, 3B). Based on this literature overview of both drugs, iPS cell technology could save around three years of the drug discovery and development process, and using fewer participants can also reduce the time and cost of developing drugs.

## Potential Increasing Revenue Generation and Minimizing Animal Testing in Drug Discovery through IPS Cell Technology

Human disease models, such as organ-on-a-chip and induced pluripotent stem cells, have appeared promising biomedical research methods, significantly improving the drug development process. These models offer many advantages, such as reducing drug development timelines and development costs and decreasing reliance on animal testing (Loewa et al., 2023). The study of (Loewa et al., 2023) highlights the influence of human disease models on drug discovery and development, emphasizing their potential to decrease both the timeline and development costs while minimizing reliance on animal testing (Lowae, A. 2023).

These human disease models can accelerate drug development by simulating human-specific diseases. This simulation enables researchers to identify unique drug targets and evaluate drug efficacy within a human context. Incorporating these models during the preclinical phase expedites the drug discovery process, and more precise data can be obtained (Lowae, A. 2023). Furthermore, these models can potentially reduce false positive and false negative results,

thereby increasing the success rate during clinical trials (Swalley, 2020). Moreover, the early identification of potential failures in the drug development process can prevent costly setbacks in later stages. Human disease models such as iPS cells can reduce development costs by approximately 10-26% of the total expenses (Franzen et al., 2019).

This reduction in costs is attributed to the early identification of potential failures. Researchers can focus their efforts on the most effective and successful candidates by promptly recognizing ineffective drug candidates, thus avoiding costly late-stage setbacks. Integrating iPS cells in the drug development pipeline will reduce development costs and the required timeline (Lowae, A. 2023). This is achieved by efficiently identifying potential failures of some drug candidates, saving valuable time and resources. Consequently, the drug discovery process becomes more streamlined, facilitating the transition from preclinical studies to clinical trials (Lowae, A. 2023).

Early drug production can yield significant benefits for a pharmaceutical company in terms of revenue, competitive advantage, and reputation. By producing a drug ahead of the expected deadline, a company can gain a substantial market advantage and enjoy an extended period of exclusivity due to patent protection (Gaessler & Wagner, 2019). This exclusivity prevents other companies from producing and selling the drug or therapy until the patent expires, granting the early producer a period of market monopoly (Gaessler & Wagner, 2019). As a result, the company can generate substantial revenue during these additional years of exclusivity (Gaessler & Wagner, 2019).

Being the first drug producer provides the company with a competitive edge and enhances its reputation as an innovative player in the pharmaceutical industry (Gaessler & Wagner, 2019). The early launch of a drug allows the company to build brand loyalty and trust among customers, patients, and the healthcare industry, particularly if the drug proves to be highly successful (Taneja, 2020). This positive reputation can attract partnerships and sponsorships with other prominent industry firms and investors, fostering collaborations and further expanding the company's influence in the industry. Moreover, an early drug launch enables the company to protect partnerships, distribution agreements, and collaborations within the industry (Taneja, 2020).

By establishing these alliances, the company strengthens its market position and gains access to broader distribution networks. Additionally, it hardens the company's intellectual property

rights, making it challenging for competitors to develop similar drugs in the future. This protection provides long-term benefits as the company continues its innovative research and development of new drugs (Tenni et al., 2022). Furthermore, an early drug launch can increase investor interest in the company, leading to additional investments from shareholders and stakeholders. The company's proven ability to deliver products ahead of schedule enhances its reputation for reliability and innovation, further attracting financial support (Making the Leap From R&D to Fully Integrated Biotech for First Launch, 2023).

# Methodology

## I. Participants

The selection of participants was based on their demonstrated knowledge and experience in drug discovery or possessing adequate knowledge of induced pluripotent stem (iPS) cells, ensuring that the insights obtained were relevant and meaningful for the study's objectives [list was provided by Juan Alcauter, the Inside Sales Manager of Ncardia.]. The participants were required to be actively engaged in the life science and healthcare industry or have prior experience working in this sector. Various roles were represented among the contacted participants, such as

- Executive members and founders
- Directors and head of departments
- Senior scientists
- Investors
- Consultants
- Business developer and sales managers

The participants were contacted through LinkedIn or email in mid-April, with a reminder sent in early May. The contacted participants were geographically diverse, representing countries including the United States, Germany, Belgium, Switzerland, France, the United Kingdom, and the Netherlands. The participants were active in diverse and different organizational sizes from small start-ups to larger pharmaceutical companies and research institutes.

## II. Interview

This study utilized semi-structured interviews as a data collection method to gather valuable insights from participants with extensive expertise in the fields of drug discovery or induced pluripotent stem (iPS) cells. The semi-structured interview approach was selected due to its flexibility, allowing participants to provide detailed and personalized responses while maintaining a certain level of consistency across interviews. The interviews were scheduled between mid-April and mid may 2023. The interview consists of 14 question based on research question and the goal of the research [Appendix 1]. Prior to conducting the interviews, explicit permission was obtained from all participants to record the interview and to use the shared information in this study. The interviews were conducted in a one-on-one setting using Microsoft Teams or Zoom. Participants were informed about the estimated duration of each interview, which typically ranged from 30 to 45 minutes. The interview started with

introduction and explaining the goal of the research, followed by the first question about the background and experience of the interviewee.

## III. Date collection analysis

Thematic qualitative analysis was performed to analyze the data obtained from the semi-structured interviews conducted in this study (Caulfield, 2022). The recorded interviews were transcribed, and the transcriptions were subjected to a coding process by using Atlas.ai. The coding involved identifying and highlighting important information from the transcriptions and assigning them short, descriptive codes. Similar codes were then grouped, forming clusters of related information (Caulfield, 2022).

Subsequently, we proceeded to consolidate similar codes within each group, leading to the emergence of distinct themes. Each theme represented a coherent and meaningful pattern within the data. These themes were then organized based on the research questions, providing a structured framework for the analysis. The themes were carefully reviewed and analyzed, with relevant quotations from the participants supporting and illustrating each theme. These quotations provided valuable evidence and further context and depth to the findings. The analysis involved thoroughly examining the themes, exploring their interrelationships, and drawing meaningful conclusions based on the participants' insights and perspectives.

# Result

## I. Profile of participants

The purpose of this research project is to explore the financial and timeline impact of utilizing induced pluripotent stem (iPS) cells in drug discovery compared to traditional approaches. A group of over 200 experts specializing in drug discovery and iPS cell technology was contacted for potential participation. The list of these experts, along with their email addresses, names, and professional roles, was provided by Juan Alcauter, the Inside Sales Manager of Ncardia. It should be noted that this list is strictly confidential and cannot be shared. Unfortunately, only four experts agreed to participate in the research, as several companies blocked the email communications, and others could not disclose any information regarding their ongoing pipelines. Nonetheless, the insights gathered from the four willing participants provide valuable findings for this study.

The first participant, S.E., is an Executive Member and Director at Biogen B.V. in the USA. With a remarkable experience of over 20 years in the fields of drug discovery and iPS cell technology, S.E. brings extensive knowledge to the research. Participant 2, identified as M.N., completed a Ph.D. in drug testing at AMC in Amsterdam, focusing on applying iPS cells. M.N. has approximately 4.5 years of experience in iPS cell technology and drug testing. Similarly, participant 3, represented as L.O., shares a similar profile to Participant 2, having spent six years in the iPS cell research and drug testing domain. Finally, participant 4, J.P., serves as the Executive member at Discoveric Bio Group. With 20 years of experience in drug discovery and a specialization in iPSC-based approaches during the last three years, J.P.'s expertise significantly contributes to the investigation. All four participants possess a biomedical sciences background, adding credibility and expertise to their contributions to the study (see Table 1).

*Table 1: Participant Profiles of Individuals Contacted to Participate in the Study*

| Participants | Reference | Role | Company or institute | Background | Years of experience in drug discovery and iPSC |
|---|---|---|---|---|---|

| | | | | | |
|---|---|---|---|---|---|
| P1 | S.E | Executive Member and Director | Biogen B.V. | Bio-Medical Sciences | More than 20 years |
| P2 | M.N | Scientist | AMC Amsterdam | Bio-Medical Sciences | 4.5 |
| P3 | L.O | Scientist | AMC Amsterdam | Bio-Medical Sciences | 6 |
| P4 | J.P | Executive Member | Discoveric Bio Group | Bio-Medical Sciences | For more than 20 years, the last 3 years focus on iPSC research |

## II. The timeline impact of iPS cell technology in drug discovery

**Theme 1: reducing the timeline of the drug discovery**

The drug discovery process is very complex, and developing a new effective drug takes several years. However, using iPS technology appeared to be a promising approach to reducing the timeline of the drug development process. In this theme, participants expressed different thoughts about the role of iPS cell technology in reducing the timeline of the drug discovery process. This theme aimed to investigate the benefits of utilizing iPS cells in drug discovery. By exploring the benefits and limitations of iPS cells, researchers can gain insights and understand whether iPS cells can reduce the timeline of the drug development process. This theme was developed using codes from interviews conducted with four participants, as cited in Table 2.

Participants two and three agreed that iPS cell technology needs to be validated and optimized enough to reduce the timeline of the drug discovery process compared to the traditional approach. However, the participants believe that iPS cells is the solution to solve the caused time-consuming using traditional approaches. By utilizing iPS cells in drug testing, researchers can gather more relevant data on drug candidates. This can lead to better decision-making, helping to identify promising compounds and reducing the time spent on ineffective ones.

Participant 2 *" If we involve facilities that produce cells ready for research, such as companies offering specific cell lines, the timeline can be significantly reduced. "*

Participant 3 *" If you have a model that closely resembles the organ you want to study, using human cells and modeling specific mutations can significantly reduce the time of drug development. "*

On the other hand, participants one and four do not believe that iPS cells can now reduce the timeline of drug development. However, it is a valuable tool to be used to increase and improve the predictivity of drugs.

Participant 1 *" The use of stem cells in the drug discovery process does not shorten the time it takes for drug development. The use of stem cells is only one component of the drug discovery process and is not the primary driver for shortening timelines. "*

Participant 4 *" Currently, I do not believe using IPSCs will shorten the timeline for drug discovery. Rather, I think it will increase the productivity of in vitro studies and improve the predictability of drug development outcomes. "*

Participants' views on iPS cell technology varied, with some expressing optimism about their ability to reduce drug development timelines, while others emphasized their potential in enhancing predictivity and productivity.

**Theme 2: Accelerating the early stage of drug discovery**

Accelerating the early stage of drug discovery is essential to develop efficient drugs and increase drug development success rates. The theme emphasizes the capacity of induced pluripotent stem (iPS) cells to create disease models that closely resemble the human system. Additionally, this theme aimed to explore how iPS cell technology can accelerate the early stages of drug discovery and development and involve developing more efficient and successful drugs. This theme was developed using codes from interviews conducted with two participants, as denoted in Table 2.

Participants emphasized the significant benefits of utilizing induced pluripotent stem (iPS) cells in the early stages of drug discovery. This approach offers a distinct advantage over traditional methods, as it enables the development of drugs and models that are more relevant to the human system. By leveraging iPS cells, scientists can examine the impacts of potential drug candidates on human cells at an early stage in the drug development process. This early assessment

accelerates the identification of promising drug candidates with higher efficacy and safety profiles. That can help identify and eliminate ineffective candidates, reducing timelines and minimizing drug failures during clinical trials.

Participant 1 *" In our company, stem cells are used in the preclinical phase to mimic human tissue better and enable more accurate testing of potential drugs. "*

Participant 2 *" These human cells are still much closer to humans than mice, which is why preclinical studies using IPS cells could be beneficial. "*

Participants highlight the advantages of integrating iPS cells in the initial phases of drug discovery. This approach enables more precise and contextually appropriate testing of potential drugs, resulting in the identification of promising candidates and a reduction in overall timelines within the drug development process.

*Table 2: an overview of themes and codes, the impact of using iPSC in drug discovery*

| *Theme* | *Code and contributing participant* |
|---|---|
| **1. Reducing the timeline of the drug discovery process** | • Timeline reduction by using iPSC (P2)<br>• Impact of iPSC on the timeline (P1)<br>• Reduction timeline of drug discovery process (P3)<br>• Impact on the timeline of drug discovery (P4) |
| **2. Accelerating the early stage of drug discovery** | • Improve drug discovery process in early stage (P1)<br>• Benefits of using iPSCs in drug discovery early stages (P2) |

## III. iPS cell technology as a replacement tool for animal studies in drug discovery

The utilization of iPS cells in the preclinical phase offers the potential to reduce the dependency on animal studies, as they can closely mimic the human body. While iPS cells are not currently capable of entirely replacing animal studies, they can minimize the reliance on animal experimentation in drug discovery by reducing the number of animals used. The theme highlights the opinions of four experts in iPS cells on the role of this technology in reducing the reliance on animal studies in the drug discovery process. This theme was developed using codes from interviews conducted with four participants, as indicated in Table 3.

**Theme 1: Using iPS cells can reduce the using of animal studies in drug discovery**

Participants agreed on the significant role of induced pluripotent stem (iPS) cells in drug discovery, particularly during the preclinical phase, with the notable benefit of reducing the reliance on animal models. By incorporating iPS cells into the drug development process, there is a real opportunity to decrease the number of animals utilized for testing purposes. This reduction in animal usage aligns with ethical considerations and carries practical implications, as it can potentially expedite the drug discovery timeline by a minimum of two years.

Participant 1 *"Stem cells may help reduce the number of animals used in the drug discovery process."*

Participant 2 *" Nonetheless, using IPS cells can still result in a drastic reduction in the number of animals used for testing, which can save both time (around two years) and money."*

Participant 3 *" By using IPS cells, you can decrease the number of animal candidates for drug screening, thus reducing the overall reliance on animal testing. "*

The participants express a strong endorsement for integrating iPS cells into drug discovery as a strategy to decrease reliance on animal models. This reduction not only addresses ethical concerns but also offers practical advantages such as time and cost savings, potentially leading to a substantial acceleration in the drug development timeline.

**Theme 2: iPS cells as Complementary, Not Replacement Assays**

iPS cell technology is a promising approach to drug discovery, with the ability to revolutionize the field. However, the technology cannot fully replace traditional approaches such as animal studies. This theme is designed to identify why iPS cells can be a complementary assay and identify its limitations in the drug discovery process. This theme reflects the perspective of certain participants who believe that iPS cells can serve as a valuable complementary assay to animal studies in drug development. This theme was developed using codes from interviews conducted with four participants, as indicated in Table 3.

Induced pluripotent stem (iPS) cell technology is considered a complementary tool in drug discovery; however, it is not yet ready to completely replace animal studies in this field. The FDA and EMA regulations require animal studies as part of bringing a drug to the market. Although iPS cell technology shows promise, it still needs further optimization and validation before it can be fully implemented as a replacement for animal studies in the future. The participants in this study agreed that iPS cells could not entirely replace animal studies but could contribute to reducing their reliance. Participant 3 believes that a more sophisticated iPS cell

technology could facilitate the development of human organs and tissues. This advancement would make drug discovery more personalized and specific, potentially reducing the necessity of including animal studies in the drug discovery process.

Participant 3 *" As IPS cells become more sophisticated, we may have advanced organ and tissue systems closely mimicking the human body. IPS cells are the future, and animal models will have less importance in drug development."*

Participant 1 confirmed that iPS cells could be highly beneficial in drug discovery. However, they also acknowledged certain limitations, such as the immaturity of iPS cells and the possibility of different gene expressions compared to cells found in the human body. These differences may lead to drug failures during clinical phases. Hence, including animal studies in the drug discovery process remains crucial.

Participant 1 *" iPS cells do have limitations compared to primary human material as they are less mature and gene expression may differ."*

While acknowledging the advantages of iPS cells in drug discovery, participants highlight the existing limitations of this technology and highlight the importance of animal studies for comprehensive drug development.

**Theme 3: switching the current technology to iPS cells in drug discovery**

Many companies are incorporating iPS cells into their pipeline due to their capability to closely replicate the human body, in contrast to traditional approaches like animal studies. Nonetheless, these firms have not wholly eliminated animal studies from their pipeline because it has yet to be ready. This theme highlights the participants' perspectives regarding the potential of iPS cells to replace animal studies in drug discovery. This theme was developed using codes from interviews conducted with four participants, as indicated in Table 3.

The participants' responses indicate a lack of enthusiasm for switching from their current technology, animal studies, to induced pluripotent stem (iPS) cells in drug discovery. The reasons for their hesitation stem from the current high cost and complexity associated with iPS cells, despite their potential to better recapitulate human physiology. However, participant 4 suggests that their company may consider transitioning if the costs of iPS cell technology

decrease in the future. Participant 4's suggestion of potential future adoption highlights the willingness to explore iPS cells as a technology if the cost barrier is addressed.

Participant 4 *" However, if the cost of using IPS cells is reduced in the future, it could replace some of the immortalized cell assays. However, that is unlikely to happen for now. "*

Participant 1 emphasizes the importance of combining both iPS cells and animal studies in the drug discovery process to ensure improved results in clinical trials. These findings suggest that while iPS cells offer advantages in terms of human physiological relevance, the current financial and technical challenges make them less viable options compared to animal studies.

Participant 1 *" Moreover, confirming the results in IPS cells and animal models will help build the case that the molecule modulates the target in the desired way. "*

In conclusion, the adoption of iPS cells in drug discovery is presently limited by cost and complexity issues. However, the potential for future utilization remains if advancements in technology reduce these barriers. Combining iPS cells with animal studies appears to be a promising approach for enhancing drug development outcomes according to participant viewpoint.

*Table 3: an overview of themes and codes, iPSC as a replacement tool in drug discovery*

| *Themes* | *Codes and contributing participants* |
|---|---|
| **1. Using iPSC can reduce the use of animals in drug discovery** | ➢ Reducing animal tests in drug discovery (P1)<br>➢ Reducing animal tests (P2)<br>➢ Reducing animal tests (P3) |
| ***2.* iPSCs as Complementary, Not Replacement Assays** | ➢ Improving drug discovery process (P3)<br>➢ iPSC limitations (P1) |
| ***3.* Switching the current technology (e.g. animal studies) to iPSC drug discovery** | ➢ Switching the current technology (P1)<br>➢ Current technologies replacement (P4) |

## IV. The impact of iPS cell technology on development costs in drug discovery

**Theme 1: reduction of development costs by using iPS cell technology**

Pharmaceutical firms have a crucial goal of reducing the expensive cost of drug development. By using iPS cells, scientists can obtain valuable insights into disease mechanisms and increase the effectiveness of drug development, reducing associated costs with the development process. The theme highlights the contribution of iPS cells to reducing development costs compared to the traditional approach. This theme was developed using codes from interviews conducted with four participants, as indicated in Table 4.

Participants 1 support that incorporating induced pluripotent stem (iPS) cells into the drug discovery process can reduce overall development costs. However, she emphasized that iPS cells represent a relatively small component of the drug discovery process compared to other costly steps involved in clinical trials.

Participant 1 *" When you consider the overall cost of a drug discovery program, the cost of using IPS cells is a relatively small component. "*

Additionally, participants agreed that iPS cells could be more cost-effective than traditional approaches, such as animal studies. Participant 2 highlighted the significant benefits of iPS cells, including the ability to create better disease models and facilitate personalized medicine. By leveraging iPS cells, researchers can gain valuable insights into disease mechanisms and enhance the effectiveness of drug development, ultimately leading to higher success rates.

Participant 2 *" The cost of maintaining cell lines is a significant factor, with mice being much more expensive to maintain than IPS cells. "*

Additionally, participants expressed optimism about the future cost-effectiveness of iPS cells. They believed that as knowledge and understanding of iPS cells continue to expand and their usage becomes more widespread, the associated costs may decrease compared to traditional approaches. This suggests that iPS cells have the potential to drive cost reduction and improve efficiency in drug discovery processes.

Participant 4 *" If iPS cells become more widely used and standardized, it is possible that the price will decrease in the future, and they could replace some of the assays currently in use. "*

In conclusion, incorporating iPS cells into drug discovery holds promise for reducing development costs. The benefits offered by iPS cells, coupled with increasing knowledge and broader adoption, provide an optimistic outlook for cost-effectiveness in the field.

**Theme 2: cost reduction by using iPS cell technology in the preclinical VS clinical phase**

The early identification of the most promising drug candidates during the drug discovery process is crucial. Leveraging iPS cell technology in the preclinical phase has the potential to generate promising data that can reduce the failure rate in subsequent stages of drug development. This theme provides insights into iPS cell technology's capacity to improve disease modeling and save costs through the early identification of effective drug candidates. This theme was developed using codes from interviews conducted with four participants, as denoted in Table 4.

Participant 2 provided insights highlighting the potential benefits of using induced pluripotent stem (iPS) cells in the preclinical phase of drug discovery. He expressed that iPS cells can offer better disease modeling capabilities than traditional methods. By utilizing iPS cells, researchers can gain a closer approximation to human biology, making iPS cells a valuable resource for early testing and screening in the drug development process. Moreover, Participant 2 suggested that iPS cells have the potential to generate cost savings by enabling the identification of promising candidates at an earlier stage.

This early identification can help researchers focus their efforts and resources on the most viable candidates, ultimately reducing the overall costs associated with drug development. He also emphasized the advantages of iPS cells over animal studies. IPS cells are more human-relevant than animal models, such as mice. This closer resemblance to human biology further strengthens the case for utilizing iPS cells in the preclinical phase. When asked whether iPS cells should be used in the preclinical or clinical phases, Participant 2 implied a preference for the preclinical phase.

Participant 2 *" In my opinion, I would place my bets on preclinical studies. The reason is even though IPS cells are closer to humans than mice, they still cannot replace an actual human heart for cardiac studies.* "

Participant 4 provided valuable insights regarding the limitations of using induced pluripotent stem (iPS) cells in the clinical phases of drug development. The participant emphasized that iPS cells cannot fully replace the human body's complexity, particularly in clinical phase 1 and

phase 2, where the safety and effectiveness of the drug are tested. The limitations arise from the fact that iPS-derived cells are not fully matured and do not completely represent the adult human body. As a result, iPS cells may not accurately reflect the intricacies of human physiology, which is crucial in determining the safety and efficacy of drugs during clinical trials.

Participant 4 *" Currently, the iPS cells are prenatal and do not fully represent the patient population we want to target, especially the elderly population where cells may not function as well. "*

In conclusion, incorporating iPS cells in the preclinical phase of drug development can provide potential benefits such as improved disease modeling and cost savings through early identification of promising candidates. However, it is important to recognize that iPS cells have limitations in replicating the complexity of human physiology, necessitating the continued need for clinical trials in later stages of drug development.

*Table 4: an overview of themes and codes, The impact of iPSC on development costs in drug discovery*

| Themes | Codes and contributing participants |
|---|---|
| 1. **Reduction development costs by using iPSC** | Reduction of development costs in drug discovery (P1)<br>Reducing development costs (P2)<br>Reducing development costs (P4) |
| 2. **Cost reduction by using iPSC in preclinical vs clinical phases** | Reducing the costs of the preclinical phase (P2)<br>iPSC limitations in clinical trials (P4) |

## V. Future considerations

**Theme 1: potential increasing the company revenue by using iPS cell technology**

Reducing time and costs in drug discovery can potentially increase revenue generation. This can be achieved through improved success rates in drug development, meeting the needs of customers and patients, and enhancing firms' market position. This theme explores the potential impact of integrating iPS cells into drug discovery on the revenue generation of companies. This theme was developed using codes from interviews conducted with four participants, as denoted in Table 5.

All participants unanimously agreed that incorporating induced pluripotent stem iPS cells in their drug development pipelines can benefit and increase companies' revenue. Participant 1 emphasized the criticality of selecting a suitable model, as it can significantly impact the company's success, including revenue growth. Furthermore, potential customers are more inclined to choose drugs developed using iPS cells over those relying solely on animal studies due to the closest resemblance to the human body and higher success rates.

Participant 1*" If using IPS cells allows for a better understanding of the biology and ultimately leads to the identification of a more effective drug, it can have a huge impact on the company's bottom line. "*

Participant 2 highlighted that being an early adopter in this field provides a substantial advantage as validation of iPS cell technology progresses, positioning companies far ahead of their competitors. Using iPS cells can also lead to a reduction in the drug development timeline, enabling companies to bring drugs to market earlier than anticipated, thereby generating more revenue during the extended patent protection period, as stated by Participant 3.

Participant 2 *" However, this perception is expected to change in the next 5 to 10 years, with IPS becoming the golden standard. Companies that start investing in IPS now will be ahead of the curve when this change happens. "*

Participant 3 *" If a drug can be developed in a shorter time frame using iPSC, it could potentially provide extra years of revenue due to longer patent protection. "*

Additionally, Participant 4 emphasized that integrating iPS cells can decrease drug failure rates, resulting in cost savings. These saved costs can be reinvested in other pipelines, aiding revenue generation and reducing time and cost inefficiencies.

Participant 4 *" As IPS cells are derived directly from human tissue and maintained in a human environment, they may help to reduce the rate of failure from preclinical to clinical stages by providing a more translational model."*

In conclusion, incorporating iPS cells into drug discovery has the potential to increase revenue generation by improving success rates, meeting customer needs, and enhancing market position. Early adoption of iPS cell technology can provide a competitive advantage and extend the patent protection period while reducing drug failure rates can lead to cost savings and more efficient resource allocation.

**Theme 2: iPS cell technology as a promising investment in drug discovery**

Due to its potential to revolutionize disease modeling, enhance success rates, and lower costs, iPS cell technology is widely regarded as a promising approach to drug discovery. This technology presents an intriguing opportunity for investors looking to capitalize on advancements within the pharmaceutical industry. This theme was developed by utilizing codes generated from interviews conducted with four participants, as indicated in Table 5.

Based on the unanimous agreement among participants, investment in induced pluripotent stem (iPS) cells is regarded as a smart choice due to its ability to closely mimic human physiology and reduce animal studies in the process. Participant 1 expressed a willingness to invest in iPS cell technology pipelines but also emphasized the importance of not relying only on one technology. A smart investor should consider multiple factors before choosing the technology to invest in.

*Participant 1 " Using IPS cells or stem cell drive cells to more accurately mimic human physiology is likely to be a smart choice, but it is not the only factor to consider. "*

Participant 2 highlighted the importance of considering whether the technology is established and the desired public image for the investments. However, due to the potential to reduce animal usage in drug discovery, investing in iPS cells was seen as a better choice to avoid potential issues with animal rights activists.

*Participant 2 " With the increasing scrutiny and criticism of animal studies in the media and among animal rights activists, reducing or avoiding animal studies altogether would be the better choice. "*

This sentiment was also confirmed by Participant 3, who supported for investing in iPS cells because of its ability to address concerns related to animal welfare.

*Participant 3 " In my opinion, I would prefer to invest more in companies that focus on using IPCs and innovative approaches to the drug development process. Any method that reduces the use of animals is something I support. "*

Participant 4 expressed a belief that iPS cell technology is a promising tool for the future and would prefer to invest in iPS cell research. The closer resemblance of iPS cells to human physiology, as mentioned by Participant 4, was highlighted as a key reason for this preference.

*Participant 4 "* Using IPS cells may be a more promising approach as it provides a model that is closer to the human situation. *"*

iPS cells have the ability to closely replicate human physiology and decrease the dependence on animal studies. The interviews highlighted the importance of considering multiple factors and not solely relying in one technology.

**Theme 3: evolution and future prospects of iPS cell technology in drug discovery**

In the early phases of induced pluripotent stem (iPS) cell technology, researchers faced challenges relating to standardization and differentiation techniques, which led to limited alternatives for generating fully mature cell types. This theme highlights the future expectations of iPS cell technology in drug discovery. This theme was developed using codes from interviews conducted with four participants, as indicated in Table 5.

The participants in this study were the first researchers who worked with induced pluripotent stem (iPS) cells and shared their experiences and perspectives during the initial phase of iPS cell discovery. They unanimously agreed that iPS cells faced challenges in terms of standardization and differentiation methods, resulting in limited options for generating mature cell types. They had a problem with replicating human cells which caused significant difficulties, and the technology required extensive research and improvement during the first 10 to 15 years. The unanimity among the participants was that iPS cells lacked standardization in the early stages. Each laboratory employed its own unique approaches, resulting in a lack of stability and hindering the ability to compare and replicate experimental results effectively. Furthermore, the differentiation methods available for iPS cells were less advanced during this period, impeding the generation of fully mature and functional cell types.

Participant 1 *" However, in the early days, there were limited options for differentiating iPSCs into mature terminal cell types, and there were issues with replicating human neurons or cardiomyocytes accurately. "*

Participant 3 *" Regarding the impact of IPCs ten years ago, differentiation techniques were less advanced, and the cells did not fully resemble the in vivo situation. "*

Participant 4 *" I think the field of IPS cells was not very standardized initially, with each lab using different differentiation protocols resulting in IP neurons from one lab being completely different from those produced in another lab. "*

In contrast to the past of iPS cell technology, the participants exhibit a high level of optimism regarding the future of iPS cell technology in drug discovery. They definitely believe that iPS cells will significantly enhance the drug development process and revolutionize the effectiveness of clinical trials. In fact, they envision iPS cells becoming the major technology in drug discovery, primarily due to their potential to reduce reliance on animal studies. While further advancements are still necessary, this technology promises to outperform animal studies in addressing all aspects of the drug discovery process. iPS cell technology represents a major step in the right direction towards developing personalized and efficacious medicines by solely utilizing human cells while minimizing dependence on animal models. It is a desirable technological approach, especially as large pharmaceutical companies can outsource its implementation, making it more cost-effective than traditional animal studies.

Participant 1 *" The use of iPSC cells in drug discovery will become more prevalent over time as we continue to develop the ability to generate more cell types, fine-tune them, and increase their scale. "*

Participant 2 *" iPS cells need to develop in parallel to have enough options to be able to answer every question, and at the end of the day, it will probably replace animals completely. "*

Participant 3 *" They will become the preferred model as they can closely resemble the human in vivo situation, taking into account various variables. "*

Participant 4 *" In the future, it would be great to see more research done on using adult cells in IPC research. This would help to improve the relevance of the findings to real-world patients and improve the potential for successful clinical translation. "*

The participants expressed optimism regarding the future of iPS cell technology in drug discovery, emphasizing its potential to transform the drug development process and reduce reliance on animal models. However, they also acknowledged the need for further research to validate and refine the technology before it can fully replace animal studies.

*Table 5: an overview of themes and codes in Chapter 5 Future considerations*

| Themes | Codes and contributing participants |
|---|---|
| **1. Potential increasing the company revenue by using IPSC** | Impact on the revenue (P1)<br>Increasing revenue by using iPSC (P2)<br>Increase revenue (P3) |

| | |
|---|---|
| | Failure reducing to save costs (P4) |
| **2. Induced Pluripotent Stem Cells (iPSCs) as a Promising Investment in Drug Discovery** | Smart investment (P1)<br>Smart investment (P2)<br>Investment in iPSC (P3)<br>Investment in iPSC (P4) |
| **3. Evolution and Future Prospects of iPSCs in Drug Discovery** | Limited resources for iPSC (P1)<br>Promising tool in drug discovery (P1)<br>The future expectation of iPSC (P2)<br>Less validated iPSC (P3)<br>Promising future of IPSC (P3)<br>Not standardized iPSC (P4)<br>improvement of iPSC (P4) |

# Discussion

This research project investigates the financial and timeline implications associated with using induced pluripotent stem (iPS) cells in drug discovery, in contrast to traditional approaches. Furthermore, the study explores the potential monetary value derived from savings and increased revenue that can be attained by reducing the throughput time before drug registration or filing.

To address this question, the research project employed semi-structured interviews with experts specializing in drug discovery and iPS cells. This method was employed to gather valuable information and insights from the participants. The interviews involved four experts in the field of iPS cell technology, with the participants possessing experience ranging from 4.5 to 20 years in the drug discovery and iPS cell technology field.

How does the incorporation of iPS cell technology in drug discovery impact the timeline compared to traditional approaches?

The results of semi-structured interviews revealed varied perspectives among the participants regarding the ability of iPS cell technology to reduce timelines. Some participants expressed optimism, emphasizing the ability of iPS cells to provide more relevant data on drug candidates and expedite the identification of promising compounds. In contrast, other participants viewed the iPS cell technology as a valuable approach to enhance the productivity of drugs and improve productivity in early-stage drug discovery. The variation in viewpoints can be attributed to the specific objectives and applications of iPS cell technology. This technology has the advantage of its ability to mimic the human body and enable more accurate testing of potential drugs, which can accelerate the identification of promising candidates in a shorter time. Additionally, integrating iPS cells in early stages can allow for the identification of candidates with higher efficacy and safety profiles. This early incorporation of iPS cells can help eliminate ineffective candidates, reducing timelines and minimizing drug failures during clinical trials.

The literature has consistently supported these findings. The study conducted by (Loewa et al., 2023) demonstrated that the utilization of human disease models can significantly decrease the time required for drug discovery. Furthermore, literature revealed that the application of human disease models could lead to a reduction in drug failures and minimize the occurrence of false interpretations during preclinical trials. This failure reduction ultimately translates to fewer setbacks during clinical trials (Franzen et al., 2019). Moreover, Ncardia has showcased the efficacy of using induced pluripotent stem (iPS) cells in the preclinical phase. Their research

on Duchenne muscular dystrophy (DMD) demonstrated that integrating iPS cells in the preclinical phase enabled their partner company, Regenxbio, to advance to the clinical phase after only six months of research. This significant reduction in the timeline of the drug development process amounted to at least two years of saved time.

The impact of iPS cell technology on drug discovery timelines is a topic of ongoing debate. Further optimization and validation of iPS cell technology are essential to unlock its full potential in shortening drug development timelines. Additionally, Future research and advancements in iPS cell technology will contribute to a better understanding of its impact on timelines and overall drug development efficiency.

What is the effect of utilizing iPS cell technology in drug discovery on development costs in comparison to traditional approaches?

The outcomes from the semi-structured interviews provide valuable insights into the impact of utilizing iPS cell technology on development costs in drug discovery. Participants showed different viewpoints on the cost-effectiveness of using iPS cell technology in drug discovery compared to the traditional approaches. Some participants were optimistic about the potential of iPS cells to reduce development costs by providing better disease models and accelerating personalized medicine. They believed that leveraging iPS cells could enhance the effectiveness of drug development and increase success rates. The findings from the literature research indicated that the utilization of iPS cell technology in drug discovery holds promise for reducing the reliance on animal testing and minimizing the number of participants required in clinical trials. This, in turn, has the potential to reduce the overall costs associated with the drug development process.

However, other participants acknowledged that the cost of iPS cell technology is currently small compared to other components in drug development (e.g., clinical trials). There is an expectation that as iPS cell technology becomes more standardized and widely utilized, development costs will be reduced. The literature findings provided support for the thoughts of participants that the integration of human disease models, such as iPS cells, during the preclinical stages of drug discovery can result in a reduction of approximately 10-26% in the overall development costs (Loewa et al., 2023). Researchers can concentrate on the most promising and efficacious candidates by incorporating human disease models in the preclinical phases, leading to a streamlined drug development process and potentially significant cost reduction (Franzen et al., 2019).

What is the influence of employing iPSC technology in drug discovery on the reliance on animal models?

The majority of participants expressed support for iPS cells as a promising tool to reduce the reliance on animal models in drug discovery. They acknowledged the ethical considerations associated with animal testing and highlighted the practical benefits of incorporating iPS cells into the process. By utilizing iPS cells, researchers have the opportunity to decrease the number of animals used for testing purposes, potentially saving both time and costs. The participants emphasized that iPS cells offer a possible alternative to animal studies, particularly during the preclinical phase. The reduction in animal usage is associated with ethical considerations and has the potential to accelerate the drug discovery timeline by a minimum of two years. The literature research supported the thought that incorporating iPS cells or other human disease modeling techniques during the preclinical phases of drug discovery can effectively reduce the reliance on animal studies (Loewa et al., 2023).

Moreover, participants and literature agreed that iPS cell technology needs to be validated more to completely replace animal studies in drug discovery due to the crucial role of animal studies in testing drug toxicity (Loewa et al., 2023). Additionally, it is essential to note that animal studies are currently required by regulatory bodies such as the FDA and EMA before progressing to clinical trials (Office of the Commissioner, 2023), (Ema, 2022).

Furthermore, participants highlighted the limitations of iPS cells that contribute to the continued reliance on animal studies. The participants emphasized that iPS cells, being less mature and potentially displaying different gene expressions than the human body, have limitations that can affect the effectiveness and safety of drugs during clinical trials, leading to failures. As a result, the participants advocated for the utilization of both iPS cells and animal studies, with a reduced number of animals, to mitigate these limitations. Nevertheless, the literature also demonstrates that human models can significantly reduce reliance on animal studies in drug discovery. Human models, like iPS cells, offer a more physiologically relevant system for studying diseases and evaluating potential drug candidates. They provide insights into human-specific responses, allowing for a better understanding of drug efficacy and safety profiles in a human context (Loewa et al., 2023).

How does the utilization of iPSC technology in drug discovery impact revenue generation and potential investment opportunities in the future?

The participants unanimously agreed that incorporating induced pluripotent stem (iPS) cells in drug discovery can potentially increase company revenue. The participants believed that drugs developed using iPS cell technology are perceived as more appealing to customers due to their closer resemblance to the human body and higher success rates. As a result, this could lead to increased need and revenue generation. The participants demonstrated that being a first mover in the iPS cell industry confers significant advantages to firms, as it can bestow them with a competitive edge and position them as favorites in the market. The reduction in drug development timelines associated with iPS cells was another factor highlighted by the participants. Bringing drugs to market earlier can extend the patent protection period, allowing companies to generate more revenue during this extended timeframe. Furthermore, the integration of iPS cells can decrease drug failure rates, resulting in cost savings that can be reinvested in other pipelines.

The literature review supported these findings, emphasizing the potential for iPS cells to reduce drug development timelines and generate substantial revenue (e.g., Parkinson's disease). It revealed that the use of iPS cells could significantly reduce the drug development timeline. The findings unveiled that incorporating iPS cells can substantially diminish the drug development timeline. Furthermore, there exists a potential for drugs developed using iPS cells to benefit from an exclusive market period exceeding seven years, providing Allife Medical Science and Technology Co., Ltd with an opportunity to generate substantial revenue without facing competition.

Furthermore, the participants expressed a positive inclination towards investing in iPS cell technology projects, given its capacity to replicate human physiology and address concerns regarding animal welfare. However, investors need to consider multiple factors when making investment decisions related to iPSC technology, such as the establishment of the technology and the desired public image associated with investments.

Limitation of the project

The response rate from the contacted experts for participation in the research project was significantly lower than expected. Out of the initial list of over 200 experts specializing in drug discovery and induced pluripotent stem (iPS) cells, only four experts agreed to participate. One of the primary reasons for the low response rate was the blocking of email communications by

several companies. It is common for organizations to implement strict email filtering systems to prevent unwanted or unsolicited emails from reaching their employees' inboxes. Unfortunately, these filtering systems sometimes result in legitimate emails being blocked, leading to missed communication opportunities.

Additionally, some experts were unable to disclose any information regarding their ongoing pipelines. Pharmaceutical and biotechnology companies often have strict policies and confidentiality agreements in place to protect their intellectual property and ongoing research. These restrictions may prohibit employees from sharing specific information, especially with external research projects.

Obtaining precise information regarding the exact costs and timelines associated with drug discovery has proven to be extremely challenging. Companies are understandably hesitant to disclose such sensitive information, making it difficult to obtain specific details on these aspects of the drug development process.

## Conclusion

The incorporation of iPS cell technology in drug discovery shows promise in reducing timelines. While there were mixed perspectives among participants, iPS cells offer advantages such as more relevant data, better decision-making, and the identification of promising compounds.

Furthermore, iPS cell technology can have an effect on development costs. Participants expressed optimism about the cost-effectiveness of iPS cells, particularly in disease modeling and personalized medicine. Incorporating iPS cells in the preclinical phase can lead to cost savings by identifying promising candidates earlier.

Moreover, the utilization of iPScell technology has the potential to reduce the reliance on animal models in drug discovery. Participants highlighted the ethical considerations associated with animal testing and the practical benefits of iPS cells as an alternative. While iPS cells are not yet ready to replace animal studies completely, they offer a more human-relevant model and have the potential to expedite the drug discovery timeline.

Lastly, iPS cell technology can impact revenue generation and investment opportunities. Drugs developed using iPS cells are more likely to attract customers due to their higher success rates and closer resemblance to the human body. Early adoption of iPS cells can provide a competitive edge and extend the period of patent protection, leading to increased revenue. Participants also consider iPS cell technology as a promising choice for investors, considering factors such as human relevance, animal welfare concerns, and public image.

In conclusion, incorporating iPS cell technology in drug discovery has the potential to improve timelines, reduce costs, decrease reliance on animal models, and increase revenue generation. However, further research and optimization of iPS cell technology are necessary to fully realize its benefits. The findings suggest that iPS cells offer valuable contributions to drug discovery and present opportunities for future advancements in the field.

## Recommendations

Based on the SWOT analysis of Ncardia, several recommendations can be made to improve the company's position in the iPS cell technology industry. Firstly, Ncardia should implement strong management strategies, including training programs and documentation of key processes and expertise. This would enhance critical knowledge among team members, reduce reliance on specific individuals, and mitigate the risk of knowledge loss. Given the highly competitive and attractive nature of the industry, Ncardia should focus on creating an environment that fosters employee growth and development.

Building a strong employer brand and actively engaging with academic institutions can help attract top talents. The company can also target new research areas, such as the immune cell market, by developing and offering iPSC-derived cells and tissue models. This expansion will attract new investors, increase the customer base, and generate additional revenue streams. Investing in research and development to incorporate emerging cell types is another key recommendation. This will position Ncardia as an innovative company with innovative solutions, enabling it to capitalize on new market opportunities.

Additionally, Ncardia should focus on building new partnerships, collaborations, and sponsorships, as well as attracting new investments. These initiatives will provide opportunities to expand manufacturing capabilities and scale operations. Expanding the sales and marketing team and investing in training and development programs will help increase market reach and customer engagement. Ncardia can also consider investing in new technologies, such as organ-on-a-chip, to expand its customer base. Building strong relationships with existing customers through excellent customer support, regular communication, technical assistance, training programs, and collaboration opportunities is crucial for customer satisfaction and loyalty. Positive customer experiences and referrals can significantly contribute to expanding the customer base through word-of-mouth recommendations.

Ncardia can also focus on establishing collaborative licensing agreements with companies involved in the development of cutting-innovative technologies such as organ-on-a-chip. In particular, Ncardia can leverage its proximity to Mimetas, a neighboring company in Leiden, and license their organ-on-a-chip technology. Through the licensing of technology from Mimetas, Ncardia can leverage these advancements to create innovative products that combine both technologies. This collaboration enables Ncardia to gain access to and utilize Mimetas' intellectual property (IP), resulting in cost savings by avoiding in-house technology

development. Furthermore, this collaboration can enhance Ncardia's position in the field of drug discovery, opening up new possibilities and strengthening their overall presence in the industry.

To increase visibility, Ncardia should actively participate in industry conferences and consider presenting their services instead of relying solely on posters or booth presence. Organizing mini-conferences and inviting key players in the drug discovery and pharmaceutical industries can also help raise the company's profile. While Ncardia operates in Europe and the USA, exploring opportunities in other international markets, such as Australia, and countries in Asia like Japan and China, would facilitate further growth and expansion. Overall, implementing these recommendations will strengthen Ncardia's position in the iPSC industry, enhance innovation, attract top talent, expand its customer base, and increase revenue streams.

## Self-reflection

During my internship at Ncardia, I had the incredible opportunity to work as a marketing trainee in the marketing team. Throughout this experience, I was able to recognize the knowledge and skills I acquired during my FBE courses, particularly in the field of marketing promotion, as well as social media marketing. This internship allowed me to see personally the impact that effective marketing strategies can have on a company's position in the market.

One of the most challenging aspects of my internship was managing the situation when I encountered a low response rate on my emails. Initially, it was disheartening to see my efforts go unnoticed or unanswered. However, I quickly realized that instead of dwelling on the difficulty, it was important to take proactive steps to improve the situation. To overcome this challenge, I decided to seek feedback from my colleagues and supervisors. By asking for their input and guidance, I was able to identify areas for improvement in my communication style, email structure, and overall approach. I learned that it's essential to tailor my messages to the recipient's needs, ensuring that they are concise, engaging, and relevant. Moreover, I discovered the importance of following up on emails, as it helps to reinforce the message and increase the chances of receiving a response.

During my internship at Ncardia, I had the opportunity to engage in various marketing activities, including conducting semi-structured interviews. While this aspect of my role allowed me to gather valuable insights and feedback, I recognized that there is always room for improvement in my interview techniques. Firstly, I realized the importance of thorough preparation before conducting an interview. in addition, active listening is a crucial skill that I aim to refine. During interviews, it is essential to give interviewees ample space to express their thoughts and ideas without interruption. To further improve my skills during the internship, I actively sought feedback from my colleagues and superiors. I regularly scheduled one-on-one meetings to discuss my performance, seek advice, and gain insights into areas where I could enhance my contribution. By embracing constructive criticism and viewing it as an opportunity for growth, I was able to make tangible progress and refine my marketing skills.

Moreover, I engaged in continuous learning by attending relevant webinars, workshops, and industry conferences. These opportunities not only deepened my understanding of marketing concepts but also exposed me to real-world case studies and best practices. I eagerly absorbed new information and actively sought ways to apply my learnings to my daily tasks and projects. The Science Based Entrepreneurship course I took during the FBE courses proved to be

instrumental in teaching me how to effectively deal with setbacks and failures. This course provided me with valuable insights and strategies that have helped me develop a resilient mindset and the ability to swiftly overcome obstacles and find solutions. One of the key lessons I learned from the course was the importance of embracing failure as a natural part of the entrepreneurial journey. Rather than viewing failure as a personal defeat, the course emphasized that setbacks should be seen as valuable learning opportunities. This mindset shift allowed me to separate my self-worth from the outcomes of my project and have a more positive and proactive mindset.

I am sincerely grateful to Ncardia for providing me with this invaluable opportunity to apply the knowledge and skills I acquired during my FBE courses and gain practical insights into the dynamic world of marketing. The support and guidance I received from my colleagues and supervisor Arjen Vaalburg have been helpful in my growth and development. I am thankful for their mentorship, feedback, and belief in my potential.

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# Appendix

## Appendix 1

Interview Questions

1. What is your role? and How many years of experience do you posses in drug discovery?
2. What influence does your role have in preclinical or clinical drug discovery?
3. In your opinion, is using IPSC technology expected to reduce the timeline in the drug discovery process? If so how many years?
4. What is the average duration of the drug discovery and development process at your company?
5. What is the furthest current clinical stage of drug(s) your company has developed using iPSC?
6. In your opinion, is using IPSC technology expected to reduce the development costs by (in percentage), how?
7. Is using iPSC in the preclinical phase expected to reduce the timeline and development costs compared to the traditional approach?
8. Is using iPSC in the clinical phase expected to reduce the timeline and development costs compared to the traditional approach?
9. Do you or your company believe switching from a traditional cell line approach to iPSC for drug discovery will increase revenue? How?
10. Are you using only iPSC to model diseases in drug discovery or other technologies as well?
11. How likely is your company to change its current technology for drug discovery (target ID validation, lead optimization, etc.) to iPSC modeling?
12. How do you think this change will benefit the company? Think about revenue reputation partnership or customer.
13. In your opinion, did iPSC have an equivalent impact on drug discovery ten years ago than it does today?
14. What is your outlook on the future of iPSC for drug discovery over the next decade?

**Appendix 2A**

Study Design of **PF-06939926**

| | |
|---|---|
| Study Type | Interventional (Clinical Trial) |
| Actual Enrollment | 23 participants |
| Allocation | N/A |
| Intervention Model | Sequential Assignment |
| Masking | None (Open Label) |
| Primary Purpose | Treatment |
| Official Title | A PHASE 1B MULTICENTER, OPEN-LABEL, SINGLE ASCENDING DOSE STUDY TO EVALUATE THE SAFETY AND TOLERABILITY OF PF-06939926 IN AMBULATORY AND NON-AMBULATORY SUBJECTS WITH DUCHENNE MUSCULAR DYSTROPHY |
| First Posted | December 5, 2017 |
| Actual Study Start Date | January 23, 2018 |
| Actual Primary Completion Date | March 28, 2022 |
| Estimated Study Completion Date | March 30, 2026 |

**Appendix 2B**

Study design of **RGX-202**

| | |
|---|---|
| Study Type | Interventional (Clinical Trial) |
| Estimated Enrollment | 18 participants |
| Allocation | Non-Randomized |
| Intervention Model | Sequential Assignment |
| Intervention Model Description | Dose Evaluation |
| Masking | None (Open Label) |
| Primary Purpose | Treatment |
| Official Title | A Phase 1/2 Open-label, Dose Escalation and Dose Expansion Study to Evaluate the Safety, Tolerability, Pharmacodynamics, and Pharmacokinetics of Intravenous RGX-202 Gene Therapy in Males With Duchenne Muscular Dystrophy (DMD) |
| First Posted | January 20, 2023 |
| Actual Study Start Date | January 4, 2023 |
| Estimated Primary Completion Date | December 2025 |
| Estimated Study Completion Date | December 2025 |

**Appendix 3A**

**Study Design of Prasinezumab**

| | |
|---|---|
| Study Type | Interventional (Clinical Trial) |
| Actual Enrollment | 316 participants |
| Allocation | Randomized |
| Intervention Model | Parallel Assignment |
| Masking | Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor) |
| Primary Purpose | Treatment |
| Official Title | A Randomized, Double-Blind, Placebo-Controlled, 52-Week Phase II Study to Evaluate the Efficacy of Intravenous RO7046015/Prasinezumab (PRX002) in Participants With Early Parkinson's Disease With a 6-Year All-Participants-on-Treatment Extension |
| First Posted | April 4, 2017 |
| Actual Study Start Date | June 27, 2017 |
| Actual Primary Completion Date | November 27, 2019 |
| Estimated Study Completion Date | September 14, 2026 |

**Appendix 3B**

**Study Design**

| | |
|---|---|
| Study Type | Interventional (Clinical Trial) |
| Estimated Enrollment | 10 participants |
| Allocation | N/A |
| Intervention Model | Single Group Assignment |
| Masking | None (Open Label) |
| Primary Purpose | Health Services Research |
| Official Title | Clinical Study of the Safety and Efficacy of Autologous Neural Stem Cells in the Treatment of Parkinson's Disease |
| First Posted | January 24, 2019 |
| Estimated Study Start Date | February 1, 2019 |
| Estimated Primary Completion Date | February 1, 2020 |
| Estimated Study Completion Date | February 1, 2021 |